A COMPARITIVE STUDY ON OUTCOME OF DIABETIC FOOT INFECTIONS TREATED ACCORDING TO DEEP TISSUE CULTURE AND SWAB CULTURE IN GRH, MADURAI.

M.S. DEGREE EXAMINATION
BRANCH I- GENERAL SURGERY

DEPARTMENT OF GENERAL SURGERY
MADURAI MEDICAL COLLEGE AND GOVT RAJAJI HOSPITAL
MADURAI – 20

THE TAMILNADU
DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.
BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled “A COMPARITIVE STUDY ON OUTCOME OF DIABETIC FOOT INFECTIONS TREATED ACCORDING TO DEEP TISSUE CULTURE AND SWAB CULTURE IN GRH, MADURAI” Submitted by Dr.A.SRINIVASAN to The TamilNadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.S. Degree Branch I (General Surgery), is a bonafide research work carried out by her under my direct supervision & guidance.

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Date:
Place: Madurai
CERTIFICATE BY THE DEAN

This is to certify that the dissertation “A COMPARITIVE STUDY ON OUTCOME OF DIABETIC FOOT INFECTIONS TREATED ACCORDING TO DEEP TISSUE CULTURE AND SWAB CULTURE IN GRH, MADURAI” is a bonafide research work done by Dr.A.SRINIVASAN, Post Graduate Student, Department of General Surgery, MADURAI MEDICAL COLLEGE AND GOVERNMENT RAJAJI HOSPITAL, MADURAI, under the guidance and supervision of Dr.D.MARUTHU PANDIAN M.S., F.I.A.S., F.I.C.S Professor Department of Surgery, MADURAI MEDICAL COLLEGE AND GOVERNMENT RAJAJI HOSPITAL, MADURAI.

Date:
Place: Madurai
DECLARATION BY THE CANDIDATE

I declare that this dissertation entitled “A COMPARITIVE STUDY ON OUTCOME OF DIABETIC FOOT INFECTIONS TREATED ACCORDING TO DEEP TISSUE CULTURE AND SWAB CULTURE IN GRH, MADURAI” is prepared by me under the direct guidance and supervision of Dr. D. MARUTHU PANDIAN M.S., F.I.A.S., F.I.C.S Professor, Department of General Surgery, MADURAI MEDICAL COLLEGE AND GOVERNMENT RAJAJI HOSPITAL, MADURAI. This is submitted to The Tamil Nadu DR.M.G.R. Medical University, Chennai, in partial fulfillment of the regulations for the award of MS degree (Branch I) General Surgery course on April 2018.

Date:
Place: Madurai

Dr. A. SRINIVASAN
Post-graduate student,
Department of General Surgery
ACKNOWLEDGEMENT

I take this opportunity to extend my gratitude and sincere thanks to all those who have helped me complete this dissertation.

I am extremely indebted and remain grateful forever to my guide, Dr. D. MARUTHU PANDIAN M.S., F.I.A.S., F.I.C.S, Professor of Surgery, for his constantable guidance and constant encouragement in preparing this dissertation and during my post-graduate course.

It gives me immense pleasure to express my deep sense of gratitude to my Professor and Head of Department of Surgery, Dr. D. MARUTHU PANDIAN M.S., F.I.A.S., F.I.C.S, the person who has mastered the art of surgical skills, for his excellent guidance, encouragement and constant inspiration during my P.G. Course.

It gives me immense pleasure to express my deep sense of guidance sincere thanks to Dr. D. LATHA M.S., Dr. C. SARAVANAN M.S., Dr. S. THIRUMALAI KANNAN M.S., Dr. S. MUTHUKUMAR M.S., MCh (Endocrine), Dr. C. RAJKUMAR M.S., MCh, for their guidance and encouragement during my postgraduate course.

I thank the dean of Madurai Medical College and Govt. Rajaji Hospital, Dr. D. MARUTHU PANDIAN M.S., F.I.A.S., F.I.C.S for
permitting me to conduct this study in the Department of General Surgery of the Govt. Rajaji medical college and Hospital, Madurai.

I extend my sincere thanks to my Post-graduate Colleagues, and Friends, who had helped me in preparing this dissertation.

I must give my sincere thanks to my PARENTS for their moral support, constant encouragement and sincere advices throughout my career.

Last but not the least my heartful thanks to all patients who formed this study group and co-operated whole heartedly.

I thank the Almighty.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Sl. NO</th>
<th>CONTENTS</th>
<th>PAGE NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>AIM OF THE STUDY</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>REVIEW OF LITERATURE</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>MATERIALS AND METHODS</td>
<td>68</td>
</tr>
<tr>
<td>5</td>
<td>RESULTS AND INTERPRETATION</td>
<td>73</td>
</tr>
<tr>
<td>6</td>
<td>DISCUSSION</td>
<td>88</td>
</tr>
<tr>
<td>7</td>
<td>CONCLUSION</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>ANNEXURES</td>
<td></td>
</tr>
<tr>
<td></td>
<td>I. PROFORMA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>II. KEY TO MASTER CHART</td>
<td></td>
</tr>
<tr>
<td></td>
<td>III BIBLIOGRAPHY</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV ETHICAL COMMITTEE CERTIFICATE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>V ANTI-PLAGIARISM CERTIFICATE</td>
<td></td>
</tr>
</tbody>
</table>
INTRODUCTION

Diabetic Foot infections are one of the leading causes of hospitalization. It typically begin most often in a neuropathic ulceration. Its prevention requires early detection and intervention. It requires careful attention & coordinated management, preferably by a multidisciplinary foot-care team. The presence of infection is defined by more than or equals to 2 classic findings of inflammation or purulence. Infections are then classified into

- Mild (superficial and limited in size & depth),
- Moderate (deeper or more extensive),
- Severe (systemic signs or metabolic perturbations).

There are two major classifications of diabetes; Type 1 and Type 2. Type 1 diabetes, which affects 10-15% of all people with diabetes, is primarily the result of the inability to produce insulin due to beta cell destruction in the pancreas. While Type I diabetes accounts for fewer individuals with diabetes, it results in a disproportionately higher frequency of diabetes related complications. Type 2 diabetes, affecting over 80% of those diagnosed with diabetes, results from a combination of insufficient insulin production and/or resistance of the cells of the body to the actions of insulin. Control of blood glucose levels is paramount to
minimizing complications related to diabetes. This is achieved through lowering serum glucose using oral hypoglycemic agents, and/or subcutaneous injections of insulin, dietary restriction and regular exercise. Other factors contributing to delayed onset of complications include control of hypertension, hyperlipidemia and hyperinsulinemia. Unfortunately, these treatments may not completely control the progression of diabetes-related changes including neuropathy.

Regardless of the type of diabetes classification, over time, failure to achieve optimal glycemic control can cause damage to the body’s small and large blood vessels and nerves. Damage to these vessels and nerves can affect all organs in the body. The eyes, heart, kidneys, and skin are most commonly affected in patients with diabetes. These changes along with those previously mentioned lead to a cascade of events resulting in changes to the foot itself. According to Boulton, Vileikyte, irsner, (2004), the “triad of neuropathy, deformity and trauma is present in almost two thirds of patients with foot ulcers”. The structural changes along with vascular insufficiency, infection and pressure predispose the person with diabetes (PWD) to develop a foot ulceration.

Vascular assessment is an important tool which helps to determine the need for hospitalization, surgical interventions. DFIs are polymicrobial, with staphylococci (aerobic gram-positive cocci), the MC
causative organism. Aerobic gram-negative bacilli are definite copathogens in chronic wounds & followed after antibiotic treatment. Obligate anaerobes may be copathogens in ischemic or necrotic wounds. Wounds without evidence any infection do not require antibiotic therapy. For infected ulcer, a post-debridement specimen is an important tool for aerobic and anaerobic culture. Broader spectrum regimens for chronic and severe infections. Osteomyelitis can be difficult to diagnose and treat. Many DFIs require surgical intervention, ranging from minor (debridement) to major (resection, amputation). Proper dressing with of loading the pressure & adequate follow up is necessary. An ischemic foot may require revascularization, few non responding patients may benefit from selected adjunctive measures.

Non healing chronic ulcers, inspite of daily dressing with local applications, it does not heal. This problem is especially seen in diabetic ulcers, venous ulcers and pressure ulcers. Treating these wound is a constant challenge for the surgeon.

The peculiarity of a chronic wound is that, they refuse to heal. Wound debridement and dressings, improving the nutritional status are all important factor in wound healing. Various studies were done on dressings in the management of DFIs. Inspite of all these, treating the microbes of native wound is far most important and nidus in the
management. Various debates going on for the best method of specimen collection whether it is swabbing or deep tissue culturing. There were studies which proved deep tissue culture, the best method of identifying the microbes. But still in many peripheral even in tertiary centres many clinicians following the SWAB TECHNIQUE for microbes culturing.

This study was to compare the efficacy in identifying the organisms and the best method of specimen collection for culture study by comparing the culture of SWAB VS DEEP TISSUE.
AIM AND OBJECTIVES

• To compare the efficacy in the management of diabetic foot infections based on culture of SWAB VS DEEP TISSUE.

• To identify the best method of specimen collection for culture study in identifying infectious organisms in diabetic foot infections.

Parameters observed

• Organisms isolated by the two different culture in different grades of ulcer.

• Days required for good healing response {granulation tissue formation, wound discharge status, pain intensity, surrounding erythema}
HISTORICAL ASPECTS OF WOUND CARE

- The earliest wound care products was BEER. The Sumerians found out 19 different types of beer.

MESOPOTAMIAN Culture – “Pound together furturpentine, pine turpentine, tamrisk, Daisy, flour of inninu strain; mix in milk and beer in a small copper pan; spread on skin, bind on him, and he shall recover”

EGYPTIANS: First one who used adhesive bandages for dressings. They were using Honey, Grease {animal fat}, Lint {vegetables}. Honey & grease for antibacterial action. Lint for drainage.

GREEKS: They recommended washing the wound with boiled water, vinegar and wine.

COTTON SWAB: First invented by polish immigrant LeGerstenzang in 1923.

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
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<tbody>
<tr>
<td>1998</td>
<td>The United Kingdom Prospective Diabetics Study - identified the importance of glucose control &amp; blood pressure control in the prevention &amp; delayed complications in DM 2. Elliot Joslin and his colleagues in Boston began to investigate new medical and surgical strategies to save feet and legs from amputation due to complications of diabetes.</td>
</tr>
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</table>
Ambulatory casting for neuropathic plantar ulcers was first used by Dr. Milroy Paul, an orthopedist working in Sri Lanka in the patients with leprosy.

Dr. Joseph Kahn in India, who described the use of casting as an off-loading alternative to prolonged, expensive periods of hospital bed rest for leprous ulcers.

Dr. Paul Brand, an orthopaedic surgeon working in India adopted this technique. Brand and his associates continued to refine and popularize the current casting technique for patients with diabetes and similar neuropathic foot ulcers.

Shaw and colleagues determined that snug-fitting, well-molded casts extending to just below the knee transfer approximately 30% of the weight-bearing load to the cast wall, thereby decreasing pressure on the plantar aspect of the foot.

More recently, Leibner and colleagues confirmed this observation by removing the proximal shank portion of TCCs, increasing the average plantar force during walking by 31%. Therefore, the utility of below-knee TCC consists in reducing peak plantar pressures through increasing the contact surface area throughout both the foot and the leg.
Then many offloading devices came into practice including which are mentioned in the title need for study. One among them is Mandakini offloading device mentioned by Kari in Indian journal of surgery in the year 2010 and accepted as economical offloading device to offload diabetic foot ulcers.

WHY SPECIMEN COLLECTION IN CULTURING METHOD IS SO IMPORTANT?

By 2025, 300 million people will be affected by diabetes mellitus world wide. Even more concerning, 6 million people will develop a lower limb ulceration placing them at risk of infection, deformity and death. With this growing statistic it is essential to collect accurate wound cultures to choose appropriate antibiotic treatment. Inadequate or inappropriate antibiotics may lead to superinfection, amputation or death.
1. PILOT STUDY FOR IDENTIFYING CONCORDANCE BETWEEN SWAB AND TISSUE BIOPSY TECHNIQUE

Vinod V. Prabhu, Aslam A. Shivani, Shilpa Shah, Alka D. Gore

Sample size of 50 cases were studied for isolates. 28 cases were non diabetic and the rest diabetics. There was only a significant disconcordance of isolates in diabetics {81.8%} as compared to non diabetics {21.4%}.

2. DEEP TISSUE BIOPSY VS. SUPERFICIAL SWAB CULTURE MONITORING IN THE MICROBIOLOGICAL ASSESSMENT OF LIMB-THREATENING DIABETIC FOOT INFECTION

G. Pellizzer, M. Strazzabosco³, S. Presi³, F. Furlan*, L. Lora³, P. Benedetti, M. Bonato², G. Erle³ and F. de Lalla

At enrolment, the mean number of isolates per patient was 2.34 by swabbing and 2.07 by tissue biopsy sampling; the rate of isolation for anaerobes with the two methods was 35% and 25%, respectively; no statistical differences could be observed between the two procedures in terms of either species or frequency of isolation. Anaerobic species were
never detected after the first 2 weeks of appropriate treatment, and those ulcers which were still active at day 30 yielded almost exclusively Gram-positive bacteria. At the end of follow-up, deep tissue cultures appeared to exhibit a higher diagnostic sensitivity with respect to swabs.

3. INTRA-OPERATIVE CULTURE SWABS VS DEEP TISSUE SPECIMENS: ASSESSING CONCORDANCE OF ISOLATES COLLECTED FROM DIABETIC FOOT INFECTIONs

Mitzi L. Williams, DPM

Thirty-two patients with diabetes were included in this study. Each patient had a UT grade 2 or 3 infected foot ulceration requiring surgical intervention. The mean number of isolates cultured from each UT Grade 2 or 3 diabetic foot ulceration per swabbing and tissue biopsy sampling was 2.06 and 1.88 respectively. Their results demonstrated a poor concordance between swab cultures and deep tissue biopsy results. Swabs identified the same isolates as deep tissue biopsy sampling 37.5% (12/32) of the time. In deep ulcerations with bone exposure, swabs isolated different species as compared with the corresponding tissue specimen. This study indicates a poor concordance between isolates cultured from swabs and deep tissue biopsy sampling of deep ulcerations with bone exposure. Deep Tissue specimens isolated fewer colonizers and did not fail to isolate pathogenic micro-organisms.
4. COMPARISON OF TISSUE VERSUS SWAB CULTURING OF INFECTED DIABETIC FOOT WOUNDS

Ying Huang, Ying Cao, Mengchen Zou, Xiangrong Luo, Ya Jiang, Yaoming Xue, and Fang Gao

Swab culturing identified all of the microorganisms isolated from the corresponding deep tissue specimens in 9/10 of grade 2 wounds (90.0%), and this proportion decreased to 12/29 (41.4%) and 7/17 (41.2%) for grades 3 and 4 wounds, respectively ($p = 0.02$).

Moreover, the sensitivity for identifying Gram-negative bacteria, such as *E. coli* and *Citrobacter*, by swabbing was low (33.3%). In addition, some Gram-negative bacteria, such as *Serratia* and *Ralstonia pickettii*, were isolated from deep tissues but not from swabs. Swab culturing may be reliable for identification of pathogens in diabetic foot wounds classified as grade 2. However, it is advisable to culture deep tissue specimens for wounds of grade $\geq 3$ because swab culturing is associated with a high risk of missing pathogens, especially Gram-negative bacteria.
5. COMPARISON OF MICROBIOLOGICAL RESULTS OF DEEP TISSUE BIOPSY AND SUPERFICIAL SWAB IN DIABETIC FOOT INFECTIONS

Fatma Bozkurt1, Serda Gülsün1, Recep Tekin2, Salih Hoşoğlu2, Hamit Acemoğlu3

In 75 patients with osteomyelitis, the compatibility rate in deep tissue biopsy culture with superficial swab culture was 58.7% whereas in STI group this rate was 89.1% (p<0.001). Of 41 superficial swap cultures, 33 of them (81%) had the same microorganisms with the identified microorganisms in deep tissue cultures. *Staphylococcus aureus* was the predominant pathogen isolated from deep tissue biopsy cultures and also from superficial swap cultures. The distributions of microorganisms in deep tissue culture and swap cultures were similar.

This study indicates that superficial swab culture could be valuable to identify the pathogens in infected diabetic wounds without osteomyelitis. The accuracy of swab specimens diminishes when osteomyelitis develops. Deep tissue culture seems more sensitive and reliable in osteomyelitis group.
DIABETIC FOOT INFECTIONS

Diabetic foot infections are the most common foot problems in India. Foot infections should be defined according to the signs of inflammation or pus and then classify by severity. It helps clinicians to make decisions about hospitalization of the patient or for any imaging procedure or to intervene surgically. DFIs are most commonly polymicrobial but Gram positive (staph) are the most common. Clinically uninfected foot ulcers don’t require antibiotics empirical antibiotics may be given based on clinical & epidemiological data but the drug of choice depends on cultures of infected tissue. Patient with DFI should be investigated for vascular disease.

It is most frequently described as a disease caused by a microbial pathogen that occurs when the presence of replicating organisms is associated with tissue damage. The American College of Surgeons defined infection as the product of the entrance, growth, metabolic activities, and resultant pathophysiological effects of microorganisms in the tissues of the patient. More specifically, White et al. defined infection as the presence of multiplying bacteria in body tissues, resulting in spreading cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response (host reaction).
In some situations, such as when established pathogens are isolated from properly obtained specimens of normally sterile fluid or tissues, diagnosing infection is easy. The presence of microorganisms in a wound, however, does not in itself define a clinical infection. It is important to recognize that there is a spectrum, or continuum, of disease. All wounds are exposed to skin commensals, and their microflora will represent the surrounding environment. These contaminating microbes can quickly become established within a wound, reaching a state of colonization. Colonization is defined as the presence of multiplying bacteria with no overt host immunologic reaction. Diabetic foot ulcers are commonly colonized with multiple species of organisms that do not normally interfere with healing. Multiplication of bacteria within the wound can reach a stage of “critical colonization, in which the host defenses are unable to maintain a balance, thus resulting in delayed healing. Infection results when the invading organisms overwhelm the host defenses, either by their sheer numbers or by impairing the host's immunity.

Infection confined to an ulcer bed can be described as local infection. This is typically manifest as purulent secretions, often accompanied by inflammatory signs. Untreated, local infection can progress to involve the surrounding and deeper tissues. Superficial soft
tissue infection may be accompanied by painful spreading erythema, known as cellulitis. Superficial infections involve the skin but do not extend to fascia, muscle, tendon, bone, or joint, as defined by the International Consensus on the Diabetic Foot. Deep infections are those with evidence of abscess, septic arthritis, osteomyelitis, or septic tenosynovitis. The International Consensus on the Diabetic Foot distinguishes bone infections as osteitis, infection of the cortical bone only, and osteomyelitis, in which the bone marrow is involved.

**MECHANISMS OF INFECTION:** Although microorganisms are responsible for infection, there is debate as to the exact mechanisms by which they cause their adverse consequences and their effect on a nonhealing chronic wound. Several factors are thought to be involved, including the bacterial burden, or load, within a wound. Many authors have reported healing to be delayed in a variety of wounds by an excessive bacterial burden, and the likelihood of infection rises as the bacterial burden increases. Controversy persists over whether the mere presence of a high bacterial bio burden warrants antimicrobial therapy. Some have proposed that a burden of >10^5 cfu of bacteria per gram of tissue is required to cause wound infection. However, particularly virulent organisms, such as β-hemolytic streptococci, secrete toxins that
allow rapid spread through the host's tissue planes and are capable of producing clinical infection at a lower burden.

In diabetic foot disease, we should aim to diagnose infection at an early stage before it progresses toward deep infection and damage to underlying tissue. Obtaining a rapid and accurate diagnosis is, however, compounded by several factors. Because the clinical signs of infection and microbiological analysis may be misleading, it is important to combine all information available and not rely on any single laboratory report. Sometimes subtle findings, such as failure of a wound to heal within the expected time frame, may suggest infection.
PATHOGENESIS OF DIABETIC FOOT ULCER
CLASSIFICATION OF DFIS

- IWGDF (PEDIS) and IDSA – IWGDF
- Wagner—Wagner, in collaboration with Meggitt
- S(AD)/SAD
- SINBAD
- University of Texas (UT)
- Ulcer Severity Index
- Diabetic Ulcer Severity Score (DUSS) & MAID
- DFI Wound Score

Infectious Disease Society of America and International Working Group on the Diabetic Foot Classifications of Diabetic Foot Infections

<table>
<thead>
<tr>
<th>Clinical Manifestation of Infection</th>
<th>PEDIS Grade</th>
<th>IDSA Infection Severity</th>
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<tbody>
<tr>
<td>No symptoms or signs of infection</td>
<td>1</td>
<td>Uninfected</td>
</tr>
<tr>
<td>Infection present, as defined by the presence of at least 2 of the following items:</td>
<td></td>
<td></td>
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<tr>
<td>• Local swelling or induration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Erythema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Local tenderness or pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Local warmth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Purulent discharge (thick, opaque to white or sanguineous secretion)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). If erythema, must be &gt;0.5 cm to ≤2 cm around the ulcer. Exclude other causes of an inflammatory response of the skin (eg, trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis).</td>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>Local infection (as described above) with erythema &gt; 2 cm, or involving structures deeper than skin and subcutaneous tissues (eg, abscess, osteomyelitis, septic arthritis, fasciitis), and No systemic inflammatory response signs (as described below)</td>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>Local infection (as described above) with the signs of SIRS, as manifested by ≥2 of the following:</td>
<td>4</td>
<td>Severe&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Temperature &gt;38°C or &lt;36°C</td>
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<td></td>
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<tr>
<td>• Heart rate &gt;90 beats/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Respiratory rate &gt;20 breaths/min or PaCO&lt;sub&gt;2&lt;/sub&gt; &lt; 32 mm Hg</td>
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<tr>
<td>• White blood cell count &lt;12,000 or &lt;4,000 cells/L, or ≥10% immature (band) forms</td>
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</tbody>
</table>

Abbreviations: IDSA, Infectious Diseases Society of America; PaCO<sub>2</sub>, partial pressure of arterial carbon dioxide; PEDIS, perfusion, extent/size, depth/tissue loss, infection, and sensation; SIRS, systemic inflammatory response syndrome.

<sup>a</sup> Ischemia may increase the severity of any infection, and the presence of critical ischemia often makes the infection severe. Systemic infection may sometimes manifest with other clinical findings, such as hypotension, confusion, vomiting, or evidence of metabolic disturbances, such as acidosis, severe hyperglycemia, and new-onset septicemia [39, 43, 44].
VASCULAR STATUS

The affected foot must have adequate blood flow to support healing. The literature supports the notion that peripheral arterial disease (PAD), also known as peripheral vascular disease (PVD), is not the cause of skin breakdown alone, but can prolong wound healing and increase the risk of subsequent amputation. In persons with diabetes seen at a younger age, PAD is often bilateral. Moreover, risk of PAD increases with the duration of the disease. Furthermore the risk of PAD increases by ten-fold in those with diabetes and concurrent renal failure (Apelqvist, 1998; Eggers et al., 1999). The presence of peripheral pedal pulses represents a minimum systolic pressure of 80 mmHg (Lavery & Gazewood, 2000). The National Evidence Based Guidelines for the Management of Type 2 Diabetes Mellitus states that the absence of peripheral pulses has prognostic significance for future amputation in people with or without foot ulceration. With the distal nature of the disease process, persons with diabetes may have ischemia in the presence of dorsalis pedis pulses.
One of the first classical symptoms of vascular insufficiency is claudication (calf pain). However, in patients with diabetes, this classic symptom can be masked by the presence of neuropathy (Calhoun et al., 2002). A cohort study by Eneroth, Apelqvist & Stenstrom (1997), found that claudication was an insignificant predictor or symptom of vascular disease. A positive history of lower limb intermittent claudication combined with non-palpable pedal pulses bilaterally increases the probability of vascular insufficiency in diabetes (Boyko, Ahroni, Davignon, Stensel, Prigeon & Smith, 1997). Capillary refill is defined as abnormal if it takes longer than 5 seconds for the tissue to return to its normal colour after applying pressure and releasing it. The colour of the foot should be assessed for rubor on dependency, pallor on elevation, mottling and dry gangrene, all of which are signs of ischemia (Bowker & Pfeifer, 2001). A vascular surgery referral is recommended for patients with signs of arterial insufficiency in order that a comprehensive vascular assessment can be completed.
INTERPRETATION OF ABI

<table>
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<tr>
<th>ABI</th>
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<tr>
<td>&gt;1.30</td>
<td>Poorly compressible vessels, arterial calcification</td>
</tr>
<tr>
<td>0.90–1.30</td>
<td>Normal</td>
</tr>
<tr>
<td>0.60–0.89</td>
<td>Mild arterial obstruction</td>
</tr>
<tr>
<td>0.40–0.59</td>
<td>Moderate obstruction</td>
</tr>
<tr>
<td>&lt;0.40</td>
<td>Severe obstruction</td>
</tr>
</tbody>
</table>

Abbreviation: ABI, ankle-brachial index.

* Obtained by measuring the systolic blood pressure (using a properly sized sphygmomanometer) in the ankle divided by that in the brachial artery. The presence of arterial calcification can lead to an overestimate in the index.

INFECTION

Persons with diabetic foot ulcers may not be able to mount an inflammatory response due to impaired immunodefense, decreased peripheral circulation and metabolic control (Armstrong, Lavery, Sariaya & Ashry, 1996; Eneroth et al., 1997). In addition, increased comorbidities associated with aging places the person with diabetes at a higher risk for infection. Identifying infection in a chronic wound can be a challenge since the clinical assessment for infection in chronic wounds differs from acute wounds. Gardner, Frantz & Doebbling (2001) validated the work by Cutting & Harding (1994) and provided a checklist to aid the clinician in identifying the clinical signs of infection in chronic wounds. Gardner et al. (2001), in a cross-sectional design study, identified the following signs and symptoms:
- Increased pain (100% specificity)
- Wound breakdown (100% specificity)
- Friable granulation tissue (76% specificity)
- Foul odour (88% specificity)

Deep infection will often cause erythema and warmth extending 2 cm or more beyond the wound margin. This increased inflammatory response is painful and will cause the wound to increase in size or lead to satellite areas of tissue breakdown which cause adjacent ulceration. Deep infections, especially in ulcers of long duration can often lead to osteomyelitis. Probing to bone is a simple, non-invasive technique for rapid identification of osteomyelitis and should be included in the initial assessment of all patients with infected pedal ulcers (Grayson, Balaugh, Levin & Karchmer, 1995). When combined with clinical evaluation and radiographic interpretation, probing to bone is a cost-effective and specific assessment tool (Caputo, Cavanagh, Ulbrecht, Gibbons & Karchmer, 1994). With infection, the wound may change in odour, colour, tissue quality and exudates. A healthy wound has a faint but not unpleasant odour, infections usually result in a distinctive and slightly unpleasant smell (Cutting & Harding, 1994). Deep foot infections are serious, potentially limb threatening and have been identified as the immediate cause of 25-51% of amputations in persons with diabetes.
NEUROPATHY

There are three components to peripheral neuropathy. Listed below are the effects of each form of neuropathy that the patient with diabetes may present with that will increase the risk of ulcer development:

**FOOT DEFORMITY AND PRESSURE**

Studies have demonstrated that while trauma to a neuropathic foot may be related to a single event, ulcers frequently occur as a result of repeated minor trauma such as from footwear or elevated pressure on the
bottom of the foot. Foot deformities such as prominent metatarsal heads, clawing of the toes and limited joint mobility alters the gait or mechanics of walking resulting in abnormal forces on the foot, poor shock absorption, and shearing and stress to soft tissues (RNAO, 2004; Shaw & Boulton, 1997). People with diabetes should be assessed regularly to detect foot deformities and should have interventions to reduce foot pressure and ulcer risk (Australian Centre for Diabetes Strategies, 2001; Royal Melbourne Hospital, 2002).

**GAIT ABNORMALITY**

Gait is the manner or style of walking. The neurodegenerative process is accelerated in diabetes and this results in a decline in motor
control and a pathology-related decline in postural stability/foot posture, and abnormal weight bearing (Mason O’Keefee, McIntosh, Hutchinson, Booth & Young, 1999b; Meier, Desrosiers, Bourassa & Blaszczyk, 2001). Alterations in gait, balance and mobility are caused by sensory ataxia, poor vision, debilitation and/or neuropathy in the patient with diabetes (Sinacore & Mueller, 2000). Assessment of gait is important because patients with diabetes and neuropathy have a 15 times greater risk of experiencing a fall compared to those without neuropathy (Sinacore & Mueller, 2000). Some gait patterns that may be observed in a patient with diabetes are: ataxic (unsteady, uncoordinated, employing a wide base of support), steppage (lift the foot higher to accommodate for foot drop and/or poor ankle-joint mobility) and antalgic (a limp, usually signifying discomfort).

ASSESSING THE PATIENT

A comprehensive assessment is required for all patients who present with diabetic foot ulceration. This assessment must include the etiology, factors that influence healing and the patient’s biopsychosocial status. History of Presenting Illness

- Initiating event
- Duration of ulceration
- Treatments prescribed
- Outcome of the treatments.
The evaluation of the patient with a diabetic foot ulcer requires a detailed history and physical examination, appropriate diagnostic tests, and identification of risk factors for ulceration. People with diabetic foot ulcers should be identified as high risk for amputation.

**Past Medical/Surgical History**

A careful history is required to determine general health, diabetes control and complications. This should include:

- All other medical conditions (co-morbidities) and complications associated with diabetes
- Any surgeries and/or previous amputation related to diabetes
- History of previous ulcers related to diabetes.
- Co-morbidities and complications associated with Diabetes:

**Renal impairment**

Eggers et al. (1999), identified that patients with diabetes mellitus and end stage renal disease (ESRD), accounted for 50% of amputations within this patient population. Those with ESRD only, without diabetes mellitus had one-fifth the rate of amputations. Those with ESRD from other causes but had diabetes mellitus as a risk factor accounted for approximately 25% of the amputations. In the ESRD post amputation population, the survival rate at two years was 33%.
Hypertension

Results of the Hypertension Optimal Treatment and United Kingdom Prospective Diabetes Study (UKPDS) trials report clinically important reductions in microvascular and macrovascular complications and diabetes related death (CDA, 2003). Individuals with co-existing hypertension have a five-fold increased risk of developing peripheral vascular disease (PVD) and therefore are at increased risk for amputation, compared to normotensive individuals with diabetes (Royal Melbourne Hospital, 2002). Adler, Stratton, Neil, Yudkin, Matthews, Cull et al. (2000) demonstrated that macro and microvascular (retinopathy, nephropathy) complications are linked to elevated blood pressure.

Retinopathy

Reiber, Vileikyte, Boyko, Del Aguila, Smith, Lavery et al. (1999) reviewed seven studies indicating that retinopathy is an independent predictor of amputation, possibly due to microvascular disease.

Hospital admissions and previous surgeries:

A history of previous amputation is a strong predictor of future amputations. Up to 34% of patients develop another ulcer within one year after healing while the 5 year rate of re-ulceration has been shown to be 70% (Frykberg et al., 2000).
Medications

Medication records will provide the health practitioner with information regarding diabetes management, as well as potential drug interactions, and those that may impair wound healing.

ASSESS FOR PRESSURE

Elevated foot pressure is an important risk factor for foot complications (Lavery et al., 2003). The plantar surface of the forefoot is found to be the most common location for the development of an ulcer (ADA, 1999). Forefoot and rear foot pressure ratios are increased in the severe diabetic neuropathic foot indicating an imbalance in pressure distribution. Equinus deformity with severe peripheral neuropathy may be an important factor in ulcer etiology (Caselli, Pham, Giurini, Armstrong & Veves, 2002). Reduced plantar soft tissue thickness at the metatarsal heads is associated with increased foot pressure and may predict development of diabetic foot ulcer (Abouaesha, van Schie, Griffiths, Young & Boulton, 2001). Pressure over bony prominences can lead to callus formation and in the absence of protective sensation may predispose the area to breakdown (Australian Centre for Diabetes Strategies, 2001; Boyko et al., 1999; Frykberg et al., 1998; Hutchinson et al., 2000). Callus may act as a foreign body elevating plantar pressures and there is significant reduction in pressure when the callus is removed.
IDENTIFY STRUCTURAL DEFORMITIES

The physical examination of a person with diabetes should include assessment and intervention for foot deformity (Australian Centre for Diabetes Strategies, 2001; Royal Melbourne Hospital, 2002). There is significant evidence that with increased number of deformities, there is an increased risk and magnitude of plantar pressure (Lavery et al., 2003). Deformities may include, but are not limited to, hammer toe, claw toe, hallux deformity, pes planus, pes cavus and Charcot arthropathy.

With atrophy of the intrinsic muscles of the foot, especially the toe plantarflexors, the flexor/extensor balance at the metatarso-phalangeal joints is altered. This causes clawing at the toe and possible subluxation of the metatarso-phalangeal joints. As a result, the submetatarsal fat pads are displaced.
and there is reduced pressure absorbing subcutaneous tissue at the metatarsal heads. In addition, glycosalation of collagen from hyperglycemia results in thickened, waxy skin which affects joint mobility. All these factors contribute to foot deformity and ulcer risk.

Pes planus produces flattening of the foot. Pes planus feet have increased lateral talometatarsal angle and increased second metatarsal length (Ledoux, Shofer, Ahroni, Smith, Sangeorzan & Boyko, 2003). There are many reasons for this condition, the first of which is heredity. Many have this condition and never have any problems of any kind. However, others will have this condition created through years in soft, unsupportive shoes on hard surfaces, injury, pregnancy, or other factors. This often leads to other problems. The arch in the foot is caused by a broad band of fibrous connective tissue, called the longitudinal ligament. A ligament is nothing more than connective tissue that connects bone to
bone. The longitudinal ligament connects the metatarsal phalangeal joints to the os calcis or heel bone. Like a string on a bow, they hold the two ends together and create an arch. This arch is a shock absorption structure and it also helps to maintain all the tarsals in proper erect anatomic position. As this arch decreases, impact from the concrete becomes worse. When the arch ligament stretches or tears, the arch falls. If it falls far enough, the tarsals may begin to shift to the inside or create pronation or a valgus (greater than 90 degree erect) position at the ankle. This can cause problems in the origin area, (the metatarsals) or in the heel. It also may cause pressure on the medial (inner) knee and perhaps the hip and back. It is like pulling the string on a marionette too tight, the result is a kinked mass on one side. The human body is much the same, put too much tension on major muscle groups and the joints kink and yell back.

In pes cavus, the arch is abnormally high on weight bearing. The heel is often tilted inwards at the ankle (but not always). In many, the toes will appear clawed. When not standing the front half of the foot (forefoot) will appear to be dropped below the level of the rear foot. Ledoux et al. (2003) identified biomechanical differences among pes planus and pes cavus feet in persons with diabetes. They found pes cavus feet had more prominent metatarsal heads, bony prominences, hammer/claw toes, increased hallux dorsiflexion and Pes Cavus decreased hallux plantarflexion.
WHEN TO HOSPITALIZE

✓ Severe infections
✓ Uncontrolled diabetes
✓ Osteomyelitis
✓ Patients with poor compliance

DIAGNOSTIC TESTS

X-ray

X-rays are useful primarily as imaging tools to identify possible osteomyelitis, foreign bodies, tissue gas, or bony abnormalities (Royal Melbourne Hospital, 2002).

Pressure Map

Pressure mapping measures foot pressures in standing and walking positions. Lavery et al. (1998) identified high plantar pressure (65 N/cm²) as a significant factor associated with the presence of foot ulceration. Pham, Armstrong, Harvey, Harkless, Giurini & Veves (2000) using an F-Scan mat system, found that foot pressures > 6kg/cm² put patients at risk for foot ulcerations.

Identification of Ulcer on the Lower Extremity

Location of a foot ulcer is determined by the site of trauma. In three large prospective studies, 53% of ulcers involved the toes and 22%
involved the first metatarsal area (Apelqvist et al., 2000; Armstrong, Lavery & Harkless, 1998a; Reiber et al., 1999).

**ASSESSMENT AND MANAGEMENT OF FOOT ULCERS FOR PEOPLE WITH DIABETES.**

**Measuring the Length and Width**

✓ A systematic review evaluated treatments for diabetic foot ulcers by calculating length and width (Margolis, Kantor & Berlin, 1999). As length and width decreased, the wound was classified as healing. It is important when measuring a wound that the measurements are done using a consistent method such as tracings (Krasner & Sibbald, 2001). This will greatly increase reliability in determining progress towards closure. Clinical studies have shown that a reduction in ulcer area (approximately 20 to 40%) after 2 to 4 weeks of treatment is a good predictor of healing (Margolis et al., 1999; Tallman, Muscare, Carson, Eaglstein & Falanga, 1997; van Rijswijk & Polansky, 1994).

**Measuring the Depth:**

✓ Wound depth is most commonly measured and quantified by gently inserting a sterile swab stick or probe into the wound. Find the deepest point and put a gloved forefinger on the swab stick at the skin level. Place next to a measuring guide. The presence or absence of undermining, a space between the surrounding skin and wound bed, and
tunneling can also be determined in this manner. If tunneling or undermining is present, use the “clock” system to document location (e.g., area of the wound closest to the head is the 12 o’clock position. Standardizing the procedure for measurement is crucial in order to evaluate whether the wound is moving in the direction of the goal of care. The University of Texas Health Science Center San Antonio Diabetic Wound Classification System (see Appendix E) is an example of a grading system to stage the depth of the wound.

**Microbiological sampling:** Traditional methods of sampling to determine the causative agents of a wound infection include rubbing the wound surface with a cotton swab, aspirating purulent secretions, and obtaining tissue by curettage or biopsy. Surface swabbing will collect skin contaminants, which may or may not be pathogenic. Furthermore, routine processing of swabs in clinical microbiology laboratories is rarely sufficient to isolate anaerobic or fastidious bacteria; this results both from the inadequate collection and/or transport method and variations in laboratory processing and incubation. Culture of aspirated fluid or pus is more likely to reveal the pathogenic organism, especially if taken from a deep pocket within the wound. Culture of debrided infected tissue is an excellent method for diagnosis in diabetic foot ulcers. Removing superficial debris before sampling will eliminate surface contaminants.
and provide more specific results. Tissue biopsy is generally regarded as the reference standard for diagnosing infection. Quantitative analysis of the deep tissue can identify heavily inoculated wounds (>10^5 cfu/g of tissue), but the clinical significance of this finding is unclear, because it requires expertise in obtaining the sample and specialist laboratory processing. If osteomyelitis is suspected, a specimen of bone obtained at surgery or by percutaneous biopsy is the most useful sample for culture. Although culture and histological examination of a specimen is the most accurate method for diagnosing infection, it not always easily obtainable. The technique used to obtain a microbiological sample is crucial. Although some methods are clearly superior, those selected sometimes depend on local clinical and laboratory expertise.

**Hematologic and biochemical markers:** Blood tests, such as WBC count, erythrocyte sedimentation rate, and C-reactive protein level, are commonly requested to aid diagnosis. However, they are neither sensitive nor specific and are unlikely to be elevated in local or superficial infection. Up to 50% of patients with a deep foot infection will not have leukocytosis; therefore, normal results do not preclude infection. Inflammatory blood markers are simple and relatively inexpensive to detect and may help guide the clinician in assessing treatment responses in severe infection, when used in combination with other factors. The
erythrocyte sedimentation rate is frequently used to monitor the response to treatment for osteomyelitis.

C-reactive protein levels have been demonstrated to be elevated in diabetic foot ulceration, and other acute-phase proteins, such as ferritin, α1-antitrypsin, and haptoglobulins, are currently under investigation. Blood glucose and hemoglobin A1c levels may rise in infection.

**Radiological diagnosis of osteomyelitis:** Many imaging techniques have been used to confirm or refute the presence of bone infection. Plain radiographs are useful as an initial evaluation and can be used as comparisons for later assessments. Radiography can also detect gas in soft tissues, which may represent severe soft tissue infection by anaerobic organisms and possible abscess formation. Osteolytic bone changes or periosteal elevation are suggestive of osteomyelitis. However, these changes may not be present in the first few weeks of infection, and their absence does not exclude osteomyelitis. Follow-up radiography is usually done 2–6 weeks later, although there is no agreed best interval. If the diagnosis remains in doubt, further investigations may include an isotope bone scan or labeled WBC scan, infrared thermography, ultrasound, or MRI. Among these, MRI has been found to be more sensitive and far
more specific than bone scans for diagnosis of osteomyelitis in diabetic feet.

**CLINICAL DIAGNOSIS OF INFECTION:** The most important diagnostic tool for infection is bedside clinical evaluation. The patient should be asked about an increase in pain, odor, or exudate. Local infection of an ulcer can be difficult for inexperienced clinicians to recognize. Cutting and Harding described signs of infection in a granulating wound: delayed healing, friable tissue, offensive odor, secretion of pus, increase in lesion size, pain or discomfort, and prolonged exudate production. Although symptoms may be absent in the neuropathic foot, the clinical signs of abnormal granulation tissue, such as a change in color from bright red to dark red, brown, or gray and increased fragility and contact bleeding, should alert the clinician to the possibility of infection. Spreading superficial infection, usually represented by warmth, erythema, and edema, may be less obvious in the diabetic foot. Systemic signs, such as pyrexia, chills, and lymphadenopathy, are usually absent. Even if infection is present, it can be difficult to differentiate from acute neuro-osteoarthropathy (Charcot's foot). Radiological and clinical assessments, together with laboratory tests, should aid differentiation of infectious from noninfectious bone lesions.
If bone is visibly exposed within the wound, or can be detected on gentle probing with a sterile instrument, osteomyelitis is likely. In a study of 75 patients with 76 ulcers, osteomyelitis was confirmed in 50 ulcers (66%). Thirty-three of these ulcers had bone detectable on probing, whereas 4 with underlying osteomyelitis did not, giving a sensitivity of 66%, a specificity of 85%, and a positive predictive value of 89%. Other deep structures exposed within the wound, such as tendon or joint capsule, also signify deep infection. Probing a wound can also detect foreign bodies and sinus tracts. It is essential that a wound is carefully probed with a narrow, blunt instrument able to convey to the user the presence of hard material within the wound. It is among the quickest and easiest procedures to do when evaluating a diabetic foot ulcer, and among the most important.

**ASSESSING THE ULCER BED:**

The aim of wound bed assessment is to identify and plan the management of factors that will promote an optimal healing environment (Vowden & Vowden, 2002). The condition of the periwound area provides important information about the status of the wound and can influence choice of treatment. Surrounding skin assessment includes evaluating colour, callus formation, induration, moisture and edema. Redness can be indicative of unrelieved pressure or prolonged
inflammation (Boulton, 1991). When the surrounding skin has been exposed to moisture for a prolonged period of time, signs of maceration (pale, white or grey tissue) may be observed. Callus formation is indicative of ongoing pressure to the affected area. Debridement of callus is generally performed to facilitate accurate assessment of the wound. Induration (an abnormal firmness of the tissue) and edema are assessed by gently pressing the skin within 4 cm of the wound. Nursing Best Practice Guideline Wound exudate characteristics, e.g., type and amount of drainage, provide important information about the status of the wound. Rating the amount of drainage is useful only if a description of each rating is provided. Wound is dry = no exudate Moist wound = scant or small Wet/saturated = heavy In addition to amount, the type of exudate should be described. Serous = clear yellow fluid without blood, pus or debris Serosanguinous = thin, watery, pale red to pink fluid Sanguinous = bloody, bright red Purulent = thick, cloudy, mustard yellow or tan All wounds, especially those treated with moisture retentive dressings, can emit an odour. Necrotic wounds tend to have more offensive odour than clean wounds, while wounds infected with anaerobes tend to produce a distinct acrid or putrid odour. A descriptive odour assessment can provide important information, as a change in odour may be indicative of an alteration in bacterial balance.
FACTORS AFFECTING HEALING POTENTIAL

The primary goal in the treatment of diabetic foot ulcers is to obtain wound closure as expeditiously as possible. The resolution of foot ulcers and decreasing the rate of re-ocurrence can lower the probability of lower extremity amputation in patients with diabetes. According to the American Diabetes Association (1999) Consensus Development Conference of Diabetic Foot Wound Care, foot wounds in patients with diabetes should be treated for several reasons – improve function and quality of life; control infection; maintain health status; prevent amputation; and reduce costs. Healing of foot wounds improves the appearance of the foot and may allow the patient to return to ambulation in appropriate footwear. Improving function and return to well-being are important goals of therapy (ADA, 1999). With impaired mobility, foot wounds often lead to general deconditioning and psychosocial dysfunction.
MANAGEMENT

The Principles of Management should include:

- Vascular management of ischemia and existing co-morbidities
- Infection control and removal of necrotic tissue
- Plantar pressure offloading – intrinsic and extrinsic

Framework For Treatment of Persons With Diabetic Foot Ulcers (PWDFU)

Diabetes management

Glycemic Control

The complications from diabetes are strongly related to high blood glucose levels. Improved glycemic control reduces complications. The United Kingdom Prospective Diabetes Study (UKPDS) showed that
intensive control of blood glucose resulted in a substantial reduction of the risk of complications of type 2 diabetes. Each 1% reduction in $A_1C$ produced significant decreases in complications. $A_1C$ values in the normal range (<6%) comprised the lowest risk (Stratton, Adler, Neil, Matthews, Manley, Cull et al., 2000). The DCCT Research Group (1993) concluded that intensive therapy to maintain blood glucose levels close to the normal range effectively delayed the onset and slowed the progression of diabetic retinopathy, nephropathy and neuropathy in patients with insulin dependent diabetes (IDDM), now identified as type 1.

A Japanese study examining glycemic control and microvascular complications concluded that intensive glycemic control can delay onset and progression of diabetic retinopathy, nephropathy and neuropathy in Japanese patients with NIDDM (type 2 diabetes) (Ohkubo, Kishikawa, Araki, Miyata, Isami, Motoyoshi et al., 1995).

The CDA Clinical Practice Guidelines (2003) recommends the following targets for glycemic control for most patients with type 1 and type 2 diabetes:

- $A_1C < 7.0\%$ to reduce the risk of microvascular and macrovascular complications.
- Fasting plasma glucose of 4.0 to 7.0 mmol/L and 2-hour postprandial plasma glucose targets of 5.0 to 10.0 mmol/L.
The CDA (2003) advises that treatment goals and strategies must be individualized according to risk factors such as complications and co-morbidities.

**Infection Control**

Infections in a diabetic patient must be treated urgently. Diabetic foot infections can rapidly progress to limb- or life-threatening situations. The amputation rate in diabetic populations with foot infections has been reported to range from 12-92% (Tennvall et al., 2000).

Management of diabetic foot ulcer infections should focus on four integrated parameters of care:

- Controlling bacterial balance
- Host response/defence;
- Complete pressure offloading;
- Local wound care.

According to Peacock and Van Winkle (1976), infection occurs when the number of organisms exceeds the ability of local tissue defenses to handle them. Maximizing the host ability to fight the infections should be a major consideration. This includes correction of hyperglycemia, stabilization of other co-morbidities, good nutrition and rest. Local wound care should include wound cleansing and debridement.
to remove devitalized tissue and reduce bacterial load in the wound (Saap & Falanga, 2002; Steed et al., 1996). Antimicrobial management of diabetic foot infection should be based on the Ontario Anti-infective Guidelines for Community Acquired Infections (Ontario Anti-infective Review Panel, 2001). The prescribed antibiotic(s) should be based on the results of the culture and sensitivity of the organism(s) in conjunction with the physician’s clinical judgement. Once a treatment plan is developed and initiated, an evaluation period should be established to determine the patient’s response to treatment.

A. Non-Limb-Threatening Infections

Ulceration does not need to be present since non-limb-threatening infections can result from small puncture wounds, scratches, nail trauma or heel (fissure) cracks. Mild to moderate infection can usually be managed on an outpatient basis with close supervision by the medical practitioner. Topical antimicrobials can be used to reduce bacterial burden in superficial infections. There are several iodine and silver preparations now available that are safe, effective and economical (Sibbald et al., 2003). Systemic antibiotics may be prescribed by the physician or the Registered Nurse/Extended Class (RN/EC) in the community. See Appendix M for a list of Topical Antimicrobial Agents. If the wound still fails to heal and there is evidence of increased
superficial bacterial burden or delayed healing with no evidence of deep infection, use local antimicrobials with debridement and moisture balance. If there is evidence of deep infection, or if the wound fails to demonstrate signs of healing within two weeks with topical antimicrobials, systemic antibiotics may be considered.

B. Limb-Threatening Infections

Diabetic foot infections in this category may have cellulitis that extends greater than 2 cm beyond the wound border including cardinal signs of infections such as fever, edema, lymphangitis, hyperglycemia, leukocytosis, and/or ischemia (Frykberg et al., 2000). An ulcer that probes to the bone or joint is highly predictive of osteomyelitis (Grayson et al., 1995). Since the patient with diabetes with a relatively severe infection may not necessarily present with these signs and symptoms, it is important to review the entire clinical assessment to guide the clinician to the proper course of treatment. A patient presenting with wet gangrene, deep abscesses, and advancing cellulitis must be transferred to a medical facility for urgent care. Hospitalization is required in order to treat the infection as well as the systemic sequelae. Patients with poor vascular status and deep infections may require vascular surgery and infectious disease consultation. Urgent surgical intervention may be required. Although many wound drainage procedures can be done at the bedside
for patients with diabetic ulcers, most will require thorough debridement in the operating room (Frykberg et al., 2000). Even the sickest of patients should be considered for emergent incision, drainage, and debridement procedures since their illness is directly attributable to the severity of their infection. Lifethreatening infections necessitate immediate surgical attention and such procedures should not be delayed while waiting for radiologic or medical workup of other co-morbid conditions (Frykberg et al., 2000). Polymicrobial infection should be anticipated in patients with a diabetic foot ulcer, with a variety of grampositive cocci, gram-negative rods, and anaerobic organisms predominating. Empirical antibiotic therapy typically includes broad-spectrum coverage for more common isolates from each of these three categories (Frykberg et al., 2000). Once wound culture results have been obtained, the initial antimicrobial therapy may require adjustment to provide more specific coverage or to provide therapy against resistant organisms. If there is persistent infection while on antibiotic therapy, surgical assessment and wound culture should be revisited. Methicillin-resistant staphylococci aureus (MRSA) has been emerging as an important pathogen in chronic diabetic foot ulcers (Frykberg et al., 2000).
C. Osteomyelitis

Osteomyelitis and joint infection will require excision of bone for microbiological and histopathological evaluation (Frykberg et al., 2000). If the affected bone has been completely resected or amputated, the infection may be treated as a soft-tissue infection. However, if residual bone is present in the wound, the patient will likely require 4-8 weeks of antibiotic therapy based on the culture results (Frykberg et al., 2000). Intravenous or oral agents may be used, depending on the microbial isolates and the infection severity. Moisture Balance Dressing selection should promote a moist wound environment that minimizes trauma and risk of infection. Selection should be based on the wound to provide local moisture balance. Modern, moist interactive dressings used for diabetic foot ulcers include foams (high absorbency), calcium alginites (absorbent, hemostasis), hydrogels (moisture balance), hydrocolloids (occlusion), and adhesive membranes (protection) (Inlow et al., 2000).

ANTIBIOTIC PRESCRIPTION

Some diabetic foot ulcers may lack clinical signs of infection, it may be subclinically infected with high “bioburden” of bacteria (more than 106 microbes per gm of tissue) its leads to critical colonization that affects wound healing.
Majority of mild and moderate infections can be treated with narrow spectrum antibiotics. Severe infections should be treated with broad spectrum antibiotics should cover Gram negative and also obligate anaerobes. For mild and moderate infections oral antibiotics can be given in patients without absorption problems, for severe infections it is better to start with parenteral therapy. Clinicians should consider the C/S results in light of clinical response of the DFI to the empiric regimen. Cultures may yield common contaminants (CONS, corynebacteria) but these may be true pathogens. These organisms are mostly resistant to prescribed antibiotics so we must decide whether these are the true pathogens that require targeted therapy if there is good clinical response after empirical therapy regimen may be continued or even narrow down (DE ESCALATION THERAPY) if the patient does not respond therapy should be widened to include all isolated oraganisms.

Both IDSA and IDWGDF classifications allowing standardization of severity scoring in recent trials on DFI antibiotics. Based on results no single or combination of agents appears to be superior to each other. The FDA approved (2004) three antibiotic for the treatment of complicated skin and skin structure infections including DFI.
**DURATION OF THERAPY**

It should be based on the severity of the infection, the presence or absence of bone infection & clinical response to therapy. There is no proper evidence to support continuing antibiotics until the ulcer is healed to achieve early closure & prevent subsequent infections.

<table>
<thead>
<tr>
<th>Infection Severity</th>
<th>Probable Pathogen(s)</th>
<th>Antibiotic Agent</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (usually treated with oral agent)</td>
<td>Staphylococcus aureus (MRSA), Streptococcus sp.</td>
<td>Dicloxacillin</td>
<td>Requires QID dosing; narrow-spectrum; inexpensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clindamycin&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Usually active against community-associated MRSA, but check macrolide sensitivity and consider ordering a “Chest” before using for MRSA. Inhibits protein synthesis of some bacterial toxins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cephalexin&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Requires QID dosing; inexpensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levofloxacin&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Once-daily dosing; suboptimal against S. aureus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amoxicillin-clavulanate&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Relatively broad-spectrum oral agent that includes anaerobic coverage</td>
</tr>
<tr>
<td></td>
<td>Methicillin-resistant S. aureus (MRSA)</td>
<td>Doxycycline</td>
<td>Active against many MRSA &amp; some Gram-negative, uncertain against streptococcal species</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trimethoprim-sulfamethoxazole</td>
<td>Active against many MRSA &amp; some Gram-negative, uncertain activity against streptococci</td>
</tr>
<tr>
<td>Moderate (may be treated with oral or initial parenteral agent(s) or severe (usually treated with parenteral agent(s))</td>
<td>MSSA; Streptococcus sp.; Enterobacteriaceae; dilute anaerobes</td>
<td>Levofloxacin&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Once-daily dosing; suboptimal against S. aureus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefoxitin&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Second-generation cephalosporin with anaerobic coverage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ceftriaxone</td>
<td>Once-daily dosing; third-generation cephalosporin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ampicillin-sulbactam&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Adequate in low suspicion of P. aeruginosa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meropenem&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Once-daily dosing; relatively broad-spectrum, including most obligate anaerobic organisms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ertapenem&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Once-daily dosing; relatively broad-spectrum including anaerobes, but not active against P. aeruginosa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tigecycline&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Active against MRSA. Spectrum may be excessively broad. High rates of nausea and vomiting and increased mortality warning. Non-equivalent to ertapenem + vancomycin in randomized clinical trial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levofloxacin&lt;sup&gt;6&lt;/sup&gt; or ciprofloxacin&lt;sup&gt;6&lt;/sup&gt; with clindamycin</td>
<td>Limited evidence supporting clindamycin for severe S. aureus infections; PO &amp; IV formulations for both drugs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Imipenem-cilastatin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Very broad spectrum (but not against MRSA), use only when this is required. Consider when ESBL-producing pathogens suspected</td>
</tr>
<tr>
<td>MRSA</td>
<td>Linezolid&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Expensive; increased risk of toxicities when used &gt;2 wk.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daptomycin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Once-daily dosing; requires serial monitoring of PCT</td>
</tr>
</tbody>
</table>
EXTRINSIC FACTORS

Ninety four percent of diabetic foot ulcers occur at areas of increased pressure (Fleischli, Lavery, Vela, Ashry & Lavery, 1997). Elevated plantar pressures coupled with neuropathy (lack of sensation) can lead to callus formation. The callus build-up (hyperkeratosis) is a normal response to the stress of elevated pressures on the foot and if untreated leads to ulcer formation. For a diabetic foot ulcer to heal the repetitive pressure must be reduced. This can be accomplished by the application of a number of external devices. It is important that there is a member of the team skilled in the fabrication and modification of offloading devices, such as a foot care specialist. One randomized controlled trial showed that total contact casting (TCC) was effective in treating well vascularized non-infected plantar forefoot diabetic foot wounds. Healing rates range from 72% to 100% over a course of five to seven weeks (Armstrong, Nguyen, Lavery, van Schie, Boulton &
Harkless, 2001). Spencer (2004) conducted a systematic review evaluating the effectiveness of various offloading modalities to treat diabetic foot ulcers. One randomized controlled trial on total contact casting was identified showing weak evidence on its effectiveness in the treatment of diabetic foot ulcers. It is important that the patient with a diabetic foot ulcer recognizes that pressure is the cause of their foot ulcer and the offloading is required whenever they are on their feet. In a study by Armstrong, Lavery, Kimbriel, Nixon and Boulton (2003) describing adherence to offloading devices, subjects were found to be only 25% compliant with their prescribed device.

**SURGICAL INTERVENTIONS**

It ranging from minor (drainage & excision of infected and necrotic tissues) to major (reconstruction of soft tissue or bony defects, revascularization & lower limb amputation). We should evaluate patient who has unexplained persistent foot pain or tenderness or evidence of a deep-space infection or abscess. The absence of fever or leukocytosis should not indicate no need for surgical exploration. The MC site is the plantar surface. A plantar wound with dorsal erythema or fluctuance likely require drainage. Prompt surgical debridement like limited resections & amputations may decrease the need for extensive amputations. Progressive abscess with in the foot can lead to rapid
irreversible damage. Good careful dissection & longitudinal skin incisions over the specific compartments lead to a durable weight bearing & non painful plantar surface. For patients with evolving infection it is better to delay surgery to avoid scar and deformity. Patients with non-severe infections observe the effectiveness of medical therapy and line of demarcation between non-viable and viable tissue, before doing surgery is essential. The surgical approach should be in the way to optimize the healing process while preserving the function of limb as much as possible. Doing high level amputations that results in a more functional residual stump is better than preserving a mechanically unsound found {i.e. unlikely to heal or prone to further ulceration}.

In case of vascular pathology of lower limb, like atherosclerosis it is easily managed with angioplasty or vascular bypass. In severe diseases it is mandatory to use aggressive endovascular therapy & distal bypass procedures.

**WOUND MANAGEMENT**

**WOUND DRESSINGS**

- Consideration should be given to the following when choosing a moist **wound dressing** for a diabetic foot ulcer (Sibbald, Williamson, Orsted, Campbell, Keast, Krasner et al., 2000):
• Assess the wound bed for bacterial balance, exudate level and the need for debridement.

• Select a dressing or combination of dressings that can manage and control the above wound environment.

• Use a dressing that will keep the wound bed continuously moist and the peri-wound skin dry.

• Choose a dressing that controls exudate but does not dry the ulcer bed.

• Consider the caregiver time when selecting a dressing.

• Eliminate wound dead space by loosely filling all cavities with dressing material.

• Assure that the patient is aware that there is to be reduced pressure to the affected area.

• Evaluate the wound frequently to determine efficacy of treatment plan. Systematic reviews in the past have shown no differences in chronic wound healing outcomes (Hutchinson et al., 2000; Ovington, 1999). However, in a recent systematic review by Smith (2004), hydrogels were shown to be of some benefit in improving diabetic foot ulcers. Consideration of caregiver time is essential to cost efficiency.
✓ Principal function - to help achieve an optimal healing environment. It promotes the wound healing, prevents the infection

**GOAL**

- Promote granulation by means of moist environment
- Angiogenesis
- Autolytic processes
- Rapid migration of epidermal cells into the wound base.

**Selection should be based on the wound bed characteristics**

✓ Dry - should be hydrated;
✓ Draining - the exudate should be absorbed;
✓ Necrotic - should be debrided.

**Dressing types**

✓ Continuously moistened saline gauze
✓ Hydrogels
✓ Films
✓ Alginates
✓ Hydrocolloids
✓ Foams
Topical Antimicrobials

A controversial concept. In addition to their cost and its local adverse effects, may further promote the emergence of bacterial resistance. Due to lack of evidence of any advantages, it is better not to use topical antimicrobials for most clinically uninfected wounds.

Debridement

It involves trimming any surrounding hyperkeratosis, removal of necrotic or nonviable tissue, slough, or foreign material from the wound. It further removes colonizing bacteria thus paves for granulation tissue formation and re-epithelialization. It facilitates the specimen collection for organism culture & allow us to examine deep tissue involvement.

It is efficacious to use sharp debridement. If non viable tissue continues to form debridement should be repeated. After every debridement, morphology of the wound should be recorded.

Although debridement methods vary, common methods of debridement for diabetic foot ulcers include:

- Mechanical irrigation with saline solution
- Use of autolytic agents (e.g., hydrogels)
- Sharp, using a scalpel or scissors (method of choice in an infected wound)
• Surgical (occurs in the operating room with anesthesia and surgical instruments) The frequency of debridement is scheduled at the discretion of the clinician (Inlow et al., 2000). Callus Reduction Debridement of callus can significantly reduce pressure at the callus site by approximately 30% (Pitei, Foster & Edmonds, 1999; Young et al., 1992). Debridement of callus is within the nurse’s scope of practice, assuming that the nurse has the knowledge, skill and judgement to perform this procedure. Tissue Debridement The removal of nonviable, contaminated and infected tissue from the wound area has been shown to increase the rate of healing of diabetic foot ulcers (Inlow et al., 2000; Rodeheaver, 2001). In a post-hoc analysis conducted by Steed, Donohoe, Webster & Lindsley (1996), lower rates of healing were correlated with less frequent debridement practices. These observations were confirmed in a prospective trial where sharp debridement may be associated with better outcomes in patients with diabetic foot ulcers (Saap & Falanga, 2002). Smith (2004) conducted a systematic review to determine the effectiveness of debridement methods for diabetic foot ulcers. Five randomized controlled trials (RCTs) were identified: three involved the use of hydrogels and two involved the use of sharp debridement. The results suggest that
hydrogels were significantly more effective than gauze or standard care in healing diabetic foot ulcers.

**Off-loading Pressure**

It is a vital part of wound care. The choice should be based on the location of ulcer, associated PAD, severity of infection & their psychological and social situation. The “gold standard” one is the TOTAL CONTACT DEVICE, redistributes pressure to the entire weight bearing surface to accelerate healing. Its advantages are easy application, less expensive, and efficacious.

**NON HEALING DIABETIC FOOT INFECTIONS**

While complete wound closure is widely accepted to be an objective endpoint in wound healing, this may not always be appropriate in assessing outcomes in chronic wounds (Enoch & Price, 2004). There are various factors that can contribute to the chronicity of such wounds. Examples of factors contributing to poor healing outcomes include:

- Inadequate blood supply;
- Poor glycemic control;
- Non-adherence with treatment plan;
- End-stage renal disease;
• Transplant recipients;

• Differing individual goals;

• Malnutrition;

• Connective tissue disorders;

• Systemic conditions such as sickle cell disease;

• Osteomyelitis;

• Immobility;

• Heart disease;

• Dementia;

• Cancer;

• Advancing age.

Goals of care must be mutually agreed upon by the individual and the healthcare team, reflecting a realistic outcome based on quality of life. The significance of managing exudate, controlling infection, relieving pain, and minimizing odour in a non-healing wound must be established and accepted as legitimate outcome measures (Enoch & Price, 2004).
When healing is not the goal, wound management should incorporate

- A palliative wound management model that includes pain control, infection control, exudate management and odour control.

- Keep wound bed dry, moist wound care is not recommended:
  - If the patient cannot fight infection the moist wound will be a breeding ground for infection.
  - Use dry dressing.
  - Using a topical, cost effective and potentially cytotoxic antiseptic such as povidine iodine can be considered when the risk of infection outweighs the healing potential.

Re assess

Inspite of good wound care, if the DFU fails to heal the clinician should re evaluate for perfusion of the limb and presence of any infections, rarely for malignancy. So in such cases take biopsy of a recalcitrant or atypical wound.

Other modalities

Care for diabetic foot ulcers that have not healed at the expected rate may include the use of:
• Biological agents

• Adjunctive therapies

• Surgery (e.g., skin graft, Achilles tendon lengthening, bony reconstruction).

**Platelet-derived growth factors**

Although an initial study demonstrated benefit, subsequent investigations have not shown these treatments to improve healing, or they have been conducted in a fashion where the data cannot be interpreted in the context of routine care.

**Granulocyte colony-stimulating factor (G-CSF)**

It did not significantly affect the likelihood of resolution of infection or wound healing, It was associated with a significant reduction in likelihood of lower extremity surgical interventions & reduce the hospital stay, but not duration of systemic antibiotic therapy. But data are not sufficiently robust to support the routine use of this therapy.

**Bioengineered skin equivalents**

There was no sufficient data to support the effectiveness of these products.
**Topical negative pressure**

It may safely improve healing of a diabetic foot ulcer that too after a surgical procedure (eg, wide debridement or partial amputation), but there is no high-level evidence to support its use in an infected wound.

<table>
<thead>
<tr>
<th>Type of Adjunctive Therapy</th>
<th>Description and Evidence</th>
</tr>
</thead>
</table>
| Electrical Stimulation     | - This procedure involves applying a low level electrical current to the base of the wound or the peri-wound using conductive electrodes.  
- It must be performed by trained healthcare professionals.  

Evidence:  
A *meta analysis* (Grose, Smith, Taylor, Zinke & Houghton, 2004) of 17 RCTs showed that electrical stimulation was effective in treating chronic wounds (*p* < 0.0001), included in this analysis were 3 RCTs with patients with diabetic foot ulcers (Baker, Chambers, DeVita & Villar, 1997; Lundberg, Eriksson & Malin, 1992; Peters, Leary, Armstrong & Fleischl, 2001).  
*(Level of Evidence = 1a)* |
| Hyperbaric Oxygen Therapy (HBOT) | - In this procedure, systemic (inhaled) subatmospheric oxygen is delivered via hyperbaric chamber.  
- It increases oxygen tension in the tissues.  

Evidence:  
The routine management of diabetic foot ulcers with HBOT is not justified by the evidence found in the systematic review conducted by Kranke, Bennett & Roeckl-Wiedmann (2004). Although HBOT significantly reduced the risk of major amputation and may improve the chance of healing at one year, economic evaluations should be undertaken. With methodological shortcomings and poor reporting of the studies that were reviewed, Kranke et al. (2004) cautions that any benefit from HBOT will need to be examined further using rigorous randomized trials.  
*(Level of Evidence = III)* |
<table>
<thead>
<tr>
<th>Type of Adjunctive Therapy</th>
<th>Description and Evidence</th>
</tr>
</thead>
</table>
| Topical Negative Pressure (TNP) Therapy | - It is a subatmospheric pressure device delivered to the wound by an open cell foam dressing covered with a clear membrane over the wound.  
- The dressing is attached to a pump that delivers equalized intermittent or continuous suction within a prescribed range of settings.  
- Vacuum Assisted Closure (VAC®) Therapy is a commercial brand of topical negative pressure.  

**Evidence:**  
*The two small trials that evaluated the effectiveness of TNP on chronic wound healing provide weak evidence suggesting that TNP may be superior to saline gauze dressings in healing chronic human wounds.*  
**Findings:** *Due to the small sample sizes and methodological limitations of these trials, there is weak evidence to date.*  

*The effect of TNP on cost, quality of life, pain and comfort was not reported. It was not possible to determine which was the optimum TNP regimen* (Armstrong, Lavery, Abu-Rumman, Espensen, Vazquez, Nixon et al., 2002; Ballard & McGregor, 2001; Clare, Fitzgibbons, McMullen, Stice, Hayes & Henkel, 2002; McCallon, Knight, Vallilus, Cunningham, McCulloch & Farinas, 2000; Sibbald, Mahoney & VAC Therapy Canadian Consensus Group, 2003).  

*A case series of 31 patients with diabetic foot ulcers showed a statistical reduction in wound size at four weeks on the continuous setting at ~100 mm Hg (League, Newbatt, Zschape, Daniels, Rankine, Hoeflock et al., 2004). (Level of Evidence = 1b)*

<table>
<thead>
<tr>
<th>Biological Agents</th>
<th>Description and Evidence</th>
</tr>
</thead>
</table>
| Growth Factors            | - Wound bed vascularization can be achieved by applying recombinant human platelet derived growth factor BB(PDGF)  
- Becaplermin gel, also known as Regranex®, is an example of a growth factor.  
- The biological activity of becaplermin is similar to that of naturally occurring PDGF and includes promoting chemotactic requirement and proliferation of cells involved in the wound repair process (Smieł, 1998).  

**Evidence:**  
*Four multicentre, randomized parallel group studies found that once-daily topical administration of becaplermin gel in conjunction with good ulcer care was effective and well tolerated in patients with full-thickness, lower extremity diabetic ulcers (Smieł, Wieman, Steed, Perry, Sampson & Schwab, 1999). (Level of Evidence = 1b)*
### Biological Agents

<table>
<thead>
<tr>
<th>Description and Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Bioactive agents can be acellular or cellular and have the potential to stimulate, through topical activation the normal or enhanced activity of mechanisms involved in tissue repair.</td>
</tr>
<tr>
<td>■ Dermagraft® is an example of living tissue equivalents.</td>
</tr>
<tr>
<td>■ Dermagraft® is a cultured human dermis. It consists of human neonatal and dermal fibroblasts cultured in vitro onto a bioabsorbable mesh to produce a living metabolically active tissue containing normal matrix proteins and cytokines (Gentzkow, Iwasaki, Hershon, Mengel, Prendergast, Ricotta et al., 1996; Gentzkow, Jensen, Pollak, Kroeker, Lerner, Lerner et al., 1999; Marston, Hanft, Norwood &amp; Pollak, 2003) (Level of Evidence = 1b)</td>
</tr>
<tr>
<td>■ Oasis®, Promogran® and Hyalofill® are examples of acellular bioactive agents.</td>
</tr>
<tr>
<td>■ Oasis® is a freeze dried wound matrix derived from porcine (pig) small intestinal submucousa (Brown-Ettris, Cutshall &amp; Hiles, 2002).</td>
</tr>
<tr>
<td>■ Xenograft: Oasis®, a relatively new product, is a xenogeneic, acellular, collagen matrix derived from porcine small intestinal submucosan in a way that allows extracellular matrix and natural growth factors to remain intact. This provides a scaffold for inducing wound healing.</td>
</tr>
</tbody>
</table>

#### Evidence:

> In a small multicentre clinical study evaluating the efficacy of Oasis® compared to Regranex®, Niezgoda (2004) found similar wound healing outcomes in both treatment groups. (Level of Evidence = Ila)

> Promogran® is a freeze dried sponge prepared from bovine collagen and oxidized regenerated cellulose prepared in acetic acid. It reduces protease MMPs known to promote inflammation in chronic wounds and protect endogenous growth factors.

#### Evidence:

> One RCT comparing Promogran® to moistened gauze dressings showed that at 12 weeks, no statistical differences were found in the healing rates between the two groups (Veves, Sheehan & Pham, 2002). Ghatnaker, Willis & Persson (2002) suggest that Promogran® may be cost effective as a result of reduced dressing frequency. (Level of Evidence = Ib)

> Hyalofill® is a hyaluronic acid ester which is thought to provide structural support, developmental regulation and assists with receptor mediated gene expression as a major molecule in the extra cellular matrix. It affects inflammation, regulation, angiogenesis, granulation formation and re-epithelialization. To date, only anecdotal results are available. (Level of Evidence = IV)
<table>
<thead>
<tr>
<th>Surgery</th>
<th>Description and Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgical (Skin Graft – Autologous)</strong></td>
<td>This procedure requires surgical transplant of epidermis and dermis from the same patient’s donor site.</td>
</tr>
<tr>
<td></td>
<td><em>(Level of Evidence = IV)</em></td>
</tr>
<tr>
<td><strong>Surgical (Achilles tendon lengthening)</strong></td>
<td>Lengthening the tendon or an attached calf muscle increases ankle dorsiflexion, thus reducing wound healing time and ulcer re-occurrence</td>
</tr>
<tr>
<td></td>
<td><em>(Level of Evidence = 1b)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Evidence:</strong></td>
</tr>
<tr>
<td></td>
<td><em>Mueller et al. (2004) compared the effect of Achilles tendon lengthening to treatment with total contact casting. The outcomes measured were healing rates and ulcer re-occurrence at seven-months follow up and two-year follow up. Although the initial wound healing outcomes were similar, statistical reduction in ulcer re-occurrence was noted at seven-months and at two-years follow up.</em></td>
</tr>
<tr>
<td><strong>Other surgical procedures</strong></td>
<td>Surgery for foot deformities can be beneficial in preventing the development and re-occurrence of ulcers.</td>
</tr>
<tr>
<td></td>
<td>Careful patient selection is critical, primarily with regard to an intact vascular supply.</td>
</tr>
<tr>
<td></td>
<td>In appropriate cases, arthroplasty, digital amputation, bunionectomy, metatarsal osteotomy or ray resection, may be indicated <em>(Muh a, 1999).</em></td>
</tr>
<tr>
<td></td>
<td>To date, only anecdotal results are available. <em>(Level of Evidence = IV)</em></td>
</tr>
</tbody>
</table>
Diabetic patient with a foot wound

- Cleanse, debride, and probe wound
- Determine the depth and tissues involved
- Assess for neuropathy (protective sensation) and foot deformity
- Assess for ischemia (pedal pulses)
- Assess for evidence of inflammation

Is the wound clinically infected?

Yes

See Algorithm 1, part 2: infected foot wound

No

- Ensure appropriate wound care
- Off-load local foot pressure
- Ensure proper footwear
- Optimize glycemic control
- Consult (podiatrist, vascular surgeon, etc.) as needed
- No antimicrobial therapy

Is the wound healing?

Yes

- Monitor until healed
- Reinforce preventive foot care

No

- Re-evaluate wound management
- Check patient's wound-care compliance
- Re-evaluate for infection
- Re-evaluate vascular status
- Consider foot radiographs

Figure 1. Algorithm 1, part 1: approach to treating a diabetic patient with a foot wound
Algorithm 2: approach to selecting antibiotic therapy for a diabetic patient with a foot infection. MRSA, methicillin-resistant Staphylococcus aureus.
CULTURING METHODS

One of the parameters used in the prevention of the complications in ulcer foot.

Superficial swabbing [LEVINE TECHNIQUE]

SWABBING TECHNIQUES

- Wound exudate
- Z- technique
- Levine technique

Most accurate results: Levine technique

DIAGNOSTIC VALIDITY OF THREE SWAB TECHNIQUES FOR IDENTIFYING CHRONIC WOUND INFECTION

Sue E.Gardener PhD, RN, Rita A.Frantz PhD, RN, Charles L. Saltzman M.D

1. Deep tissue sampling [Using scalpel or punch biopsy or curettage take viable tissue]

2. Needle biopsy

3. Bone biopsy
MATERIALS AND METHODS

- Study design: hospital based non randomized control trial
- Study period: 4 months
- Study population: patients aged 40 – 60 yrs in both sexes with diabetic foot infections at GRH, MADURAI.
- Sample size: 100
- Sampling method: convenient sampling method
- Measuring tools:
  - Questionnaire.
  - Culturing method.
  - Basic blood investigations
  - Urine routine
  - Viral marker

A. Inclusion criteria

- Patients aged 40- 60 years in both sexes presenting with diabetic ulcer foot of grade more than 1 (IDSA/IWGDF CLASSIFICATION)
- Patients who have given written consent for this study
**B. Exclusion criteria**

- Hb < 9gm.
- Albumin < 3gm.
- Creatinine >2.
- Immunocompromised state other than diabetes.
- Non palpable pulse in peripheries.
- Gangrene foot
- Patient who have not consented for inclusion in the study.

**DATA COLLECTION METHODS**

- Grading the patients according to IDSA/IWGDF CLASSIFICATION patients’ GRADE more than 1 are taken for this study

- They will be numbered from 1 to 100. Every alternate one will be chosen. Odd one will be subjected to SWAB group, even number to TISSUE group.

**PROCEDURE**

- Two cultures were simultaneously taken from each patient after the wound had been cleansed (using sterile saline and gauze) and debrided (removal of necrotic tissue, foreign material, calluses, and
undermined wound edges) in the lack of systemic antibiotic therapy for at least 4 weeks before swabbing and deep tissue culture (DTC). No antimicrobial agent (e.g., alcohol or iodine) or antiseptic was introduced into the wound before specimen collection. Superficial swab cultures (SC) were taken using the Levine technique, involving rotation of a wound swab over a 1 cm² area of the wound for 5 seconds, using sufficient pressure to extract fluid from the inner part of the wound. DTC samples about 4mm in diameter were taken from the junction of non-viable and viable tissue by using forceps. All non-viable tissue removed from the wounds & extension of sinus tract or abscess was performed in the deep tissue debridement. Samples were inserted into a transport tube containing brain infusion broth suitable for both aerobic and anaerobic microorganisms and delivered to the laboratory, for immediate processing, within 15 min after collection. Only one site was sampled from each patient. Culturing of aerobic and anaerobes species were inoculated on to blood agar, EMB (Eosin Metilen Blue) agar, Sabouraud agar and Wilkins- Chagren anaerobe agar at 35-37°C for 24-48 hours. The hemolysis reaction, catalase test, optochin, bacitracin and co-trimoxazole susceptibility testing was performed for Gram-positive bacteria, while oxidase test were applied for gram-negative bacteria. Kirby bauer Disc diffusion sensitivity testing was performed.
- Patient will be given empirical antibiotic initially then treating infection according to swab C/S for ‘S’ group and deep tissue C/S for ‘T’ group.

- After thorough debridement and respective antibiotic coverage patient has to be follow up and data will be recorded.

- Now comparing the efficacy in management of DFIs by comparing the culture of swab technique and deep tissue biopsy method by analyzing the outcome of their wound healing.

In this study for 90 patients, specimen were taken at the time of admission \(T_1\) then the patients were started on Empirical antibiotics. From 5\(^{th}\) day onwards culture sensitive antibiotic \{tissue group – tissue C/S, swab group – swab C/S\} were given. Then the second specimen for the same patient was taken on 11\(^{th}\) day of admission \(T_{11}\) then on 15\(^{th}\) of admission revised culture sensitive antibiotic was given. 3\(^{rd}\) specimen was taken on 20\(^{th}\) day \(T_{20}\). For all patients wound was thoroughly debrided and dressing done. Wound was examined for healing response. For 90 patients totally 540 specimens \{270 each for swab and tissue\} were taken. Patients with grade 4 ulcer mostly having underlying abscess, these patients were treated under high care with proper wound debridement and higher antibiotics.
The results obtained were statistically evaluated and the main parameters which were analysed were

- Organisms identified in different grades of ulcer as well as in different settings of wound culture.
- Healing response in terms of granulation tissue, wound discharge, surrounding skin, pain intensity \{Lego pain assessment tool\}
OBSERVATION AND RESULTS

In this study 100 Patients subjected to two groups deep tissue culture & swab culture. Among them 10 were excluded from the study. Because of the following reasons

1. Amputation
2. Expired
3. Lost follow up

During the course of study, we lost 2 patients for follow up; 3 patients were expired due to sudden MI; and 5 patients Underwent amputation who all had severe sepsis.
AGE & GENDER

Mean age group of patients was 55 – 57. Most of the patients lie in the age group of >50. There was no significant difference \( P = 0.654 \) in the comparison of two groups by means of age. Except 11 patients all are Male gender.
ULCER GRADING

According to IDSA classification, patients subjected to study are divided among 3 grades.

Grade 2 – 26 patients

Grade 3 – 34 patients

Grade 4 – 30 patients.

Most of the patients belongs to grade 3 ulcer group.

Patients compared between Tissue vs swab group:

<table>
<thead>
<tr>
<th>Ulcer grade</th>
<th>Tissue group</th>
<th>Swab group</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>16</td>
</tr>
</tbody>
</table>

There was no significant difference between tissue and swabbing group by means of ulcer grade \(P=0.405\).
A total of 1107 microorganisms (an average of 12.3 per wound for 3 sittings of specimen) were isolated from both the swab and tissue specimens from 90 wounds.

In Overall Gram-positive bacteria were predominant in grades 3 ulcer, as determined by either swab or tissue culturing. Gram negative bacteria were predominant in Grade 4 ulcer, as determined by either swab or tissue culturing.
At the enrolment, Gram positive bacteria were frequently isolated from SWAB technique \( p = 0.266 \) whereas after the 20 days of follow up it was frequently isolated from TISSUE biopsy technique \( p = 0.833 \). But both are statistically insignificant.
At the enrolment, Gram negative bacteria were frequently isolated from SWAB technique \( p = 0.002 \) significant one, where as after the 20 days of follow up it was frequently isolated from TISSUE biopsy technique \( p = 0.001 \). Statistically highly significant. It shows initially SWABBING better isolates the gram negative than TISSUE biopsy. So in long follow up cases TISSUE biopsy isolates gram negative better than the SWAB.
The prevalence of polymicrobial infection diagnosed by TISSUE culture increased from 28.9% for grade 2 wounds to 31.8% and 33% for grade 3 and grade 4 wounds, respectively where as for SWAB culture it was 40.8%, 32.6% & 26.5% respectively. In the isolation of polymicrobes TISSUE shows significant difference comparing to SWAB {P= 0.047}. The MC polymicrobial combination is E.faecalis, staph.aureus, pseudomonas.
CONCORDANCE

- Swabbing allowed for identification of all of the microorganisms isolated from the corresponding deep tissue specimens (percentage):

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>76.9</td>
<td>58.8</td>
<td>25</td>
</tr>
<tr>
<td>Day 11</td>
<td>61.5</td>
<td>44.1</td>
<td>15</td>
</tr>
<tr>
<td>Day 20</td>
<td>61.5</td>
<td>38.2</td>
<td>12.5</td>
</tr>
</tbody>
</table>

- Proportion of swab specimens lacking microorganisms isolated from the deep tissue specimens (percentage):

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>23.1</td>
<td>41.2</td>
<td>75</td>
</tr>
<tr>
<td>Day 11</td>
<td>38.5</td>
<td>55.9</td>
<td>85</td>
</tr>
<tr>
<td>Day 20</td>
<td>38.5</td>
<td>61.8</td>
<td>97.5</td>
</tr>
</tbody>
</table>

- Diptheroids which was isolated at enrolment as well as after 20 days follow up in four cases by SWABBING and in no case by TISSUE biopsy.
> Citrobacter spp. which was isolated at enrolment as well as after 20 days follow up in 5 cases by TISSUE biopsy and in no case by SWABBING.
MICROBIAL LOAD

- At enrolment, the overall numbers of bacterial isolates yielded from swabbing and tissue sampling were 55.8% and 44.2%, respectively ($P = 0.002$). After 20 days follow up numbers of bacterial isolates yielded from swabbing and tissue sampling were 45.1% & 54.9%, respectively ($P = 0.007$). Statistically significant.

- The average number of isolates per patient detected by swab and biopsy, respectively, was 2.32 vs. 1.84 at the enrolment ($P = 0.239$), where as it declines after 20 days follow up with net result of 1.3 vs 2.4 ($P = 0.217$) not significant statically.

- At the enrolment among Gram positive microbes Staph. aureus was the MC isolated species both in TISSUE & SWAB with percentage of 29.9% 35.5% respectively. After 20 days follow up Staph. aureus was the MC isolated species, appearing in 35.8% of the tissue specimens and CONS was the MC one in 32.6% of the swab specimens.
At the enrollement among Gram negative microbes E.coli & proteus was the MC isolated species both in TISSUE & E.coli alone in SWAB with percentage of 27%,37.1% respectively. Among the Gram-negative organisms, proteus spp. were the most prevalent, being isolated from 31.5% of the biopsied wounds and pseudomonas were the MC one from swabbed wounds about 34.1% after 20 days follow up.
CULTURE NEGATIVE

- After a 25-day follow-up, only 17 patients displayed both clinical and microbiological cure among TISSUE group and only 5 patients among SWAB group \( P=0.041 \).

HEALING RESPONSE

- In this study with in a period of 15 days follow up 12 & 30 patients were showed good healing response among SWAB & TISSUE groups respectively. \( P=0.004 \) significant

- Even after 20 days follow up 18 patients still have signs of infections in SWAB group and only 9 patients in TISSUE group. \( P=NS \)
DISCUSSION

This study was done as a prospective non randomized controlled comparative study

➢ To compare the efficacy in the management of diabetic foot infections based on culture of SWAB VS DEEP TISSUE.

➢ To identify the best method of specimen collection for culture study in identifying infectious organisms in diabetic foot infections.

A reliable sampling technique is needful to identify pathogens present in infected diabetic foot wounds. A systematic review of diagnosis of infections in diabetic foot ulcers has concluded that the available evidence is too weak to determine the optimal sampling technique. To date, most researchers consider that tissue biopsy is the best method for the identification of pathogens in DFIs because deep biopsy is not prone to superficial contamination.

Nelson et al. have carried out a large, prospective, multicenter trial to assess the concordance between culture results for swab and tissue specimens in patients with clinical DFIs. Previous studies have ignored the fact that the microbial species detected in wounds of varying depths and severities can significantly differ. Furthermore, the accuracy of swabbing has not been assessed with respect to the PEDIS infection
grade. Thus, we reappraised the concordance between swab and tissue culturing according to the PEDIS infection grade of diabetic foot wounds.

Pellizzer et al. found the mean number of isolates per patient as 2.34 by swabbing and 2.07 by tissue biopsy sampling.

Kessler et al. found the mean number of microorganisms isolated by needle puncture significantly lower compared with that obtained by superficial swabbing: 1.09 vs. 2.04 (P<0.02). However, they also observed that the swab specimen identified 13 microorganisms (62%) isolated from the needle puncture culture.

In this study there was significant difference in no. of isolates identified by TISSUE and SWAB. At the enrollement SWAB isolates more microbes than TISSUE but for chronic infections TISSUE will be the better one.

But the no. of isolates per patient by TISSUE {1.84 to 2.4} was increased in 25 days follow up comparing to SWAB{2.32 to 1.3} but statistically not significant.

Our results are not compatible with Sharp et al. and Sapico et al. study reports. They reported that swabs do not accurately identify bacterial pathogens in diabetic foot wounds. However, these studies were restricted to patients who underwent amputation. Therefore, the poor
performance of swabs in these studies might have been due to the excessive growth of colonizers at the site of the wound after the foot or limb had lost its viability. In contrast, our protocol excluded specimens from infectious gangrene and amputations.

As with Pellizzer et al study, this study denotes Gram negative microbes have been better isolated by TISSUE biopsy comparing to SWAB in chronic infection patients. As the chronicity \{GRADE 2 - 23.1 to 38.5\%, GRADE 3 – 75\% to 97.5\%\} and Grading of ulcer increases SWAB lacks to isolate microbes as the TISSUE can. Out of 45 patient’s 17 patients have both clinical& microbiological cure in TISSUE group comparing to only 5 with SWAB group. This shows significant improvement in the management of DFIs by treating the patients with TISSUE C/S antibiotic and the significant improvement in healing response too.

Few studies have prospectively compared superficial swabbing with deep tissue culture in the microbiological monitoring of severe diabetic foot. Polymicrobism and anaerobic infection appear to be the features that most closely correlate with the severity of the clinical setting. Therefore, whatever sampling method is used, it should be sensitive enough to detect the range of potential pathogens and prevent the loss of obligate anaerobes. When infection is unresolved after standard
treatment, the microbiological features of severe polymicrobial ulcers tend to resemble those observed in typically monomicrobial infections of superficial ulcers, and Gram-positive species, particularly staphylococci, are frequently isolated. It is unclear whether the higher prevalence of Gram positive species detected in properly treated long-standing ulcers represents a marker of either colonization or true infection. Indeed, the presence of facultative pathogens and S. aureus has been frequently observed to be associated with delayed wound healing, and a study by Bowler PG, Davies JB. Et al has suggested that the role of microbial synergistic interactions in the pathogenesis of chronic wound infection may be of greater clinical importance than the isolated involvement of any specific potential pathogen.
LIMITATIONS OF THE STUDY

The most important limitation of the present study is the technical issues in identifying the anaerobic culture, because of the patients financial status and lack of resources during the project work we couldn’t make out that. But we covered all the patients with available anaerobes covering Antibiotics.
CONCLUSION

- Humid environment of an ulcer likely to promote the overgrowth of skin opportunistic flora.

- Treating according to superficial culture may lead to overtreatment of that wound {superficial swab contains contaminants}

- To prevent chronicity or non-healing ulcer {rural set up} – superficial swab along with deep tissue culture should be done.

In conclusion, our experience suggests that swabbing and biopsy of the ulcer base may be equally reliable for the initial follow-up of empirical therapy in limb-threatening diabetic foot infection, provided that laboratory processing is adequate. In contrast, the microbiology of foot ulcers that are still active after 2 weeks of appropriate treatment appears better assessed by deep tissue culturing. Swab cultures may be reliable for guiding the antibiotic treatment of diabetic patients with grade 2 foot wounds. However, it is necessary to perform deep tissue biopsy for wounds of grade $\geq 3$. In such cases, swab culturing is associated with a high risk of missing pathogens, especially Gram-negative bacteria.
PHOTOGRAPHS

VARIOUS DIABETIC FOOT ULCER
COLLECTION OF TISSUE SAMPLE USING ALLIS
COLLECTION OF PUS SAMPLE USING SWAB
CULTURE METHODS

SWAB USED FOR SPECIMEN COLLECTION

KIRBY BAUER ANTIBIOTIC SENSITIVITY TEST
KLEBSEILLA PNEUMONIA

BETA HEMOLYSIS OF STAPH AUREUS
HEALING RESPONSES
CONSENT FOR THE STUDY

THE PATIENTS WHO WERE ALL SUBJECTED TO THIS STUDY, EXPLAINED ABOUT THE STUDY IN DETAIL IN THEIR NATIVE LANGUAGE AND ALSO ABOUT NIL RISK IN THIS STUDY AND WE GOT WRITTEN CONSENT FOR THIS STUDY.

ANNEXURE – 1

PROFORMA

<table>
<thead>
<tr>
<th>Name:</th>
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<tr>
<td>Age:</td>
<td>Occupation:</td>
</tr>
<tr>
<td>Sex:</td>
<td>Ph.Number:</td>
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Chief complaints

RELEVANT HISTORY

Known diabetic for --- years

History regarding immunocompromised state

H/O treatment : Insulin/OHA    Regular/Irregular

H/O trauma:+/-                 H/O bleeding disorder:+/-

H/O recurrent ulcer : +/-      H/O visual problems: +/-
H/O numbness : +/-  
H/O discoloration of foot: +/-

O/E: Temperature –  Pallor +/-  
Signs of hypoproteinemia : +/-

Peripheral pulses – palpable / not palpable

Heart Rate

**ULCER**

Dimension:     Edge:     Floor:

ExudateGangrene : +/-

Bone involvement: +/-Pain: +/-  
Abscess cavity: +/-

**INVESTIGATIONS**

Hb-      PCV-

WBC

Serum Proteins:T      A      G

RFT :

Viral markers: HIV/HBsAg/HCV

Urine:albumin / sugar / deposit

USG Abd/ Pelvis :
### Culture report:

<table>
<thead>
<tr>
<th>Day</th>
<th>Date</th>
<th>Culturing method</th>
<th>Organism</th>
<th>Antibiotic Sensitivity</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>G+</td>
<td>G-</td>
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<tr>
<td>1</td>
<td></td>
<td>Tissue Swab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Tissue Swab</td>
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<tr>
<td>12</td>
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<tr>
<td>20</td>
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<tr>
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<tr>
<td></td>
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<td>Tissue Swab</td>
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Empirical antibiotic:

Treated according to Tissue /Swab Culture:

Wound healing :

<table>
<thead>
<tr>
<th>Day</th>
<th>Edge</th>
<th>Floor</th>
<th>Exudate</th>
<th>Surrounding Skin inflammation</th>
<th>Pain</th>
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## ANNEXURE – 2

### KEY TO MASTER CHART

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<tr>
<th>Sl.no</th>
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<tbody>
<tr>
<td>G</td>
<td>Granulation tissue</td>
</tr>
<tr>
<td>R /L</td>
<td>Right / left side</td>
</tr>
<tr>
<td>M</td>
<td>Male</td>
</tr>
<tr>
<td>F</td>
<td>female</td>
</tr>
<tr>
<td>P</td>
<td>pus</td>
</tr>
<tr>
<td>S</td>
<td>serous</td>
</tr>
<tr>
<td>p/D</td>
<td>Pus decreased</td>
</tr>
<tr>
<td>SA</td>
<td>STAPH AUREUS</td>
</tr>
<tr>
<td>KLEB</td>
<td>Klebsiella</td>
</tr>
<tr>
<td>PM</td>
<td>Pseudomonas</td>
</tr>
<tr>
<td>CITROBA</td>
<td>Citrobacter</td>
</tr>
<tr>
<td>EB</td>
<td>Enterobacter aerogenes</td>
</tr>
<tr>
<td>SP</td>
<td>Streptococcus pyogenes</td>
</tr>
<tr>
<td>S.PNEUMO</td>
<td>Streptococcal pneumoniae</td>
</tr>
<tr>
<td>EF</td>
<td>enterococcus faecalis</td>
</tr>
<tr>
<td>CONS</td>
<td>COAGULASE NEGATIVE STAPH</td>
</tr>
<tr>
<td>Drug</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>CFS</td>
<td>Cefaparzone + sulbactum</td>
</tr>
<tr>
<td>CFOT</td>
<td>Cefotaxime</td>
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<td>CLOX</td>
<td>Cloxacillin</td>
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<td>AMPI</td>
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<td>Ceftriazone</td>
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<td>CIPRO</td>
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<tr>
<td>GM</td>
<td>Gentmycin</td>
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<td>CAZ</td>
<td>Ceftazidime</td>
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<tr>
<td>VANCO</td>
<td>Vancomycin</td>
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<tr>
<td>OFLOX</td>
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<td>PIPTAZ</td>
<td>Pipericillin + tazobactum</td>
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<tr>
<td>AZITHRO</td>
<td>azithromycin</td>
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</tbody>
</table>
ANNEXURE – 3

BIBLIOGRAPHY


ANNEXURE – 4

ETHICAL COMMITTEE CERTIFICATE

MADURAI MEDICAL COLLEGE
MADurai, TAMILNADU, INDIA -625 020

(Affiliated to The Tamilnadu Dr.MGR Medical University,
Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate: Dr. A. Srinivasan

Course: PG in MS, General Surgery

Period of Study: 2015-2018

College: MADURAI MEDICAL COLLEGE

Research Topic: Comparative study on outcome of Diabetic foot infections treated according to deep tissue culture and swab culture in GRH, Madurai

Ethical Committee as on: 02.06.2017

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary

Chairman

Dean / Co-ordinator

Madurai Medical College
Madurai-29
noreply@urkund.se

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</tr>
<tr>
<td>Receiver</td>
<td><a href="mailto:srinivasan.mgmu@analysis.urkund.com">srinivasan.mgmu@analysis.urkund.com</a></td>
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Alternative sources

Sources not used
CERTIFICATE – II

This is to certify that this dissertation work titled **A COMPARITIVE STUDY ON OUTCOME OF DIABETIC FOOT INFECTIONS TREATED ACCORDING TO DEEP TISSUE CULTURE AND SWAB CULTURE IN GRH, MADURAI**, of the candidate **Dr. A. SRINIVASAN** with registration Number **221511119** for the award of **MS Degree** in the branch of **GENERAL SURGERY**, I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion **99** pages and result shows **1%** of plagiarism in the dissertation.

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https://academic.oup.com/cid/article/54/12/e132/455959/2012-Infectious-Diseases-Society-of-America

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