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From Complex to Closure:

Diabetic Foot Ulcer Assessment and Management

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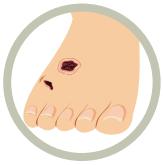
Overview and Epidemiology of Diabetic Foot Ulcers

The World Health Organization Global Report on Diabetes estimates that, globally, 422 million adults are living with diabetes mellitus, which is the sixth leading cause of death in the United States.[1] Of persons in the United States with this life-long condition, 25% will develop diabetic foot ulcers (DFUs), and the rate of recurrence can be as high as 70% within five years of the first ulceration.[2] These wounds increase both the risk of amputation and mortality rates.[2] A study by Hicks et al. showed that the direct medical cost—estimated at $176 billion in 2012—associated with treating patients with diabetes is 2.3 times higher than those costs related to the care and treatment of patients with other conditions.[3] The study also showed that 33% of these costs are directly linked to the treatment of DFUs, and the cost is rising exponentially year after year. [4] The purpose of this paper is to discuss the pathophysiology, assessment, and management of DFUs to help prevent recurrence, reduce complications and control health care costs.

Pathophysiology of Diabetic Foot Ulcers

Numerous biochemical factors accelerate the development of neuropathy and vascular foot changes in individuals with diabetes mellitus. Hyperglycemia inhibits the activation of endothelial nitric oxide synthesis, and proteins reacting with sugars trigger additional complications and aging.[2] The pathophysiology of diabetic foot ulcers can be described as the perfect storm of neuropathy, ischemia from peripheral vascular disease, and infection. Each of these factors can severely impact any individual, but for patients with diabetes, the combination of these issues occurring simultaneously can lead to ulceration, amputation, and death.[4] Understanding each of these causes independently allows for better comprehension of how devastating the results can be when they are combined.

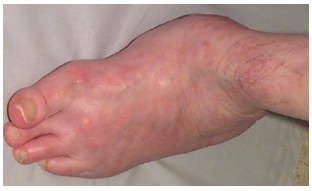
Neuropathy



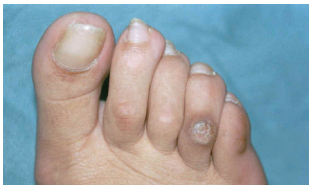
"Neuropathy plays a key role in the risk and development of DFUs."

Diabetes leads to neuropathy in many individuals and is manifested by the impact on the motor, autonomic, and sensory components of the nervous system. Neuropathy plays a key role in the risk and development of DFUs. Motor neuropathy refers to physical or structural changes that occur, symptoms of which may include muscle weakness, loss of control of coordination, muscle twitching, and muscle paralysis. Damage to nerves in the feet leads to improper flexion and extension functions of foot muscles. This dysfunction, in turn, leads to altered foot anatomy and alterations in the individual's gait. As deformities progress, so does the creation of abnormal bony prominences and pressure points, gradually causing skin breakdown and ulceration.[2] Common physical findings caused by motor neuropathy include[5]:

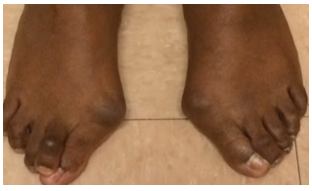
- **Charcot foot –** results from weakening of the bones of the foot and ankle leading to fracture. Secondary to loss of pain sensation, the person continues to walk on the foot, and it gradually changes shape, altering its weight-bearing pressure points.



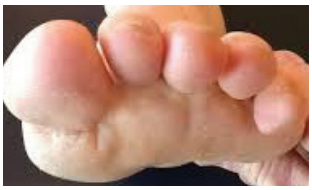
- **Hammer toes –** result from an imbalance in the muscles, tendons, and ligaments that normally hold the toe straight. It occurs when the middle joint of the toes becomes permanently in a bent position and usually only impacts one or two toes.



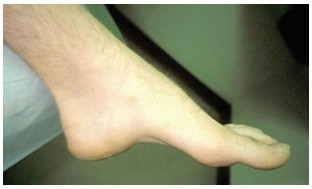
- **Claw toe –** results when the two distal toe joints bend and curl under while the joint at the ball of the foot bends slightly upward. This causes the toes to have a claw-like appearance and usually impacts all the toes of the involved foot at once.



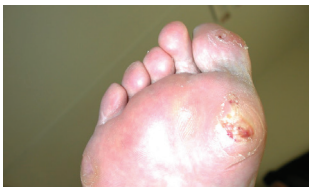
- **Prominent metatarsal heads –** occur when the plantar heads of the metatarsals are physically palpable.



- **Pes cavus –** occurs when there is an abnormally high medial longitudinal arch, which extends between the first metatarsal head and the calcaneus.



- **Excessive callous formation over bony pressure points –** excessive hyperkeratotic tissue formation as a result of shear stresses over or near bony prominences. With loss of protective sensation and continued pressure, callosities thicken, hemorrhage underneath, and ulcerate.



The autonomic nervous system works without our will, by controlling many organ functions and aiding the body in adapting to changes in the internal and external environment. Diabetic autonomic neuropathy (DAN) increases morbidity and mortality in patients with both type 1 and type 2 diabetes mellitus and impacts every organ system of the body. DAN is almost always asymptomatic in the early stages, so it is easy to miss opportunities for early diagnosis and treatment. Clinical manifestations may occur in the cardiovascular, gastrointestinal, genitourinary, pupillomotor, thermoregulatory, and other organs and systems. In individuals with pre-diabetes, hypoglycemia, and diabetes who develop DFUs, it significantly impacts the integumentary system or the skin. With DAN, there is a change in the sympathetic nervous system, rendering changes to involuntary functions such as the ability to perspire and sweat. As the skin becomes drier, cracks and fissures form, allowing further skin deterioration, the entry of bacteria, and, ultimately, infection.[6,7]

Sensory neuropathy alters tactile sensation, especially pain perception. This is called loss of protective sensation. The loss of sensation also increases the risk of injury resulting from trauma because the individual is unable to feel the insult or injury to the skin. There may be numbness, impaired temperature perception, weakness, a variety of paresthesias, and unusual pain such as tingling, stabbing pain, burning, and other abnormal sensations.[8] Approximately 10% to 26% of patients with diabetes develop painful neuropathy severe enough to impact quality of life and that results from small-fiber dysfunction. This discomfort occurs in those patients with poor long-term glycemic control. Other factors contributing to the increase in pain include age, obesity, smoking, hypertension, dyslipidemia, and peripheral artery disease.[9] Loss of vibratory and position

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sensation may also occur. The inability to perceive pain and tactile stimulus accurately puts the patient at risk for trauma, friction injury, and ulceration. Because there may be absence of pain, the individual may not notice the ulceration, or if it is noticed, he or she may feel that it is of little consequence until the ulceration becomes progressively painful as a result of infection. Weight bearing, shearing, and repetitive pressure on damaged tissue results in further deterioration of the area. Bone demineralization and impaired vascular smooth muscle also result from autonomic denervation.[2]

Peripheral Vascular Disease and Ischemia

Individuals with and without diabetes can develop atherosclerosis. However, in persons with diabetes, it occurs prematurely and progresses more rapidly. Manifestations may be coronary artery (CAD), cerebrovascular (CVD), or peripheral vascular disease (PVD). Patients with PVD typically have CAD, but those with a primary diagnosis of CAD are less likely to have PVD. Occurring at all levels of the vascular tree, PVD of the lower extremities is either macrovascular or microvascular. When sufficient blood flow in these vessels is impaired, it can result in ischemia, which leads to increased risk of infection and tissue death. Only 10% of DFUs are purely ischemic, and the remaining 90% are caused by neuropathy or neuropathy and ischemia combined (i.e., neuroischemic).[9] Macrovascular PVD results in atheromas commonly found at the bends and bifurcations of blood vessels, such as the aortoiliac segment, the superficial femoral artery, and more distal vessels below the trifurcations at the peroneal, anterior, and posterior tibialis. However, the dorsalis pedis is frequently spared.[2] Microvascular PVD combined with neuropathy predisposes patients with diabetes to an increased risk of foot infections, which can range from simple superficial cellulitis to chronic osteomyelitis. It also makes these infections more difficult to treat because poor microvascular circulation inhibits access of phagocytic cells to the area or the delivery of antibiotics to infected tissues.[10]

Infection

Infections associated with diabetic foot ulcers are not only difficult to treat, but also can become limb and life threatening. The anatomy of the lower limb, especially the foot, makes these infections more devastating than infections in other parts of the body. Because of the compartmental structure of the foot, infection can spread rapidly from one to the other. This can be especially exacerbated by neuropathy, which makes it possible for the individual to remain ambulatory, thus facilitating the further spread of infection and subsequent tissue destruction. Soft tissues of the foot, such as the plantar aponeurosis, tendons, muscle, and fascia, are more susceptible to spreading infection. The infection—along with neuropathy, ischemia, and hyperglycemia—further compromises the body's natural defenses.[2]

"Infections associated with diabetic foot ulcers are not only difficult to treat, but also can become limb and life threatening."

Most deep, long duration foot infections are associated with osteomyelitis, which develops when the infection spreads through the deep soft tissue to the bone cortex and into the bone marrow.[11] It is estimated that 44% to 68% of patients with DFU will develop osteomyelitis; this disease is the leading cause of amputation among these patients. Gram-positive organisms such as *Staphylococcus aureus* and beta-hemolytic *streptococci* are the primary responsible organisms. Most DFU cultures reveal that the infections are monomicrobial. Only 3% to 14% of DFU infections are caused by anaerobic organisms.[12]

Diagnosing osteomyelitis is difficult because it is clinically challenging to differentiate soft tissue infection from bone infection by visual inspection and assessment alone. Focal osteopenia, cortical erosion, or periosteal reaction is typically what is seen in plain films of the foot. The simplest clinical test for osteomyelitis is to use a sterile metal probe and insert into the ulcer. If it penetrates to the bone, it is generally diagnostic of osteomyelitis. Other clinical indicators are chronic draining sinuses or sausage-like appearance of the toe. Computed tomography (CT) scans, positive emission tomography (PET) scans, three-phase bone scans, and magnetic resonance imaging (MRI) can be utilized for clinical correlation, but definitive diagnosis should be made by obtaining a bone biopsy and sending the specimen for both pathology examination and culture.[11]

Assessment of the Diabetic Foot Ulcer

"Assessment should always include the whole patient, not just the patient's wound..."

Assessment should always include the whole patient, not just the patient's wound; this is especially true for patients with DFUs. A complete social and medical history should be obtained including previous ulcerations, surgery, trauma, or amputations. Remember that the individual who has had a previous amputation is at a higher risk for loss of the other limb.

Physical Examination of the Feet

Physical examination of the feet of the patient with diabetes should be an integral part of routine examinations and skin care. Observations should include neuropathic changes such as dry skin, cracks and fissures, deformities, callus formations, hemorrhagic callus formation, abnormal foot shape or deformity, condition of the nails, and prominent veins. Special attention should be paid to the interdigital spaces. The metatarsal heads should be examined on the plantar surface of the foot to determine whether they have become prominent or have developed callus over them.[13]

Peripheral neuropathy characteristics include loss of vibratory and position sense, loss of deep tendon reflexes (especially ankle jerk), trophic ulceration, foot drop, muscle atrophy, and excessive callus formation, especially over bony prominences, such as the metatarsal heads and calcaneus. Sensory perception should be evaluated using a 5.07 monofilament. In the event that this equipment is not available, cotton swabs, a pinprick, or a tuning fork may be used to detect the level of sensation. This will help in determining whether the individual has lost protective sensation, thus posing a higher risk of DFU formation.[14]

Characteristics of ischemia will include decreased temperature in the affected extremity, dependent rubor, elevational pallor, loss of hair on the dorsal foot, and faint or absent dorsalis pedis and posterior tibial pulses. The femoral artery should be palpated as well as auscultated for the presence of a bruit.[4] To confirm the presence or absence of pulses and to validate adequate blood supply, a hand-held Doppler device may be used. Utilizing the Doppler and a sphygmomanometer, an ankle brachial index (ABI) may be obtained. This is accomplished by taking the ankle systolic pressure and dividing it by the brachial systolic pressure. According to the Wound, Ostomy and Continence Nurses Society™, ABI values are interpreted as follows[15]:

>1.3: Non-compressible vessels

>1.0: Normal

≤ 0.9: Lower extremity peripheral vascular disease

<0.6 to 0.8: Borderline ischemia

<0.5: Severe ischemia

Additionally, toe pressures and transcutaneous oxygen pressure (TcPO2) measurements can be helpful in measuring tissue perfusion. Claudication, which is pain in the legs with walking or other exercise, and temperature difference between the feet are also signs of ischemia. When it is determined that a limb has critical ischemia, the individual should be urgently referred to a vascular surgeon. Critical ischemia is a limb-threating clinical emergency, which is characterized by the six "Ps": pulselessness, pain, pallor, perishing cold or poikilothermia, paresthesia, and paralysis.[13]

DFUs are classified into two categories: neuropathic, in which neuropathy is the dominant issue; and neuroischemic, where neuropathy is present, but ischemia is the primary issue. As discussed previously, neuropathy leads to drying and fissure development in the skin of the feet, as well as Charcot joints and digital necrosis. Friction leads to bulla formation and breaks in the skin as well. Poor blood flow or ischemia of the foot leads to pain at rest, ulcerations on the plantar surface and other pressure bearing points on the foot, digital necrosis, and the development of gangrene. Treatment strategies for each differ because the complications vary, so being able to differentiate between these categories is important.[16]

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Classification Systems

There are no universally accepted classification scales for DFUs. The two most widely accepted are the Wagner Diabetic Foot Ulcer Grade Classification System and the University of Texas Diabetic Foot Ulcer Classification System. The Wagner system is an older classification scale for foot ulcers and takes into account the depth, appearance, and presence of osteomyelitis or gangrene, and it is described by grades 0 through 5[17]:

"There are no universally accepted classification scales for DFUs."

- **Grade 0 –** intact skin
- **Grade 1 –** superficial ulcer of skin or subcutaneous tissue
- **Grade 2 –** ulcer extends into tendon, bone, or joint capsule
- **Grade 3 –** deep ulcer with osteomyelitis or abscess
- **Grade 4 –** partial foot gangrene
- **Grade 5 –** whole foot gangrene

The newer scale or system is the University of Texas Diabetic Foot Ulcer Classification System, which grades DFUs by depth and then stages, based on the presence or absence of infection and ischemia, as follows:

- **Grade 0 –** pre-ulcerative site or post-ulcerative site that has healed
- **Grade 1 –** superficial wound not involving tendon, joint capsule, or bone
- **Grade 2 –** wound penetrating to tendon or joint capsule
- **Grade 3 –** wound penetrating the bone or joint

The stages within each wound include:

- **Stage A –** clean wounds
- **Stage B –** non-ischemic infected wounds
- **Stage C –** ischemic non-infected wounds
- **Stage D –** ischemic infected wounds

Neuropathy leads to fissures, bullae, neuropathic (Charcot) joint, neuropathic edema, and digital necrosis. Ischemia leads to pain at rest, ulceration on foot margins, digital necrosis, and gangrene. Differentiating between these entities is essential because their complications are different, and they require different therapeutic strategies.

Assessment of Ulcer Characteristics

The initial assessment and documentation of the DFU establish a baseline for clinical diagnosis, development of the plan of care, initiation of treatment, and monitoring the response to treatment. The size (length × width × depth), appearance, and location should be documented. The color and status of the wound bed (which should be healthy, beefy red) and, if present, the amount

and characteristics of necrotic nonviable tissue should be recorded. The presence of exposed bone, necrosis, or gangrene may indicate osteomyelitis or worsening infection. What is the type, color, amount, presence of purulence, and odor associated with the wound drainage? The condition of the periwound skin should also be documented because maceration and spreading erythema may indicate excessive exudate and worsening of the wound. In addition, the presence of callus, edema, and undermining should be documented. Photographs are especially important at onset of treatment and periodically thereafter to monitor and document the progress toward or lack of healing.[13]

Other Assessment Parameters

Glycosylated hemoglobin (hemoglobin A1c [Hgb A1c]) levels should be obtained to see how well the individual is managing blood glucose levels. A study by Zubair et al. discussed that higher prolonged Hgb A1c levels place the individual at higher risk of developing complications, especially DFUs. Higher Hgb A1c rates were also found to delay healing in these patients.[18] The American Diabetes Association recommends maintaining Hgb A1c levels at around or below 7% to reduce microvascular and neuropathic complications.[19]

"Individuals with diabetes are already at high risk of vascular disease and stroke, which smoking only compounds."

Smoking habits should also be documented. Individuals who smoke are at high risk of developing other comorbid conditions such as coronary artery disease, peripheral vascular disease, and chronic obstructive pulmonary disease, all of which have a detrimental effect on healing.[20] It should also be determined how motivated the individual is to stop smoking. Individuals with diabetes are already at high risk of vascular disease and stroke, which smoking only compounds.

Management of Diabetic Foot Ulcers

The primary focus of DFU management is achieving wound healing. Management should consist of treating the underlying disease process, achieving and maintaining adequate perfusion by revascularization and edema management, wound care and infection control, and offloading. Identifying the underlying cause and correcting and eliminating it are essential to effective management of DFU.[13] Interventions for ischemia are the most essential to achieving wound healing and limb preservation. Patients with critical ischemia should have emergency consultation for interventions that will reestablish and maintain blood supply. Managing other risk factors such as hypertension, high cholesterol, smoking, and malnutrition is essential to keep DFUs on a healing trajectory. Identifying the cause of trauma or potential for repetitive trauma is important as well. This would also include assessing the patient's footwear for proper fit, wear and tear, and possible foreign bodies such as rocks, pieces of glass, pins, needles, or pet dander, which have the potential to induce trauma. It is also important to keep in mind that footwear should accommodate the dressing, or other foot protection should be chosen.[2]

Optimal wound care is also essential and should include a focus on initial and serial debridement to keep the wound in an acute state free of debris and non-viable tissue; as well as frequent assessment and dressing interventions that aid in bacterial control and maintain a moist healing environment without the risk of maceration. Additionally, offloading of at-risk and ulcerated areas of the foot aids in maximizing pressure redistribution across the plantar surface of the foot, thus helping maintain perfusion and aid healing.[21]

"Optimal wound care is also essential and should include a focus on initial and serial debridement..."

Topical therapy is inclusive of appropriate dressings tailored to dynamic wound characteristics, with attention to moisture and exudate levels. Advanced therapies for DFUs include negative pressure wound therapy (NPWT), cellular and/or tissue-based products (CTPs), growth factors (GFs), and hyperbaric oxygen therapy (HBOT). These modalities may be considered after four weeks of traditional standard therapy has failed to demonstrate at least 50% reduction in wound surface area. NPWT has demonstrated benefits in decreasing the lengths of inpatient hospital stays and DFU complication rates. In some trials, CTPs may decrease the risk for amputation and improve the rate of closure compared with standard care.[22] GFs, specifically, platelet-derived growth factor (PDGF), demonstrated some evidence in providing higher rates of closure in groups treated with standard care plus PDGF versus standard care only.[23] HBOT studies show decreased time to closure and chance of amputation in DFUs in which at least 30 days of standard therapy have failed in patients with improved TcPO2 (tissue oxygenation) testing after HBOT.[2] No general consensus has been reached on recommendation of these therapies for regular use in routine care of the DFU, and throughout wound assessment appropriate grading and classification is paramount to selecting appropriate treatment, including the use of advanced modalities referenced previously.

Although there are multiple devices available to provide offloading, total contact casting is the gold standard for offloading DFUs. This is a padded foot and lower leg cast with an opening over the DFU. The cast provides the offloading, and the opening in the cast provides access to the wound for dressing changes. It also provides a method of ensuring patients' compliance because it is very difficult to remove. Total contact casting has also been found to reduce healing time by as much as six weeks.[9] Contraindications for total contact cast include infected DFUs and osteomyelitis, because of difficult observation, and patients with critical ischemia, because of the risk of increasing ischemia.

Patient Education for Diabetic Foot Ulcers

Successful prevention of DFUs is a result of partnerships between caregivers and patients. Studies have shown that with effective patient education, DFUs can be prevented by up to 50%, thus reinforcing the fact that self-management should be the foundation of DFU prevention.[9] Emphasis on positive health practices, especially for patients with diabetes, will help prevent foot ulcers and possible amputation. Effective programs include an array of methods from brief education to comprehensive education, which includes hands-on teaching and teach-back methods. Priority topics should be on management of risk factors, proper foot care with visual self-inspection, monitoring of skin temperature and hair growth, proper foot hygiene and footwear choices, and glycemic control. This comprehensive approach not only reduces the frequency of amputations but also decreases the rate of amputations and mortality associated with DFUs.[14]

"Emphasis on positive health practices, especially for patients with diabetes, will help prevent foot ulcers and possible amputation."

Patients need information simplified into laymen's terms so that it is easy to comprehend. Ascertaining their comprehension level is imperative to developing an effective personalized education program. If patients do not understand what is being done or the rationale and purpose, it is very difficult to promote compliance with the plan of care. For example, patients must understand how reduction of pressure on the wound and proper offloading can stop the repetitive trauma and callus formation that inhibits wound healing. Many times, it takes repetitive education to drive the point home and ensure that understanding is achieved. As outcomes improve, patients appreciate their role in preventing and caring for DFUs, and this appreciation also drives and promotes adherence to the plan of care.[24]

Conclusion

Unfortunately, DFUs are dreaded and common maladies for patients with diabetes that often lead to frequent hospitalizations, lower limb amputation, and, in some cases, death. Targeted management strategies can lead to successful healing outcomes and include education, glycemic control, wound debridement, infection control, offloading, surgical interventions, and advanced therapies. Screening for DFUs should be completed in all care settings, and self-assessment should be taught as part of the patient's self-management plan. Utilization of an interprofessional approach can support patients in the prevention and management of DFUs.

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SANTYL Ointment is indicated for debriding chronic dermal ulcers and severely burned areas.

Use of SANTYL Ointment should be terminated when debridement is complete and granulation tissue is well established.

One case of systemic hypersensitivity has been reported after 1 year of treatment with collagenase and cortisone. Occasional slight transient erythema has been noted in surrounding tissue when applied outside the wound.

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Collagenase SANTYL®

Ointment 250 units/g

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DESCRIPTION

Collagenase Santyl® Ointment is a sterile enzymatic debriding ointment which contains 250 collagenase units per gram of white petrolatum USP. The enzyme collagenase is derived from the fermentation by *Clostridium histolyticum*. It possesses the unique ability to digest collagen in necrotic tissue.

CLINICAL PHARMACOLOGY

Since collagen accounts for 75% of the dry weight of skin tissue, the ability of collagenase to digest collagen in the physiological pH and temperature range makes it particularly effective in the removal of detritus.[1]

Collagenase thus contributes towards the formation of granulation tissue and subsequent epithelialization of dermal ulcers and severely burned areas.[2, 3, 4, 5, 6] Collagen in healthy tissue or in newly formed granulation tissue is not attacked.[2, 3, 4, 5, 6, 7, 8] There is no information available on collagenase absorption through skin or its concentration in body fluids associated with therapeutic and/or toxic effects, degree of binding to plasma proteins, degree of uptake by a particular organ or in the fetus, and passage across the blood brain barrier.

INDICATIONS AND USAGE

Collagenase Santyl® Ointment is indicated for debriding chronic dermal ulcers[2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18] and severely burned areas.[3, 4, 5, 7, 16, 19, 20, 21]

CONTRAINDICATIONS

Collagenase Santyl® Ointment is contraindicated in patients who have shown local or systemic hypersensitivity to collagenase.

PRECAUTIONS

The optimal pH range of collagenase is 6 to 8. Higher or lower pH conditions will decrease the enzyme's activity and appropriate precautions should be taken. The enzymatic activity is also adversely affected by certain detergents, and heavy metal ions such as mercury and silver which are used in some antiseptics. When it is suspected such materials have been used, the site should be carefully cleansed by repeated washings with normal saline before Collagenase Santyl® Ointment is applied. Soaks containing metal ions or acidic solutions should be avoided because of the metal ion and low pH. Cleansing materials such as Dakin's solution and normal saline are compatible with Collagenase Santyl® Ointment.

Debilitated patients should be closely monitored for systemic bacterial infections because of the theoretical possibility that debriding enzymes may increase the risk of bacteremia.

A slight transient erythema has been noted occasionally in the surrounding tissue, particularly when Collagenase Santyl® Ointment was not confined to the wound. Therefore, the ointment should be applied carefully within the area of the wound. Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

No allergic sensitivity or toxic reactions have been noted in clinical use when used as directed. However, one case of systemic manifestations of hypersensitivity to collagenase in a patient treated for more than one year with a combination of collagenase and cortisone has been reported.

OVERDOSAGE

No systemic or local reaction attributed to overdose has been observed in clinical investigations and clinical use. If deemed necessary the enzyme may be inactivated by washing the area with povidone iodine.

DOSAGE AND ADMINISTRATION

Collagenase Santyl® Ointment should be applied once daily (or more frequently if the dressing becomes soiled, as from incontinence). When clinically indicated, crosshatching thick eschar with a #10 blade allows Collagenase Santyl® Ointment more surface contact with necrotic debris. It is also desirable to remove, with forceps and scissors, as much loosened detritus as can be done readily. Use Collagenase Santyl® Ointment in the following manner:

1 – Prior to application the wound should be cleansed of debris and digested material by gently rubbing with a gauze pad saturated with normal saline solution, or with the desired cleansing agent compatible with Collagenase Santyl® Ointment (See **PRECAUTIONS**), followed by a normal saline solution rinse.

2 – Whenever infection is present, it is desirable to use an appropriate topical antibiotic powder. The antibiotic should be applied to the wound prior to the application of Collagenase Santyl® Ointment. Should the infection not respond, therapy with Collagenase Santyl® Ointment should be discontinued until remission of the infection.

3 – Collagenase Santyl® Ointment may be applied directly to the wound or to a sterile gauze pad which is then applied to the wound and properly secured.

4 – Use of Collagenase Santyl® Ointment should be terminated when debridement of necrotic tissue is complete and granulation tissue is well established.

HOW SUPPLIED

Collagenase Santyl® Ointment contains 250 units of collagenase enzyme per gram of white petrolatum USP.

Do not store above 25˚C (77˚F). Sterility guaranteed until tube is opened.

Collagenase Santyl® Ointment is available in the following sizes:
30 g tube NDC 50484-010-30
90 g tube NDC 50484-010-90

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