Management Of Chronic Leg Ulcers In Nigeria: An Update.

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A wound is an area of compromised tissue integrity[1]. This definition includes all compromised tissues with or without loss of lining. An ulcer, which is a type of wound, is a site on or in the body where the surface lining has been lost or deepithelised. Although the aetiology of wounds is all embracing, often when used unqualified, it is due to trauma and typically there is associated loss of substance. Deeper injuries to the muscle tissue, the skeletal system, or the inner organs are defined as complicated wounds[2].

According to Ellermann and Röthel[3] when a wound is healing by second intention, it is said to be chronic if it does not show any healing tendency under appropriate causal and local therapy within eight weeks. Mekkes et al[4], however set the time limit to four weeks. Oluwasanmi[5] working in Ibadan had indicated a time frame of six weeks in a retrospective review of chronic leg ulcers. Chronic wounds or ulcers are usually the end stage of progressive tissue breakdown due to certain aetiopathogenetic factors some of which are outlined below.

The two main criteria for definition of a chronic ulcer are "full thickness loss" and "slow healing". Mekkes et al[4] have suggested that the slow healing tendency is not simply explained by depth and size, but caused by an underlying pathogenetic factor that needs to be removed to induce healing. An understanding of these is required for a successful management of this condition. Often however, when this understanding is lacking, patients with this disease present with recurrence and more recurrence compounds the problem further presenting with a greater difficulty in healing. The aim of this communication is to appraise the problems encountered in management of the commonest aetiological varieties of this disease in Nigeria with an updated overview.

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Epidemiology of chronic lower limb ulcer

Chronic lower limb ulceration is frequently encountered in clinical practice. Information about its prevalence and natural history in Nigeria is however scarce. Such information can only be obtained by screening a large population and with the current organization of the Health sector that would be difficult.

On the other hand, for example in the UK, treatment of leg ulceration is largely through community services. From there referrals for aetiologies other than venous disease are sent to the hospitals[6]. Community nursing is provided by one agency within a geographical area. More than 80% of patients are treated by these nurses either in the patient's home or in general practice clinics[7]. This makes identification of patients a relatively simple exercise in the UK.

Where figures are available, the prevalence of chronic ulceration of the lower leg is about 1-2 per 1000 of the general population[8,9], and 3-5% in the population over 65 years of age[4]. Studies of small populations have suggested that about one percent of people have leg ulcers at some time[10,11].

In the UK and USA, chronic lower limb ulcers are largely due to venous and arterial disease, and complications of diabetes and rheumatoid arthritis[12,13]. In Nigeria however, while these

(except rheumatoid arthritis) are common, factors like pressure, and other traumas, haemoglobinopathy, and malignancies are frequently seen. Few studies[5] have suggested trauma as the most common aetiology in Nigeria.

Abroad, the incidence of chronic lower limb ulcer is rising as a result of the ageing population and increased risk factors for atherosclerotic occlusion such as smoking, obesity and diabetes[4]. In addition to these, however, in Nigeria, rising incidence may be attributable to an increase in trauma notably road traffic accidents in amidst poor primary health care delivery.

Aetiopathogenesis of chronic lower limb ulcer:

An awareness of the differential diagnosis in addition to a detailed knowledge of the presentation, pathogenesis and treatment modalities is essential for a rational approach towards patients with chronic lower limb ulcers. Because an incorrect diagnosis usually leads to incorrect treatment (a classic example is pyoderma gangrenosum treated with antibiotics), which may cause serious harm to patients, early careful assessment is crucial[4].

The common aetiological factors, figure I, of chronic lower limb ulcer in Nigeria are trauma, venous valve insufficiency, lower extremity arterial disease, diabetes, and haematological diseases. Less frequent conditions are malignancies and infections which may be chronic ab initio (as in mycobacterial and fungal infections) or a chronicity from an acute infection. Rarer conditions are vasculitis and ulcerating skin diseases such as pyoderma gangrenosum. Proper treatment of patients with leg ulcers requires a thorough knowledge of the large differential diagnosis of leg ulceration.

The mechanisms that produce a chronic ulcer are similar. Although the deficiencies in nutrient delivery and metabolite removal are due to diseases in vessels, they finally all lead to tissue hypoxia and cell ischemia and necroses. The events at molecular level are similar in all cases, figure II. Here, the orderly process of wound healing usually seen in acute wounds becomes disrupted. The extracellular matrix gets disorganized with an increased level of matrix metalloproteinases (MMPs) and proinflamatory cytokines. The levels of inhibitors of MMPs are reduced and fibroblast synthesis of collagen also becomes diminished. In the sections below some of these aetiological factors and the mechanism with which they cause ulceration will be dealt with to a greater detail and will be related to current management.

Trauma:

The commonest aetiological factor for chronic lower limb ulcer in Ibadan is trauma. Chronic post traumatic leg ulcer results from inadequate primary treatment of a trauma or from complications during primary treatment. Typical causes for the chronic course of a post traumatic wound are soft-tissue contusion, skin avulsion, skin necrosis, osteitis, implant infection, joint involvement and infection, or deep soft-tissue infection. In most cases, the disadvantageous development is due to initial under-estimation of the soft-tissue injuries that accompanies the primary trauma[3].

Leg traumas in Nigeria are often treated initially by unqualified personnel with cleansing solutions which are often deleterious to the wound healing process. Apart from being deleterious, they are often used in concentrations that are not standardized. Iodine solutions, hydrogen peroxide and hypochlorites like EUSOL and JIK are often counterproductive in wounds. Inappropriate use of topical antibiotics like penicillin and "M and B" powder also contribute to chronicity.

An ulcer of several years duration may consist of a rather fibrous base and surrounding. The granulation tissue floor may be pale. Pale granulating and sloughy floors should be considered not ready for skin grafting. After desloughing and during the conditioning period of treatment, an application of the molecular knowledge is in the use of low dose sub antimicrobial dose of the tetracycline product called doxycycline[14,15]. This antibiotic is known to antagonize MMPs. Hypertrophic pink granulation is not a contraindication for skin grafting. At surgery, it can be excised and skin

graft laid over. On the same note, fibrous base can be excised down to fascia but the tenuous film of suprafascial arterial plexus must be left intact to ensure graft take.

When there is an open fracture, contaminations may produce soft-tissue and bone infections that often run a chronic course. Open fractures are best managed by a combined team of plastic and orthopaedic surgeons and that simultaneously not one after the other. In addition, the best timing for such management should be during the acute phase which is within the first five days post injury[16]. Major soft tissue coverage should be avoided during the subacute phase until six weeks post trauma.

Sometimes excision of the ulcer base with the underlying osteitis, and or radical debridement of chronic osteomyelitis produces a large defect which presents reconstructive challenges. The problem usually posed by inadequate availability of local tissues is being surmounted through discoveries of innovative flaps such as the sural artery flap[17,18] while the armamentarium of free tissue transfers[19,20] remain possible where the expertise is available.

Pressure ulceration involving the maleoli and the heel region is a special form of chronic lower limb ulcer. Extrinsic and intrinsic factors contribute to its formation. Extrinsic factors include pressure (causing mechanical damage, blockage of blood vessels), shear, and friction[21] (which strips outermost layer of skin). Intrinsic factors include infection, hypoproteinaemia, anaemia, sensory loss, impaired mobility, faecal, and urinary incompetence[22]. Pressure is one of the physical factors that must be removed for a chronic wound to heal, figure III

This may be carried out by astute nursing management. For hospital managements that can afford it, beds like Low Air Loss, or Clinitron, should be used. The low air loss bed relies on the segmentation of parts of the bed allowing for introduction of air into segments at different pressure; hence, parts subject to pressure can lie on low pressure segments. Hospitals that are unable to afford these expensive beds may explore the use of fenestrated foam[23]. Pressure ulcers that present an involvement of underlying constitute indications for operative intervention. The underlying bone should be shaved and a local flap transferred.

Venous disease:

Venous ulceration results from venous hypertension which in turn is due to valvular insufficiency of the deep venous system and of the lower perforating veins, as well as an ineffective calf muscle pump. When the valves are intact but calf muscle contraction is absent as in immobility and paralysis, oedema and ulceration may ensue. The condition is known as dependency syndrome.

Although the commonest cause of valvular insufficiency is post-thrombotic syndrome, it may be caused by compression or obstruction of veins by tumours or enlarged lymph nodes, as well as congenital weakness of valves or vessels. The pathogenetic mechanisms that lead from valve insufficiency to ulceration are still not fully elucidated[24]. Functionally, there is reduction, reversion and stagnation of blood flow in the capillaries of prenecrotic skin, increased pressure in the capillaries, increased blood flow in the reticular dermal capillary network, increased blood flow and arteriovenous shunting near ulcers, and decreased skin oxygen pressure in areas at risk[25,26].

Retrograde pressure waves during calf muscle contraction with increased tension in the venous system lead to malformation of the capillaries. The capillary changes of dilatation and elongation lead to reduction of blood flow, disturbed rheological conditions[27] sludging and aggregation of cells, and finally to microthrombi formation and occlusion of capillaries[25,28].

In addition, increased pressure in the venous system increases transendothelial and interendothelial capillary passage, resulting in a protein-rich oedema[4]. Oedema in itself may contribute to tissue hypoxia by increasing the diffusion distance for oxygen around the nourishing capillaries[26]. This finally results in a fibrotic and oedematous skin area where a considerable number of capillaries are missing, while those remaining are malformed and

dysfunctional. The slightest trauma or infection in these areas disturbs the balance between oxygen supply and demand and a chronic nonhealing ulcer develops[4]. Sustained reduction in pressure differential between arterial and venous systems in the limb effectively traps or slows down polymorphonuclear leukocytes in the area. These through an inflammatory response as well as increased proteolytic activity in lipodermatosclerotic skin predispose to skin ulceration.

Clinically, chronic venous leg ulcer can generally be graded into three stages according to the severity of the dermal lesion. A stage I chronic venous leg ulcer is characterized by vein dilation along the sides of the foot with concomitant formation of oedema in the ankle region, stage II already involves hyper- and depigmentation of the skin, dermatoliposklerosis, or even atrophie blanche together with marked oedema formation on the lower legs. Stage III is the florid or healed ulcer that is preferentially located in the perimalleolar region, but can also be found at other sites of the low leg[3].

The management of venous ulceration must be comprehensive. After appropriate localizing investigations, treatment may consist of the combination of saphenofemoral junction disconnection, avulsion of the saphenous vein, and subfascial ligation of incompetent perforators. The approach for such ligation should be placed away from the medial or lateral aspects of the leg which in some cases contains bags of varicose (worms) veins. We utilise a midline posterior leg incision with an inverted U extention over tendo Achilles.

A closed subfascial ligation of incompetent perforating veins of the lower limbs which is easy to perform, not invasive, and gives encouraging results has been described[29]. It consists of making two small transverse incisions measuring 5-10 mm in length on both sides of the incompetent perforating vein. Using an aneurysmal needle, a suture (polypropylene No. 1) is placed in the subfascial plane to encircle the incompetent perforating vein from all directions and tied to ligate the perforator.

Arterial disease:

Arterial ulcer of the lower limb is uncommon in al Nigeria. It is always a sign of tissue hypoxia at rest owing to peripheral arterial blockage which has been ongoing for several years. Risk factors are age, diabetes (four to five fold increase in incidence of arterial occlusive disease) smoking, hypertension, obesity, fat embolism (hypercholesterolaemia, hyperlipidaemia), and hyperuricemia. The obliterative processes are not restricted to the periphery. Additional renal, cardiac, and cerebral dysfunctions may be present due to the generally impeded arterial supply[3].

Every non traumatic leg ulcer that is not located at the typical sites for venous ulcerations is very likely to be arterial in origin. Diagnostic features include missing popliteal, posterior tibial, and dorsalis pedis pulses, reduced walking range as defined by intermittent claudication, a cool, pale extremity, a soft, doughy oedema, as well as possible gangrenous alterations at the tip of the toe. The blood pressure index, which is the ratio of ankle to brachial blood pressure, is usually below 0.8

Diabetes Mellitus

Chronic secondary damages in diabetes mellitus become especially expressed at blood sugar levels that do not cause the acute features of diabetic coma, nor noticeably impair the patient's general condition. Among the secondary complications of diabetes, the "diabetic foot syndrome" is particularly problematic[3]. The slowly progressing changes at the feet remain mostly unnoticed and are often painless due to concomitant neuropathy. With additional wounding, the foot is in acute danger and may cause serious problems:

Classically, distal sensorimotor and autonomic neuropathy is the major cause. This is often combined with arterial insufficiency due to atherosclerotic occlusion of the tibioperoneal arteries which spares the arteries arteries of the foot[30,31]. Approximately 6070% have neuropathy only, 1520% have peripheral vascular disease only, and 1520% have a mixture of both[32].

Occlusive disease of the microcirculation is no longer considered as the major component of vascular compromise in diabetes mellitus. Morain and Colen[33] have listed factors that may influence their (diabetic's) microcirculation: stiffened red

blood cells, increased blood viscosity, susceptibility of both tibial and peronial arteries to artherosclerosis, transudation from high venous back pressure, affinity of glycosylated haemoglobin for oxygen contributing to low oxygen delivery; also impaired phagocytosis and bacterolysis which along with neuropathy and ischaemia cause increased vulnerability to infection.

In order to establish a reliable treatment regime, diabetic chronic lower limb ulcer should be assigned to one of the following groups:

- traumatic neuropathic foot
- ischemic gangrenous foot with peripheral arterial occlusion
- infected foot with diabetic polyneuropathy with or without peripheral arterial occlusion
- infection of the foot with features of diabetes but no evidence of relevant neuropathy or angiopathy.

In treating diabetic ulcers the vicious cycle of ulcer infection, progression of ischaemia and hyperglycaemia must be broken. Needless to say however, that early control of distal ischaemia through revascularization to bypass the segment of midrange vasculopathy is paramount. If progressive and extensive gangrene develops, a case should be made for appropriate amputation and early mobilization of the patient.

Haematological diseases:

In Blacks particularly where there is a high prevalence of the sickle cell gene, the sickle cell anaemias are the commonest haematological aetiological factors. Other forms of anaemia, for example, thalassaemia, hereditary spherocytosis, and glucose-6-phosphate dehydrogenase deficiency have been associated with lower leg ulceration. In sickle cell anaemia, it has been hypothesized that an interaction between sickle cells and endothelial cells causes increased expression of endothelial cell adhesion molecules, which promotes thrombotic vasoocclusion[34]. In other haematological conditions like essential thrombocythaemia, thrombotic thrombocytopenic purpura, polycythaemia, leukaemia, dysproteinaemia, microvascular thrombosis is the most likely pathogenetic factor[4]. Other factors include secondary bacterial infection, and decreased oxygen-carrying capacity of blood that interferes with proper nutrition and metabolism of blood cells.

Sickle cell leg ulcers occur either spontaneously or as a result of local trauma. Abroad, it is reported that between 8% and 10% of SS patients[35] develop leg ulceration between the ages of 10 and 50 years. In "endemic zones" however, like in West and Central Africa, and in Jamaica[36,37], higher rates of more than 40% have been described. Durosinmi et al[38] reported a prevalence of 7.5% among 630 HbSS patients at Ibadan. The healing rate of these ulcers is typically three to 16 times slower than for other forms of leg ulcers, and they tend to recur[39].

A highly significant association between leg ulceration and venous incompetence in the same leg has been demonstrated[40]. This association of venous incompetence with chronic leg ulceration suggests a further pathological mechanism that contributes to the morbidity of SS disease. However the cause of venous incompetence in this situation is unknown.

Bed rest with leg elevation and local treatment consisting of wound cleansing sometimes with topical applications like zinc, antibiotics is the treatment of choice for small mean size diameter (< 4cm) and the recurrence rate of 25% has been described[35]. We sometimes use topical antiseptics such as silver sulphadiazine. Chemical debridement with eusol or other agents should be short term. Mechanical or sharp debridement should be reserved only for the cases with necrotic tissue. Often the floor consists of sloughs as opposed to necrotic tissue.

More aggressive forms of treatment with blood transfusion therapy and skin graft are reserved for nonhealing ulcers of >8 cm in mean diameter. The recurrence rate in a study was 37% and 52% for transfusion therapy and skin graft, respectively. The difference was not significant. The high failure rate of 52% after skin graft may be due to the larger diameter of the ulcer, and chronicity. Skin grafts should be medium to thick partial thickness and should be performed after proper wound conditioning on good granulation tissue.

Fig I: Aetiopathogenesis of chronic leg ulcer

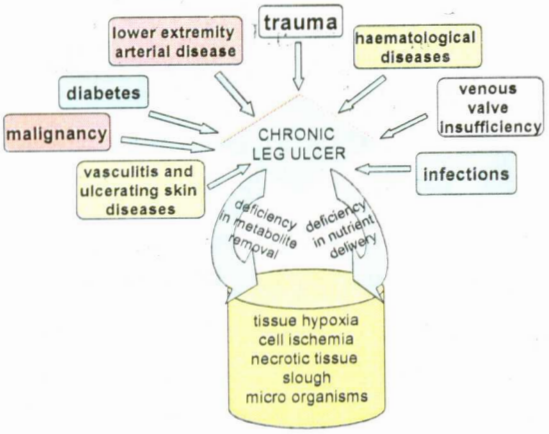


Fig II: Molecular and cellular events in chronic wound

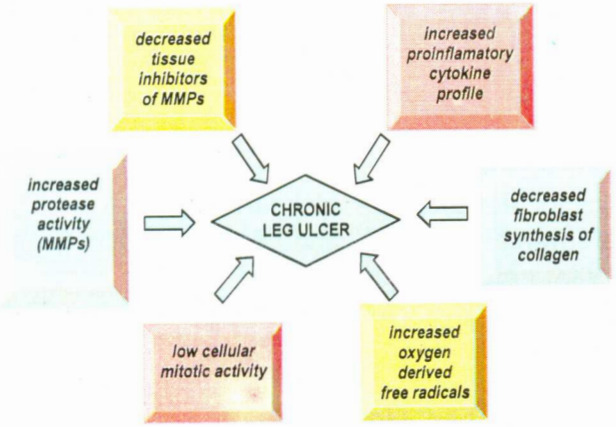
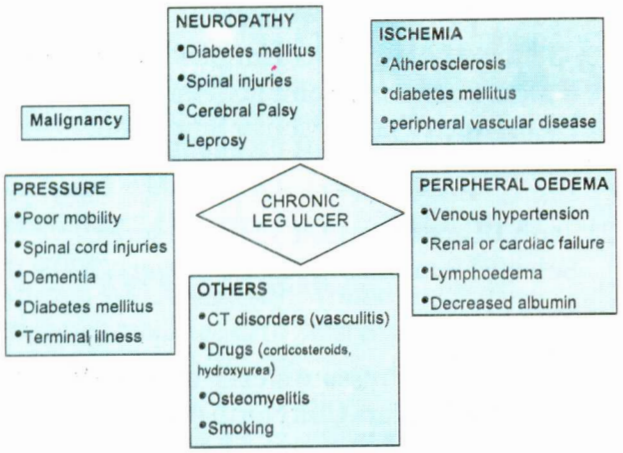


Fig III: Physical factors that lead to persistence of chronic wounds



Blood transfusion therapy may be pre and or perioperatively in form of a partial exchange transfusion with fresh AA blood. Intravenous pentoxifylline may also be used to resolve acute vaso-occlusive crises in 75% to 100% of patients with sickle cell anemia by increasing erythrocyte flexibility and decreasing blood viscosity[41].

Since haemoglobinopathic ulcers are vaso-occlusive and since there is a tendency for ulcers to occur in the malleolar regions, any surgeries performed on the lower extremities should be performed without a tourniquet to prevent vascular compromise or ulcer formation due to tourniquet trauma[39].

Apligraf, a tissue-engineered product which has the appearance and handling characteristics of human skin with both an epidermis and a dermis including living keratinocytes and fibroblasts derived from human neonatal foreskin has been used in treating sickle cell ulcers[39]. It also has the capacity to produce a variety of growth factors that are critical to wound healing and should be considered as an additional treatment option for patients with chronic sickle cell wounds.

Venous hypertension in SS patients with leg ulceration suggests that firm elastic supportive dressings might promote healing of chronic leg ulcers[40]. Caution should however be exercised bearing in mind the possibility bandage trauma. Treatment of the primary disease should focus on induction of fetal hemoglobin, modulation of erythrocyte hydration, augmentation of nitric oxide, chronic transfusion, stem cell transplantation, and gene therapy[42].

Nutritional supplementation.

Ette et al[43] found that levels of vitamin A, C and E were significantly lower than levels in healthy Nigerian controls. They also indicated that patients with chronic leg ulcers had a deficiency of zinc. The relationship of these nutrients to wound healing suggests the addition of vitamins C and E and zinc in the management of leg ulcers.

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