Assessing and controlling wound infection

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Methodology

Chronologic perspective

It is apparent that humans are not germ free. Therefore, health is not the absence of bacteria, but is kindred to an elegant balance among humans, their resident or transient flora, and flora of the environment. The intact skin and the mucous membranes are the most eloquent defenses for humans. Any damage or injury to integument disturbs this bastion and its equilibrium with the bacterial flora. Infection occurs when the bacteria accomplish penetration of the subcutaneous tissue and achieve an acute number. The objective of the surgeon is to deter the invasion of the organism when and wherever feasible, and when contamination develops, to curtail the bacterial levels so that wound healing can emanate unretarded [1].

Consequently, it is necessary to recognize that the equilibrium balance in humans is in a continual state of jeopardy. Not only is quantity crucial, but conjoined virulence factors provide the microbes with an adjunctive armamentarium that magnifies their ability to alter the balance in their favor, thus inflicting grave damage to the host. The encapsulated strain of Staphylococcus aureus “M” is capable of evading phagocytosis by preventing opsonization [2,3]. The slime of Pseudomonas aeruginosa is composed of a glycolipoprotein, which obviates phagocytosis, giving rise to a leukopenia [4]. It has been proven that group A β-hemolytic streptococci is an extremely virulent organism [5]. S pyogenes not only produces hyaluronidase, but streptolysin S is a leukotoxic component that annihil polymorphonuclears by causing the disruption of the neutrophil granule [1]. Group A streptococci also generates streptolysin O, a hemolysin that attacks red blood cells and induces them to lyse [6].

Not all microorganisms have the capability to produce virulent products; however, all microbes have the capability to inaugurate an infection. The concept that the immensity of bacterial numbers was an additional factor that could portent the genesis of infection attained creditability in 1363, when Guy de Chauliac supported the theory that open wounds should be closed in a delayed technique [7]. All of the wounds that he treated by using the delayed technique were of the class that had heavy bacterial contamination such as abscesses, bites, or indolent ulcers. Ambrose Paré determined that cleansing of a wound by debridement would abolish infection [8]. August Nelaton employed sponges that were soaked in alcohol, whereas Lister used carbolic acid, both of which were designed to diminish the incidence of wound infections [9–11].

The theory in which the quantity of bacteria in a wound established a potential for infection was generated by French surgeons during World War I [9,12–14]. If the wounds exceeded 15 hours, the wound was debrided, a culture was taken, irrigation with Dakin’s solution was instituted, and the wound was packed with flavine gauze. The soldier was then evacuated to a rear-echelon hospital with a culture plate affixed to the patient [1,12,13,15]. When the soldier arrived at the base hospital, the plate was inspected. If there were no streptococci on the plate, or if other bacteria were present at a number of less than five colonies, the wound was sutured after the pack was removed. If there was any sign of streptococci or if there were more than five colonies of any
other bacteria, the wound was allowed to remain open and to close by secondary intention. This early wound therapy not only differentiated between species differences in virulence, but concomitantly substantiated the hypothesis that quantitative assessment of the microbial contamination of the wound was invaluable [1,9,12,13].

With the discovery of anti-infectives in the post-World War I era, an emphasis on qualitative bacteriology was emphasized over quantitative assessment. With the succession of resistant bacterial strains, focus was placed on the demand for the development of organism-specific antibiotics [16]. By 1942, preliminary wound cultures had become the state of the art for the care of war wounds [17]. Major concentration was focused on anaerobic organisms in surgical infections [18]. Consequently, the evolution of topical sulfanilamide adumbrated the debridement and therapeutic approach, and became the cure-all for contaminated wounds [19]. Although the therapeutic approach of delayed closure was still widely used, it was performed without concern for the number of bacteria leading to colonization. In 1944, Churchill [20] described a 95% rate of healing with delayed closure, even in those wounds that “show[ed] a profuse and varied flora, both anaerobic and aerobic.”

In the 1950s, the emphasis began to return from qualitative to quantitative estimate for surgical decision making. In 1955, Liedberg et al [21] clarified in rabbits that graft beds infused with greater than 10^5 colony-forming units (CFUs) abolished skin grafts. In 1956, Elek [22] injected staphylococci into normal skin and demonstrated that a mean inoculum inoculation of 7.5 × 10^6 staphylococci was necessary to produce a pustule. He established that the association of a silk suture minified the necessary microbial burden by four logs. Finally, in 1957, Kass [23] correlated the bacterial burden with the presence or absence of symptomatic urinary tract infections based on quantitative assessment. He demonstrated that in 2000 patients with pyelonephritis, 95% had greater than 10^5 CFUs per mL of urine, whereas 100% of symptomatic patients were found to have a similar number of bacteria. Lindsey et al [24] proclaimed in 1959 that 96% of goats that expired from experimental clostridial wound infection had bacterial counts of greater than 10^6 CFUs per mL.

Further observations in the next decade authenticated these data. Krizek and Davis [25] demonstrated that visceral or blood cultures with microbial counts greater than 10^6 or 10^7 CFUs per gram of tissue or per mL of blood climaxed in fatal sepsis. Studies published in 1964, 1965, and 1969 from the U.S. Army Surgical Research Unit [26–28] provided further evidence that confirmed that burn wound infections for a level of bacteria at greater than 10^5 CFUs of tissue was essential. Positive cultures obtained by percutaneous transhepatic cholangiography from congested biliary tracts were peripheral to bile containing greater than 10^5 CFUs per mL [29]. Bendy et al [30] determined that decubitis ulcers would not heal until, quantitatively, bacteria were less than 10^6 CFUs per mL. Noyes et al [31] demonstrated that wound exudates should carry a microbial burden of greater than 10^6 bacterial CFUs per mL to be able to give rise to an invasive infection. These two findings led to the development of the chronic granulating wound in an experimental animal model to question the effectiveness of various topical therapeutic antibacterial creams [32].

Assessment of these data provided evidence that a range of organisms between 10^4 and 10^6 CFUs per mL apparently was necessary to induce an infection. The majority of the data, particularly the more current experimentation, pinpointed the critical bacterial burden at greater than 10^6 CFUs per gram or 10^5 CFUs per mL of body fluid [1,12,33]. The initial technique of soft tissue quantitative bacteriology was designed by Krizek and Davis [33] to assess the microbial burden necessary to cause fatal sepsis. The wound was originally cleansed with alcohol. A biopsy of the tissue was excised, and then weighed under aseptic technique, flamed, diluted at a 1:10 ratio with a bacteriological broth, and homogenized. To obtain the bacterial burden, serial tube dilutions were executed and were subsequently back plated or simultaneously pour plated [1,34,35].

After these early publications, the technique of quantitative wound bacteriology was applied in various surroundings, including acute and chronic wounds, other different wounds, and diverse classes of wound closure. First examined were 50 granulating wounds that were caused by a variety of mediators such as venous stasis ulcers, trauma, or infection. A variety of topical anti-infectives were employed to reduce the bacterial burden. On intermittent days, biopsies were obtained for quantitative evaluation. When the wounds seemed to be “ready” for closure based on clinical criteria, they were skin grafted. Those that were grafted when the wound biopsies were determined to be less than or equal to 10^5 CFUs per gram of tissue had a 94% take; those that had higher counts had less than 20% graft survival [15]. The next study examined decubitis ulcers in patients who were not considered to be candidates for closure by means of a flap. All were treated therapeutically with topical therapy, pressure-alleviating devices, and, if closure did not occur, split-thickness skin grafting.
Wound analysis was usually conducted to coincide with the quantitative assessment. In 14 cases, spontaneous healing occurred only after the microbial burden was sustained at $10^5$ or fewer CFUs per gram of tissue. The remaining 18 patients were skin grafted and responded with a $92\%$ graft survival when wounds contained $10^5$ or fewer CFUs per gram of tissue, with an increase of $80\%$ graft loss for those with elevated levels of bacterial assessment [14,16].

The next tactical maneuver was to utilize the technique in delayed closure. Delayed primary closures were performed in 41 cases of either surgical wounds delayed primarily, or incisional abscesses drained, treated, and later closed. All wounds were assessed quantitatively on intermittent days to include the day of closure. Wounds were treated by a diversity of topical anti-infective agents. Clinical criteria alone were used to determine the time to close the wound. In 10 cases containing greater than $10^5$ CFUs per gram of tissue, closure was unsuccessful, whereas in 29 of 31 cases with less than or equal to $10^5$ CFUs per gram of tissue closure was successfully [16]. Quantitative assessment is now employed currently in numerous disciplines and clinical settings, to dispense information to make clinical decisions for wound treatment and management and to minimize errors in judgment.

Methodology: yesterday versus today

I have used quantitative bacteriology routinely in both experimental and clinical settings [16]. The initial technique is to decontaminate the surface of the wound with an adequate disinfectant and obtain a biopsy. The biopsy should be obtained under aseptic conditions and collected using either a sterile scalpel and forceps, scissors, or a 6-mm biopsy punch. The tissue obtained must be of sufficient size to be diluted 10-fold. Therefore, the minimum weight of the biopsy should be no less than 250 mg or 0.25 g. The tissue sample is aseptically weighed, dipped in alcohol, and flash flamed to remove any exogenous contaminating organisms. The weight of the specimen is multiplied by a factor of 9 to provide an amount of diluent to attain a 1:10 dilution. The tissue sample is then homogenized after being diluted 1:10 with an appropriate biologic broth.

Serial 10-fold dilutions are then prepared up to $10^{-7}$, and are either back plated or pour plated to achieve a precise quantitative count. The tube dilutions and inoculated plates are incubated at $37^\circ C$ for 24 hours. The plates are read at the dilution containing 30 or more colonies per plate. The number of CFUs are then multiplied by that portion of a 1 mL inoculum used to inoculate the plate (ie, 0.5 mL is 1/2 of a milliliter; consequently, the number of colonies should be multiplied by 2 plus the logarithmic dilution and the dilution factor should be taken into consideration). Consequently, 36 colonies on the plate at the $10^4$ dilution is calculated to be 72. Therefore 72 times the $10^4$ dilution equals $7.2 \times 10^5$ CFUs per gram of tissue.

I subsequently designed a STAT method for quantitative appraisal to provide a rapid bacterial quantitative result on surgical and burn wound biopsies. The idea was based on the histologic evaluation of the U.S. Army Institute of Surgical Research. Histologic evaluation correlated when microorganisms were observed in biopsied tissue when bacteria counts were $\geq 10^5$ CFUs per gram of tissue [26,28]. Therefore, the following hypothesis was postulated: If tissue specimens that demonstrated the presence of bacteria under histologic examination it was comparable to bacterial counts greater than $10^5$ equivalent to CFUs per gram of tissue, so when tissues are diluted 1:10, which reveal the existence of one organism, this should be a positive indication of surgical or burn wound infection with counts that exceed greater than $10^5$ CFUs per gram of tissue [16,34].

This priceless procedure can arm the surgeon with the essential information regarding the microbial burden and thus avert wound dehiscence, flap failure, and fatal sepsis all within 15 to 20 minutes postbiopsy [1,16,34,35]. Recently, I have made discrete modifications to the quantitative evaluation assay. The specimen is weighed as described previously; however, it is placed in a sterile homogenizer tube containing 3 mL of sterile saline. If the tissue sample is small, then 2 mL is used instead. As described previously, the sample is then homogenized. After homogenization is complete, 0.1 mL is delivered to the appropriate culture media (ie, McConkey agar, Columbia blood agar, Colistin, Naladixic acid blood agar, or Sabourand-Dextrose agar). Then employing precalibrated loops at 10 $\mu$L and 1 $\mu$L of a known concentration is transferred from the initial dilution to each of the media described above and streaked out as for a urine colony count. The media are incubated at $35^\circ C$ overnight.

The number of organisms present on each plate is calculated according to the following formula:

$$\text{CFUs per gram of tissue} = \frac{\text{number of colonies} \times \text{volume} \times \text{dilution}}{\text{weight of biopsy}}$$

Example: Volume = 3 mL

Weight of biopsy = 0.250
Dilution = 1 mL

Colony count = 9

\[ 9 \times 3 = 108 \times 100 = 1.08 \times 10^5 \text{ CFU per gram} \]

0.250

I have also assayed and compared the outcomes of swab cultures with quantitative appraisal assays. The results showed that although swabs may furnish significant information regarding an infectious process in a wound, the results are often a polymicrobial garden that does not actually identify the etiologic agent. Quantitative appraisal assays most often yield one agent—the actual organism causing the infection—therefore giving the surgeon a more specific and direct therapeutic approach in the treatment of wound infections [33,36,37]. This approach excludes cultivating a polymicrobial garden with a polypharmacy in an endeavor to eliminate the infection [16,36].

Statistics and confidence levels

Although the quantitative assessment of a single biopsy was considered to be greater than 95% accurate, a statistical analysis of one biopsy versus multiple biopsies was not evaluated until 1979. Volenec et al [38] proved that the 95% confidence interval predicated on a single biopsy was \(1.31 \pm \text{the standard deviation}\). Therefore, they concluded that the wound biopsy is a reliable technique for quantitating organisms in a wound.

Although the significance of the burden of organisms that exist is well established, the organism's identity must be determined. Due to the idiosyncrasies of individual species, qualitative microbiology maintains its major role. The combination of both qualitative and quantitative appraisal assays, which are performed under aerobic and anaerobic environments, supplies the utmost information.

It should be emphasized that not all microbes adhere to the number of greater than \(10^5\) CFUs per gram or mL to induce complications. Specifically, the \(\beta\)-hemolytic streptococci continually have proved to be clinically significant at numbers that are much lower [5]. This is largely due to an excretion of specific enzymes that promote its invasion and destruction of host tissues. Currently no other species has been shown to be troublesome at a lower level, and thus, this could be a chance phenomenon. The “gold standard” is to not execute a skin graft or close a wound in the presence of \(\beta\)-hemolytic streptococci, regardless of its numeric assessment [5].

Wound characteristics

The tenets regarding the relationship between the quantitative bacteriology of a wound and the bacterial balance have been readily sanctioned by most surgeons. Repeatedly dealing with contaminated wounds, and demanding quality results, they have realized the importance of diagnosing the precariousness of the equilibrium and the need to restore the bacterial balance during management.

Chronic wounds

Much too frequently, chronic wounds become part of the components of diseases distinguished by all surgeons. The chronicity of these indolent wounds has continually stressed the patience of other clinicians to whom the patient first presented. Radiation ulcers, pressure ulcerations, vascular ulcers, hidradenitis suppurativa, and the cutaneous manifestation of Crohn’s disease are examples of chronic wounds. In contrast to acute potentially contaminated wounds, all chronic wounds contain a tissue level of microbial flora [39,40]. Granulation tissue, which is the dominant characteristic of these wounds, would not be present without bacteria. It is not found underneath the surface of a successfully closed wound. Hence, it has been paragoned to a pyogenic granuloma, and successful closure is founded on one’s expertise to control the microbial flora.

Tissue biopsy cultures have demonstrated that it is essential, in the clinical situation, to identify healthy granulation tissue. Clinically and experimentally favorable closure of a contaminated wound—either by wound edge approximation, delayed primary closure, spontaneous epitheliazation, or employing pedicled flaps or skin grafts—is directly associated with a bacterial level of \(10^5\) or fewer CFUs per gram of tissue.

Pressure ulceration

Chronic pressure ulcerations are a major entity confronting the patient who is paralyzed, debilitated, emaciated, or otherwise bedridden [41]. These ulcers occur habitually over the sacral, ischial, and femoral trochanteric prominences, as well as over other bony prominences such as the elbows, heels, knees, and hips. Once the ulcer has been formed, therapeutic measures must be initiated to avert exacerbation of the process and to provide for eventual healing [39,41,42].

In the chronic ulcerations that are usually found in paraplegic patients, pressure and ischemia have been incriminated in the etiology [42]. Peacock and Van-
Winkle [43] established that the morbid anatomy is not simply that observed when skin is rendered ischemic by devastation of its blood supply. The channel of events commences with the redness of the skin to complete dissolution that occurs quickly, which suggests that a localized infection with its ancillary bacterial enzymes and toxins may play a part of the etiology.

Originally, the role of bacteria in these ulcers was thought to be collateral. There is no question that bacteria do play a quiescent role. Robson and Heggers [16] determined in 32 pressure ulcers that only when the bacterial population was controlled did spontaneous healing occur. Likewise, they established that definitive coverage of the ulcer could be performed only when the bacterial population was decreased. Bendy et al [30] discovered a comparable relationship between the bacterial level in these ulcers and their rate of healing. Along with this retardation in healing, it is premised that bacteria play an early, and perchance etiologic, role [39,41,42,44–46].

In 1942, Groth [47] performed experiments in which he determined that rabbits who experienced pressure necrosis behaved differently when infected than did control animals. He also found that organisms injected into animals were centralized in areas of compression. If the bacteria were staphylococci or streptococci, they accounted for liquefaction. Coincidentally, he determined that the localization could be prevented by pretreating the rabbits with antibiotics. Husain [48] demonstrated that brief periods of local pressure intensified the susceptibility of tissue to local infection. He injected streptococci intravenously and succeeded this by localized pressure to the leg. Biopsies of the tissue determined that the streptococci were predominant in the area of pressure. Robson [42,45] showed that wounds created in controlled pressure areas permit a 100-fold greater microbial proliferation than do wounds in areas not exposed to pressure.

These observances of localization of microbes in areas of pressure can be justified in part by studies implemented by Miles and Niven [49], who determined that locally injected epinephrine temporarily diminished blood flow, accordingly curtailing the number of phagocytes to the infected area. Similarly, Miles [50] showed the effect of tissue ischemia on microbial growth. He established that the augmentation of staphylococcal and clostridial lesions in conditions of shock were enough to diminish blood pressure in the minor arteries of the skin underneath a certain number, with the distribution of microbial augmentation being directly allied to the development of ischemia.

Bacteria can alter the outcome in distinct ways in the patient whose local area has been transformed by pressure, denervation, or ischemia [39,41,42,45,46]. “Primary lodgment” could be a mechanism based on some breach of the integument, as recounted by Miles and Niven [49]. The rupture could be mechanical, or could be a modification in the chemical or physical qualities of the skin generated by denervation or ischemia. Chemical alteration in denervated skin could be caused by an edematous process. Exton-Smith [51] has demonstrated this occurrence in denervated tissue. Edema fluid or plasma is known to neutralize the normal fatty acids of the lipids of the integument, which Ricketts et al [52] had shown to contain streptococcicidal properties. Accordingly, edematous denervated skin might allow streptococcal invasion and original lodgement. Denervation could allow for an enhancement in microbial proliferation. In our laboratories, wounds generated in denervated extremities and inoculated with exact amount of bacteria accelerated proliferation in soft tissue matched with identical wounds that were innervated [41,42,44,45].

Microbes may also interact in the pathophysiology of pressure sores by their ability to insulate themselves in an organ or area of the body with a flawed local resistance, as presented earlier. Virulence factors play a major role in enhancing bacterial proliferation. In this patient population, the urinary tract is consistently the endogenous source of infection.

Because current indications suggest that these organisms may be important participants in these chronic ulcerations—not only after the ulcer occurs, but also prior to its formation—patients inclined to develop ulcers require surveillance and, when needed, therapy. Bacterial surveillance of intact skin is more formidable than that of ulcerated wounds. Surface cultures tend to be deceiving, and quantitative assessment by biopsy cultures of undamaged skin is inappropriate.

An added consequence with these patients is a flawed host defense response initiated by edema occurring in the compressed soft tissue among a firm surface and an underlying bony prominence. Therefore, edema could neutralize the host defenses against β-hemolytic streptococci, which could gain primary lodgement in edematous tissue [5,52]. Areas of incipient breakdown and ulceration appear to be clinically akin to cellulitis. Techniques to prevent the local edema and the use of systemic penicillin are warranted [39,41,42]. Diminishing the probability for the locality of pressure to act as a “locus minoris resistentiae” for endogenous infection is feasible by eliminating or controlling distant loci of infection such as the urinary tract [39,41,42].
Methods to reduce microbial levels

As opposed to the possibility of a contaminated initial ulcer area, all lesions that occur from breakdown and ulceration contain a number of specific organisms. A tissue biopsy of the lesion should be surveyed scrupulously by qualitative and quantitative assays for the existence of both aerobic and anaerobic bacteria. This allows the clinician to envision which of the multiple pathogens may account for invasion of the wound and have achieved significant tissue levels—which is important when ulcers subsist in close proximity to the rectum in individuals who may be incontinent. Organisms that are engulfing the lesion may never accomplish lodgement and may be of little clinical importance in preserving control of the soft tissue infection [39,41,42,45].

The objective of bacterial balance in the ulcerated wound is to reduce the microbial level below $10^5$ CFUs per gram of tissue. All of the procedures for diminishing bacteria to appropriate levels should be used. There is no alternative to sharp debridement; however, one must be cautious not to create a septicemia during the debridement. Glenchur et al [53] have demonstrated that transient bacteremia can occur as much as 60% of the time subsequent to debridement of decubitis ulcers.

A curtailed course of antibiotics may be considered for the peridebridement period. The pulsating jet lavage has been shown to be an adjunct to sharp debridement. In the experimental model it removes tremendously more bacteria than do the classic types of irrigation [41,54]. Consequently, granulation tissue should be continually treated until the organisms are numerically below $10^5$ CFUs per gram of tissue, and the elimination of streptococci. This can be accomplished best by topical antibacterials that can penetrate the subdermal plexus of the wound and have a profound effect on the microbial growth [41,42,45].

In a prospective randomized study of 45 pressure ulcerations, Kucan et al [41] established that silver sulfadiazine was an efficacious, safe, rapid, and effective way to reduce the bacterial load. Granulation tissue was converted into bacterial balance with a bacterial count of $10^5$ or fewer organisms per gram of tissue in all cases treated with silver sulfadiazine. Among the other treatment regimens, only 78.6% of cases treated with saline and 63.6% of cases treated with povidone–iodine solution were brought into balance (Fig. 1). Systemic antibiotics do not attain adequate tissue levels in chronic granulation tissue, and have been experimentally determined to have no effect on the bacterial level in granulating wounds [55].

The wound can be closed successfully when the colony count is equal to $10^5$ or less per gram of tissue, provided no streptococci are present. Technical procedures have classically encompassed any one of these techniques: abrogation of the ulcer, excision of the underlying bony prominences and periosteum, coverage of the bone stump with juxtaposed muscle or fascia, and mobilization of a large composite soft tissue flap [41,42,44,56,57].
Radiation ulcers

Therapeutic radiotherapy can cause a chronic granulating wound. Radiation causes incessant and lasting damage to soft tissue, and acutely, causes erythema and swelling, succeeded by flaking, blistering, bleeding. Eventually, ulceration of the integument occurs [41,42,44,58]. In lieu of complete ischemic necrosis of foundational tissue, a progressive, redundant, obliterator endarteritis evolves followed by chronic vasculitis a classic indication of radiation injury. The most severe alternation is progressive tissue ischemia, secondary infection, and necrosis. Infection is not primarily a major problem. In the more grave injury, skin breakdown commences in the initial few weeks. Open wounds, secondary infection, and ischemia contribute to trigger a cycle of ulceration, infection necrosis, and the formation of further ulcers, eventually leading to gangrene. Infection appears to be the ascendant factor in precipitating this cycle. The resulting ischemic wound is sequestered from the peripheral circulation and, therefore, from systemic antimicrobials. Consequently, the wound must be treated as a thermal burn with appropriate topical antimicrobial agents.

Leg ulcers

Another chronic wound that surgeons usually treat is the ulcerated wound on the lower extremity. The universal term “leg ulcer” has characterized these lesions as more laborious to treat. The cause of the ulcer—whether largely due to blood dyscrasias, venous hypertension, trauma, ischemia, or diabetes mellitus—must be resolved [41,42,44,46], allowing for competent and timely therapeutic approaches.

Timely management of leg ulcers encompasses controlled measures carried out as preoperative, operative, and postoperative procedures. Without specific regard to each of these, it is debatable whether one can achieve successful treatment of any leg ulcer. Management of the soft tissue infection is instituted during the conservative period. On admission, biopsies cultures for qualitative and quantitative bacterial assessment are performed. Topical antimicrobials and biologic dressings are employed as for any chronic granulating wound. Additionally, reliable techniques are imperative, depending on the cause of the lesion [12,35,39,41,44,46].

Venous stasis ulcers are prone to streptococcal irrupt because of their coalesced edema. Consequently, systemic penicillin may be administered on admission, and elevation of the lower extremities is recommended to abrogate the edema. The wound is rapidly brought into balance with topical therapy, and surgical management can be attempted when the count is equal to $10^5$ or fewer bacteria per gram of tissue and streptococci are not present (Figs. 2, 3). Timely long-term therapy requires amending the underlying venous hypertension, and excising the fibrotic, lymphatic decimated tissue, ultimately closing with a skin graft. Postoperatively, the skin graft is safe guarded by long-term protection with pressure-gradient stockings to prevent recurrence of venous hypertension or edema [39,41,42,44].

Diabetic foot ulcers

Ischemic ulcers of whatever cause have minimal blood supply at best and seldom respond to systemic antimicrobials. Eventualities of ischemia induce tissue anoxia and poor delivery of phagocytes to the wound, both of which intervene with the control of the infection. Although topical antimicrobials evidently are suggested in these ulcers, balance may not be attained prior to excision of the ulcer bed [39,41,46]. Hence, prior to any operative, noninvasive vascular
studies, or when considered appropriate, an arteriography must be performed. If a correctable vascular ulcer is present, care and treatment of the ulcer is made simpler. Patients with ischemic lesions secondary to diminished blood supply may be on systemic steroids. Topical application of vitamin A to the ulcer would annul the untoward consequences of the steroid on the granulation tissue. Vitamin A also appears to have a particular effect on averting the growth of *P aeruginosa*, an opportunistic organism that attains raised levels in these lesions [2]. Once the decision is made to graft an ischemic ulcer, it is presumably judicious to place the graft on the granulation bed, provided the wound is in bacterial balance, and to excise the lesion if the bacterial count cannot be diminished to adequate numbers. The graft is best applied without sutures to avert further necrosis of the surrounding ischemic tissue. The graft is protected for approximately 4 months with special pressure-gradient stockings. Concomitantly, the patient must be instructed on the care of the ischemic foot [41,44,46].

Lesions in the diabetic patient are amplified in localities of neuropathy, which can cause a painless ulcer that often goes untreated until infection occurs [29,40]. Infections in the feet of patients with diabetes mellitus outside of these sequelae are frequently identical to infections in normal feet. Whereas infection may change diabetic control, the presence of diabetes mellitus itself does not modify the response of local tissue to trauma and infection, except in the presence of a neuropathy or vascular deficiency [40,43,47,60]. The absence of pulses would suggest arteriosclerosis, and if infection or gangrene is present, arteriography is recommended.

The presence of amendable vascular lesion must be managed in the identical mode as the nondiabetic patient. Even if no rectifiable lesion is distinguished, a major amputation is not necessarily imperative. Robson and Edstrom [46] reported on a conservative approach that was amplified and satisfactorily applied on a large series of patients. The technique recommended was to eliminate the apparently necrotic or infected tissue and conservatively manage the wound. The canons of quantitative bacteriology, the use of topical antimicrobials, and biologic dressings coupled with judicious debridement and drainage can salvage the ulcerated infected lower extremity that was previously considered adequate for amputation in these patients. When sufficient bacterial control has been accomplished—as measured by the diagnostic precision of quantitative bacteriology performed on a tissue biopsy—the ulcer bed, including the normal-appearing margin of the wound, must be totally resected and replaced by adequate soft tissue [12,16,40,44,46,59].

**Crohn’s disease and perineal hidradenitis**

On the occasion of definitive surgery, systemic prophylactic antibiotics may be recommended. The goal is not to diminish the bacterial flora in the granulating wound itself, but to dispense a bastion of defense for the normal tissue that will be directly challenged by bacterial contamination. If bone is denuded, protracted use of systemic antimicrobial agents is suggested to gain sufficient levels of antibiotics in the bone [41,46].

There are only two additional chronic wounds that have benefited from quantitative bacteriology to facilitate care: those following radical resection of perineal hidradenitis suppurativa, and the granulating ulcerated wound that occurs in Crohn’s disease. Ariyan and Krizek [60] suggested that perineal hidradenitis suppurativa be treated by militant extensive excision and allowed to heal by secondary intention. Their approach was to treat the granulating wounds with saline soaks, and they noted that the wounds healed by
contraction, rather than by epithelization. Because bacterial counts of greater than $10^5$ CFUs retard wound contraction, Ariyan and Krizek [60] altered their procedure by using water-soluble topical antibacterial creams on the wounds. This sustains a microbial balance and allows for contraction to emanate without retardation. Similarly, cutaneous lesions of Crohn’s disease can present with a chronic non-healing wound of the perineum. These wounds have an exorbitant amount of bacteria in the tissue, but become readily manageable when treated with topical antibacterials. Once the bacterial level is reduced to $10^5$ or fewer bacteria per gram, the wounds will either heal instinctively or can be closed with either a skin graft or flap. Prior to this comprehension, the authors [60] had observed that wounds of this type lingered open for years in a chronic indolent condition.

Carcinomas of the head and neck

Indolent granulating ulcers repeatedly occur in patients with head and neck cancer cases who have disregarded medical advice. There is a daily drastic alteration of the bacterial population of the salivary bacteria in each individual. Counts of $9 \times 10^7$ CFUs are observed in the early morning after fasting, then reduced by 10-fold ($1 \times 10^7$) after a saline mouthwash, and elevated again to $5 \times 10^7$ by noon [11]. Meals throughout the day can again alter the counts, but they return to the same peak after the overnight fast. Salivary bacterial counts can be modified by therapeutic measures such as antibiotics, dental extractions, and radiation.

Surgical measures for head and neck cancer are in continual risk for disrupting the bacterial balance: the host in favor of the bacteria. Ariyan [61] stated that in these cases, surgery should be viewed as “dirty” due to the extremely virulent nature of the bacterial flora in the oral cavity. Although the incidence of infection of comparable wounds in other areas of the body is about 16%, the patient with head and neck cancer is subject to the impact of other factors that increase the potential of complications to 65% [62]. The most common complication is infection, which is also the major contributor to the necrosis of flaps, the induction of a fistulae, and the vulnerability and schism of carotid arteries [61].

It is evident that the wounds collateral to composite resections of head and neck cancer are bathed with copious buccal secretions with suffocating bacterial numbers in the millions. These counts during surgery or in the wound washings after surgery are biologically irrelevant, provided that the organisms are unable to achieve tissue lodgement and multiply. Even if the organisms encroach into the tissue, no infection will occur unless they multiply to levels exceeding $10^5$ CFUs per gram of tissue [12,16,35,41].

It is evident that the surgeon is faced with a wide diversity of contaminated or potentially contaminated wounds. The canons of quantitative bacteriology are particularly beneficial in these instances and have been demonstrated to be of immense value.

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