American Diabetes Association 60th Scientific Sessions, 2000

The Diabetic Foot

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This is the seventh in a continuing series of articles on the American Diabetes Association (ADA) 60th Scientific Sessions held in San Antonio, TX, in June 2000. It covers topics related to the diabetic foot.

Foot Ulcers
Gayle E. Reiber, Seattle, WA, gave the Roger Pecoraro Lecture on the economics of lower-limb amputations in diabetes. A number of clinicians over recent decades have implemented programs leading to substantial decreases in amputations among participants in the U.S. and Europe. However, the target of a 40% decrease in amputation rates, based on these studies and set more than a decade ago, has not been met, and rates have actually increased. With the aging of the populations of the U.S. and Europe and the greater prevalence of diabetes, amputation rates and costs may increase further.

Using the Veterans Administration system and Medicare data sets in the U.S. and the Cost of Diabetes in Europe, Type 2 (CODE-2) data set, Reiber presented trends for foot ulcers. There are ~300,000 hospitalizations annually for foot cellulitis, ulcers, and deep infections among individuals with diabetes and 400,000 hospitalizations among individuals without diabetes in the U.S. Amputation rates are increasing among patients with diabetes, while decreasing among those without diabetes. In 1999, there were ~92,000 amputations among those with and 42,000 among those without diabetes.

There are tremendous variations among regions in the U.S. in the frequency of amputations and footwear prescriptions. However, <1% of Medicare patients in the U.S. obtained therapeutic footwear in 1995. Low-level amputations comprise 53% of the total, and this fraction has increased over recent years, suggesting improved limb preservation. Direct costs in the U.S. are ~$17,000 for an episode of foot infection and $35,000 for a hospitalization leading to amputation. Reiber noted that reimbursement rates are well below these charges. Revascularization rates have tripled over the past decade, perhaps partially driven by the higher reimbursement for vascular surgery than for amputation. In the CODE-2 study, ulcers and amputation costs show a great deal of variation by country in Europe, although costs are consistently below those in the U.S.

I. Kelman Cohen of the Medical College of Virginia, Norfolk, VA, gave an overview of the diabetic wound and the role of new therapies, growth factors, skin substitutes, and antibiotics, speaking as a plastic surgeon involved in wound healing research. “My take-home message,” he said, “[is that] with proper patient skills new technologies are rarely needed,” recalling Osler’s dictum that “wounds require surgeons and not the fool of a physician.” Most wounds require excision and debridement. Cohen pointed out that enzymatic debridement has never been shown to be effective. Noting the increasing prevalence of diabetes, he pointed out that “the diabetic wound is becoming a greater and greater problem.” Once amputation is needed, he noted, “We don’t do so much better than they did in 1902.”

Fifteen percent of patients with diabetes develop foot ulcers, and 6% of individuals with diabetes require hospitalization for these, at “astronomical” cost. Further, it is necessary to correct the foot deformities rather than just get the ulcer to heal. This may require as little an intervention as an Achilles tendon lengthening. Similarly, vascular evaluation is required for these patients to promote wound healing. “One can keep the wound healed with the proper mechanics,” Cohen pointed out, but ongoing patient involvement is crucial, with education and efforts to involve patients in their own care.

Discussing the role of growth factors in diabetic ulcers, Cohen noted that platelet-derived growth factor (PDGF) is produced in wounds at the time of injury by many cellular elements in addition to platelets and that there are many other cytokines that act along with it and may be found to have a therapeutic role. It is chemotactic, stimulating proliferation of fibroblasts and smooth muscle cells, production of collagen, and angiogenesis. It is only effective after full debridement. He pointed out that wounds produce elastase, collagenase, and other proteases, which “totally wipe out” cytokines as well as their receptors, so topical application of growth factor may be of limited benefit. “One has to debride the ulcer well,” Cohen stated, totally excising bacterial products, including proteases, to make a clean wound; and in certain cases, grafts, local flaps, or free-tissue transfers with microvascular surgery may be needed to salvage the extremity. PDGF is effective, although Cohen suggested his reservations regarding the health-economic data that has been cited to suggest it is worthwhile. He noted that in the reported study the site with the highest debridement rate had the highest healing rate and the site with the lowest debridement rate had the lowest healing rate, showing the importance of this local treatment. “The Achilles heel of [this approach] is wound protease,” he pointed out, but with appropriate de-
briement, it produces up to 80% improvement in wound healing.

As far as the use of antibiotics, Cohen noted that the bacterial count “gives us the definitive answer,” because all wounds are contaminated but only wounds with $>10^5$ colonies/ml should be considered infected. In general, topical antibiotics are ineffective, and systemic antibiotics should only be administered with signs of local or systemic infection. He pointed out that osteomyelitis probably responds better to excision of infected bone than to antibiotics. Cohen pointed out the importance of further study of a variety of systemic and local antibiotic approaches in improving wound healing.

A variety of “skin substitutes” are in development, with some evidence that skin graft (Apligraf, Novartis) may be useful. These products significantly increase the rate of wound healing, but as is true of growth factors, wound proteases can destroy them, and “we do not have good cost evidence.” In concluding, Cohen stated, “Diabetologists should not attempt to manage a surgical problem.” He suggested a concern that skin substitutes will prove ineffective for diabetic ulcers, although having potential in other illnesses. He expressed greater optimism regarding cytokines such as PDGF in improving wound healing.

Aristidis Veves, Boston, MA, contributed to the discussion of the potential roles of bioengineered skin, skin substitutes, and skin equivalents in the healing of diabetic foot wounds. These products create functional analogs of normal skin as they are degraded. Dermograft is produced by 3-dimensional cultivation of human fibroblasts that secrete cytokines and growth factors. Studies in 1996 showed wound healing when applied weekly for up to 8 weeks. In a subsequent large clinical trial of patients with diabetes who had a full-thickness ulcer $>1$ cm in size, without evidence of infection and with an ankle-brachial systolic pressure ratio $>0.7$, 126 and 109 patients were randomized to control or Dermograft, respectively, with assessment over 8 months. All groups underwent surgical debridement and avoided bearing weight on the affected limb. On average, wounds had been present for 10 months before the trial, with mean baseline area $3 \text{ cm}^2$. At the conclusion of the trial, healing was seen in 32% vs. 38% of patients. The product was reformulated during the trial, however, with comparison of the 67 patients who received the less active form with the 37 who received the revised product suggesting more rapid healing. A new trial is currently being conducted with the new product.

Graftskin is a bilayer of epidermal cells and fibroblasts that is histologically similar to normal skin and produces growth factors similar to those produced by normal skin. In a trial similar to the Dermograft trial of patients with noninfected, nonischemic chronic ulcers, with 6 months’ total follow-up, extensive debridement, and off-loading, 112 and 96 patients were treated with graft-skin or control. The former group had better healing beginning after the first week, with 56 vs. 38% showing complete healing in a mean of 65 vs. 90 days. Infection, cellulitis, and other complications were similar, but osteomyelitis and amputation rates were significantly lower with active treatment. At Veves’ center, healing was seen in 75 vs. 40% of patients, suggesting “a learning curve with this product,” such that it may be particularly useful in large centers that gain experience with the approach. The most difficult issue, Veves suggested, is that of when to use this approach, as “these are expensive products and you should save them for difficult-to-heal patients.” Using a calculation of the rate of decrease in the circumference of the ulcers, the healing rate was 0.11 vs. 0.05 cm$^2$/week in control-group patients who did heal versus those who did not heal, suggesting that such measurement may be useful in determining which patients should receive this treatment.

The normal healing process involves vasodilation, secretion of PDGF, and production of collagen and other factors to close the wound, after which production of cytokines and growth factors initiate the proliferation phase with production of new vessels, leading to production of a scar. Lack of sensation, inadequate infection healing, and abnormalities of the macro- and microcirculation lead to the worse outcome of diabetic wounds. Thus, the use of skin substitutes may provide platforms for wound healing that prove clinically beneficial. Asked about the various other approaches that have been advocated, such as total-contact casting, Veves replied that there is no single and agreed-upon standard of care.

T. Jeff Wieman, Louisville, KY, discussed cytokine trials and the clinical use of PDGF. Studies of this treatment over the past decade have included ~1,000 patients. In addition to debridement, maintenance of a healthy wound environment—“neither desiccated nor macerated”—is necessary. The major factors in determining wound healing are wound size and the completeness of debridement in removing granulation tissue. Large ulcers usually require a skin graft or flap of some sort to achieve healing. There are few adverse responses to PDGF. The drug is rather expensive, costing $50–200 more per patient than standard care, but over longer follow-up, patients in such “standard care” groups have costs close to $1,000 more than those of patients treated with becaplermin (Regranex; Ortho McNeil). Wieman suggested use of digital photography to determine the rate of wound closure, with treatment in patients who fail to show a reasonable rate of closure. Asked whether there “is any evidence that patients who are using this product are doing better,” he stated that he feels this is the case at his center, but is not aware of such information. He suggested that it is appropriate in ~15% of patients.

Benjamin A. Lipsky, Seattle, WA, addressed the role of topical antibiotics in “managing the bacterial burden.” He pointed out that neuropathy plays the most important role in foot wound development—with ischemia and hyperglycemia itself also affecting wound healing—but that the final common pathway to amputation is infection. Mildly or moderately infected wounds comprise the majority of foot infections in patients with diabetes. The underlying microbiology of these infections includes organisms present on skin and rarely pathogens (such as diphtheroids), organisms present on skin and often pathogens (such as Staphylococcus aureus), and organisms that are always pathogens. If an organism is isolated in pure culture, if it is repeatedly isolated, if it is isolated from deep tissue, and if there is an inflammatory response and purulent secretion, the wound can be considered clinically infected. This approach, however, does not allow complete assessment of all patients, because, for example, erythema is often decreased by ischemia or increased by neuropathy, and bone changes similar to those of osteomyelitis may be caused by neuropathy.

The use of quantitative bacterial...
count is important as low-level bacterial contamination may actually accelerate wound healing, whereas levels $>10^2$ bacteria/g tissue appear to impede healing by producing proteases, causing migration of polymorphonuclear cells to the wound and predisposing to systemic spread. S. aureus is the most important pathogen, with gram-negative infections common and anaerobes also playing a role. Similar bacteria are found in chronic wounds that are not clinically infected, often despite prior antibiotic treatment.

A case can be made for the use of antibiotics to reduce the bacterial burden in diabetic foot wounds, particularly in view of the adverse effects of bacteria and the difficulty in distinguishing between colonized and infected wounds. Some, but not all, studies have indeed shown improved healing even of clinically noninfected wounds with this treatment. However, such treatment has not been convincingly shown to decrease bacterial isolates, particularly of gram-positive bacteria, in wound cultures. Antibiotics are expensive, may cause toxicity, and can cause antibiotic resistance. In the clinically infected diabetic foot wound, oral antibiotics are usually effective. In the U.S. in 1998, antibiotics, particularly cephalosporins and quinolones, were prescribed for 60% of visits with foot wounds in patients with diabetes.

Topical antibiotics are also frequently used, with potential advantages including high local concentration, lack of systemic toxicity, and increasing patient attention to the foot, including the need for more frequent dressing changes. Antiseptic agents such as hydrogen peroxide and chlorhexidine are safe for intact skin but toxic to human fibroblasts and other cell types, so are no longer used for diabetic foot wounds. Iodide-based agents are toxic and should not be used. Topical antibiotics include euterpicin (which is active against gram-positive bacteria), neomycin (which is effective against gram-negative bacteria but to which resistance is common), polymyxin (effective against gram-negative bacteria and with little resistance), and bacitracin (effective against both gram-positive and gram-negative bacteria). None of these, however, have been shown effective. In a study of 885 patients randomized to oral ofloxacin versus pexiganan cream, the drugs had similar efficacy. The Food and Drug Administration has advised against approval pending a placebo-controlled trial, although Lipsky pointed out that ethical concerns might preclude allowing patients to participate in such a study. Other approaches being developed are the implantation of antibiotic-impregnated beads or bovine collagen sponges with antibiotics into infected wounds. Topical antibiotics may prove effective in patients with open wounds and should be further explored.

Mechanics of Ulcer Healing and Prevention
Peter R. Cavanagh, University Park, PA, discussed “the mechanics of healing and staying healed” in the diabetic foot, noting that typical barefoot maximal pressures in the normal foot during walking are less than half of those seen with foot deformity, where these pressures may be exerted on a single abnormal area. “Healing,” he suggested, “is really the easy part—keeping healed is the difficult part.” He advocated greater use of the total-contact cast in patients without ischemia or infection. Total-contact casting is applied with a minimum of padding, unlike the usual orthopedic cast, after the area of the lesion is covered with soft foam. Potential complications include worsening of infection or development of additional ulceration, so technique is crucial. A recent meta-analysis of 526 ulcers in 493 patients reported 88% healing in a mean time of 43 days, although all studies but one used historical controls.

Cavanagh asked, “Why does a total-contact cast work so well?” The cast walls have been shown to carry $\sim 30\%$ of the load. Furthermore, because of the way in which the cast is applied, it protects the wound. Other approaches include “half shoes,” which confine weight-bearing to the heel or the forefoot, and short-leg braces, which are widely used even without data on healing efficacy, although peak pressure decreases by 60–70%. Felted foam dressings and “Scotch-cast boots” also are used, with excavation in the region of the ulcer, again without definite benefit in randomized controlled trials. None of these approaches are intended to allow the patient to resume an active lifestyle, so the best treatment may be bed rest (1).

After an ulcer heals, however, recurrence rates at may be as high as 70% at 3 years. The mechanical goal of treatment after ulcer healing is to reduce pressures so that the cumulative load is below that at which tissue damage occurs. Barefoot peak pressures $>700$ kilopascals (kP) (normal pressures do not exceed 500 kP) predict ulcer recurrence with moderate sensitivity, although some patients develop ulcers with pressure levels as low as 200 kP. Use of protective shoes reduces peak pressures to $\sim 200$ kP, suggesting good potential for prevention. Cavanagh commented that he believed that “therapeutic footwear is the most important feature of a recurrence program” but pointed out that this has not yet been proven. Indeed, a prescription for therapeutic footwear is actually a risk factor for ulcer development, presumably because clinicians have identified at-risk patients for such treatment (2). Part of the problem is that not all therapeutic shoes given in the community are effective. Indeed, the Medicare demonstration project designed to study therapeutic shoes for patients with diabetes failed to show benefit; nevertheless, Medicare has agreed to pay for one pair of shoes and three fitted inserts annually for patients with diabetes. Shoes should reduce areas of excessive pressure and have sufficient room over the toe and instep. We do not, however, have a way of assessing whether a given pair of shoes is beneficial. Indeed, “many ulcers are caused by shoes,” particularly on the sides and dorsum of the foot. What is needed includes footwear for use when getting out of bed during the night, as well as the “definitive” shoes for use during the day. The shower is another location for injury to the foot, with a hard surface that is particularly likely to cause damage, and footwear should be used there as well. Shoe covers for rain, golf shoes, horseback-riding shoes, and many other special-purpose shoes should be considered for appropriate patients.

Cavanagh noted that “load distribution is the most important” function of footwear. This can be addressed by the use of rigid-rocker shoes, patellar braces, and a variety of other special measures. At least 75% of neuropathic patients have much wider feet than normal, with 50% not adequately fitted, even with extra-wide conventional shoes, another factor requiring special attention. Insoles designed to accommodate rather than to correct foot deformities are crucial. The mechanical properties of materials used for inserts are important, with resilient
materials such as Plastozote allowing longer-lasting devices. Some soft materials only last a few weeks, and this must be taken into account in patient instructions.

How should insoles be designed? A “good place to transfer load to,” Cavanagh suggested, is the medial longitudinal arch, although not all studies show benefit of such approaches. Another approach is the use of a metatarsal bar, which is placed under the insole, transferring load from the heads to the shafts of the metatarsals. “Plugs” of soft material can also be used to redistribute load. A related approach is the use of injections of small amounts of silicone around the areas of the metatarsal heads to decrease local pressures. Outsole modification is another approach, and adding rigid “rocker” or “roller” bars to the sole of the shoe can reduce pressures by half. We do not know the optimal location for these appliances or how best to adjust these for individual patients. Making pressure measurements for optimized shoe insole design requires special equipment and is quite time consuming, so it may not be practical as a general measure. Patients must be told how to break in their new shoes by wearing them for 1 h for a few days and then by gradually increasing this time, and they should be shown how to walk with the shoes, typically with very short strides, so that the metatarsal-phalangeal joints are not extended during the stride.

Surgical approaches can be used to alter the structure of the foot, and a role in prophylaxis has been suggested. A well-performed metatarsal head resection can be effective in preventing lesions (3), and dorsal osteotomies have been proposed (4). However, these may increase the risk of subsequent Charcot neuroarthropathy. Lengthening of the Achilles tendon is another procedure used for reducing pressures in the forefoot.

A final issue is provider knowledge. A recent U.K. health district survey did not find a single primary care provider who mentioned that load relief was important in the treatment of ulcers (3). “Where,” Cavanagh asked, “is the disconnect?” Most physicians do not remove callus, another widely accepted approach. “We must not,” he stated, “get so enamored with new ways to treat ulcers that we forget the fundamental truth that putting people to bed cures ulcers.”

Lower-Extremity Vascular Disease
Cameron Akbari, Boston, MA, discussed the approach to the patient with lower-extremity vascular disease, stressing that even minor degrees of nonocclusive microcirculatory dysfunction and large vessel disease are important in the biologically compromised diabetic foot. Endothelial dysfunction, free radical production, advanced glycation end products, arteriovenous shunting, capillary basement membrane thickening, and a variety of other pathways further this biologic compromise. Furthermore, typical symptoms of ischemia, such as intermittent claudication, may be less prevalent in diabetic patients because of neuropathy. Distal ulcers are more likely ischemic, and a decreased degree of bleeding with debridement is a sign of arterial insufficiency. The most important physical finding is the absence of palpable pulses. The Doppler-derived arterial pressure measurement is used to derive the ankle-brachial ratio, which is normally >1.1 but decreases to 0.5–0.8 with single-segment occlusive disease and to <0.5 with multiple-segment disease. Medial calcification of arteries may, however, lead to noncompressible arteries falsely elevating the ankle-brachial ratio. Toe pressure measurements may be useful, but there are number of technical factors making this difficult. Doppler waveform analysis, showing loss of the normal triphasic pattern, is useful but is not quantifiable. Pulse volume analysis, which is not affected by medial calcification, also has disadvantages, including the effects of obesity and edema. Duplex plethysmography allows direct visualization of areas of turbulent flow, but it is time-consuming and may not give physiological information. Measurement of the partial pressure of oxygen diffusing through the skin is problematic in view of the higher levels in patients with neuropathy. Thus, despite the availability of multiple noninvasive tests, clinical evaluation is crucial.

Radiological evaluation was discussed by George Hartnell, Springfield, MA, who urged that interventional radiologists rather than cardiologists and vascular surgeons perform these studies. In a study of 1,409 patients, elevations in baseline creatinine were common, but renal failure occurred in only 1.5% of patients. Therefore, if appropriate hydration is found, one should consider the level of adverse consequence of these studies acceptable. Although computerized tomography gives useful information, it appears less valuable in assessing circulation in the lower extremities than in assessing circulation in other regions and does not allow measurement of pressure gradients. Magnetic resonance angiography does give information about peripheral vessels, but is often not as useful as standard contrast arteriography. An additional technique involves using carbon dioxide to enhance images.

Balloon angioplasty is the most widely available interventional technique, and laser angioplasty and newer mechanical approaches have not been shown to be more effective. Thrombolysis and stenting are useful additional approaches, which may increase success rates from >95 to close to 100%. The problem is restenosis, with 5-year patency rates ~25%. Hartnell stressed that “there is no evidence that routine use of stents improves results,” and he suggested that these only be used in selected cases. Akbari stressed the need to do careful evaluation of potential for distal arterial bypass graft surgery before making decisions about angioplasty. In >900 patients, 50–60% of bypass grafts were performed to vessels distal to the popliteal artery, with 5-year patency rates of almost 76 and 87% limb salvage at 5 years.

The Charcot Foot
At a symposium on the Charcot foot, Lee Sanders, Lebanon, PA, gave a historical introduction illustrated with a dazzling set of images from postal stamps. He pointed out the importance of Jean-Martin Charcot’s clinical-anatomic correlation studies during the latter half of the nineteenth century. “How often,” Charcot asked, “have I seen persons not familiar with this arthropathy misunderstand its real nature?” Charcot realized that “behind the disease of the joint was a disease far more important in character, and which in reality dominated the situation.” He described the classic foot deformity of tabes dorsalis as follows: “The foot deformity relates to an erosion of the tarsal bones, with a resultant flat foot, and especially marked protrusions of the medial tarsal components.” These comments remain pertinent as we enter the 21st century.

Michael Edmonds, London, U.K., reviewed the current staging concept,
which consists of an initial developmental/destructive stage, followed by a stage of coalescence/healing, and a final stage during which reconstruction may be required. Some patients exhibit an initial acute stage of rapid destruction and inflammation. Most patients show full evolution of the syndrome over a 6-month period, with a 1- to 12-month range. X-rays are often normal initially, but bone scans show increased uptake. Clinical causes include somatic and autonomic neuropathy, states of severe osteoporosis, and (pertinent in a number of individuals with diabetes) post-renal transplant and postrevascularization states, with immunosuppressive agents contributing to bone loss in the former and both associated with prolonged immobilization. Autonomic symptoms such as diarrhea, gustatory sweating, and orthostatic hypotension are seen in two-thirds of patients, with an increase in venous pressure present because of arteriovenous shunting. The hyperperfusion syndrome is common, and there is a decrease in distal lower-extremity bone mineral density. This process of neuropathic hyperperfusion leading to bone loss may contribute to the pathogenesis of fracture with relatively mild trauma, which is often difficult to explain based on peripheral sensory neuropathy alone. In addition, there is an abnormality of bone resorption in response to trauma, with increased osteoclastic activity.

Edmonds noted that “many patients have neuropathy and many are susceptible to minor trauma” and asked, “Can we identify patients who will develop Charcot?” In a comparison of eight patients with diabetes who did not develop Charcot after trauma with five who did, 80% of the latter group had an initial erythematous area on the dorsum of the foot, suggesting an abnormal vascular reflex (6). Bone markers of osteoclast activity at presentation showed an increase in those who developed Charcot lesions, although osteoblastic activity was similar, suggesting uncoupling of the two processes.

There may be “trophic nerves” acting to provide autonomic nervous system control of bone remodeling, perhaps involving the same nerve fibers that mediate pain sensation. Neural regulation of fracture healing may play a role, with the deinnervated limb in animal models showing an increase in bony callus and decreased tensile strength after fracture. Thus, dysregulation of reparative processes as well as the presence of osteopenia and increased blood flow may underlie the acute Charcot foot. Clinically, the Charcot foot is of ominous prognostic significance. Analysis of studies of >500 patients suggests amputation or death to be the outcome in >10%, with the majority having retinopathy and nephropathy as well (7), leading to the characterization of individuals with Charcot foot as “frail patients with fragile feet” (8). It is noteworthy that the diagnosis is not made at presentation in the majority of patients and that such delay is associated with greater likelihood of amputation.

Michael Pinzur, Maywood, IL, discussed surgical management of the Charcot foot, stressing the importance of prevention and the anecdotal nature of most studies. During the initial “destructive” stage, total-contact cast application and avoidance of weight-bearing have been recommended. These approaches are used in the minority of patients, however, and little data documents this approach. Pinzur recommended the use of a prefabricated orthosis in the majority of patients and suggested that weight-bearing should not routinely be avoided. During the stage of “coalescence,” defined by the development of abnormal radiological findings, external fixators are usually inadequate; rigid internal fixation devices are usually required to achieve healing of unstable stress fractures because of the severe osteopenia. Subsequent surgical procedures are often necessary to remove the implanted hardware. Lengthening of the Achilles tendon is often useful because of motor imbalance. During the third stage, “reconstruction,” surgical resection to allow eventual use of an extra-depth shoe is often required because of the development of bony prominence of the plantar foot. Pinzur pointed out that in many cases, it is uncertain whether to “go through limb salvage reconstruction” or to perform an amputation because “when we start operating on patients with ulcers” there is at least a 30% rate of severe subsequent infection. We must recall that “the goal is to keep people walking [and] not just to save a foot.”

Peter Sheehan, New York, NY, discussed a number of issues pertaining to infection, pointing out that approximately one-fifth of patients with foot ulcers have a Charcot foot and that the distinction between acute Charcot and osteomyelitis is difficult (9). Erythema, edema, and increased skin temperature characterize both processes. Radiological studies, including magnetic resonance imaging, often do not distinguish the two processes. Bone scans, Sheehan mentioned, “really have no utility,” and indium-labeled leukocyte scans have poor resolution and may be positive in the Charcot foot as well. Furthermore, he pointed out that “sepsis is an inflammatory process than can precipitate a Charcot.” The major guide to osteomyelitis, therefore, is the clinical examination, with the “probe to bone” test useful, although again not showing complete ability to detect deep infection (10). A 4- to 6-week course of antibiotics is usually required for bone infection, but it may be possible to shorten this to 2 weeks with aggressive ablation of infected tissue. Healing rates are no greater than 60–80% in most series, even with surgery, and many patients require at least partial foot amputation.

Andrew Boulton, Manchester, U.K., addressed new approaches to medical management, arguing that Voltaire’s opinion that “the art of medicine consists of amusing the patient while nature cures the disease” does not pertain to the Charcot foot. The goal of medical treatment is to reduce disease activity to allow the development of a stable foot that allows reconstruction. It may be helpful to measure skin temperature (11) as an index of disease activity. In a recent trial, bisphosphonate treatment with pamidronate (90 mg i.v.) was compared with saline placebo in 39 patients without ulceration and with a >2°C temperature difference between affected and unaffected feet. Alkaline phosphatase and urinary pyridinium collagen crosslinks fell with active treatment, but skin temperature fell similarly in both groups. As yet, there is no evidence that clinical outcome improves with bisphosphonate treatment, and there have been no randomized trials of use of a total-contact cast, administration of nonsteroidal anti-inflammatory drugs, or avoidance of weight bearing, all of which are advocated for the condition.

Neuropathy and the Diabetic Foot

A number of studies presented at the meeting discussed aspects of diabetic neuropathy and the treatment of the diabetic foot ulcer. Abouaesha et al. (abstract...
reported that among 84 patients with decreased vibration perception threshold, ultrasound-measured plantar subcutaneous tissue thickness was decreased in patients whose foot pressures at the metatarsal heads and increased callus were high, potentially a useful marker for risk of ulceration. Tesfaye et al. (abstract 137) reported a 7.3-year follow-up of 986 type 1 diabetic patients without peripheral neuropathy at baseline from 27 centers participating in the EURODIAB Prospective Complications Study: 25% developed peripheral neuropathy, 24% developed neuropathic symptoms, and 16% developed abnormal autonomic function, with age, duration of diabetes, baseline HbA1c, BMI, albumin excretion rate, triglyceride, cholesterol, systolic blood pressure, smoking history (current or past), and retinopathy as significant predictors. Devers et al. (abstract 807) reported a population survey of 11 lower-extremity amputations among 812 type 1 diabetic patients, 108 among 9,804 type 2 diabetic patients, and 271 among 305,886 nondiabetic subjects followed from January 1992 through March 1998 in Tayside, U.K. The 2.6-year postamputation mortality rates were 61 and 53% in the diabetic and nondiabetic groups, with a mean of 4 vs. 3 hospitalizations for 69 vs. 43 days, respectively.

References