

**SOME LONG-TERM SEQUELAE OF POORLY
CONTROLLED DIABETES THAT ARE FREQUENTLY
UNDIAGNOSED, MISDIAGNOSED OR MISTREATED**

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Many years of scientific studies of both animals and humans have provided overwhelming evidence that the long-term adverse sequelae of diabetes are caused by elevated blood glucose (BG). A recent meta analysis of studies of over 95,000 individuals demonstrated that even within BG ranges generally considered normal, the risk of cardiovascular events increases exponentially with blood sugar. Elevated BG adversely affects every tissue of the body, with the possible exception of hair.

Although many glucose-related biochemical mechanisms have been demonstrated to be causative of diabetic sequelae the one most commonly studied is glycosylation of proteins. Glucose that has been irreversibly bound to certain sites on amino acids can then attach to another amino acid in the same molecule or to an adjacent protein. This “gluing” of proteins or collagen can render the affected molecules inactive or even pathologic as in the case of glycosylated apoproteins of LDL particles, which can then adhere to proteins in vascular endothelium. A well-known example of this process is the glycosylation of hemoglobin, which for many years has served as a measure of BG control over the prior four months.

Since proteins (and very slowly collagen) do turn over with time, some diabetic sequelae caused by this mechanism can be reversed by BG normalization, if caught early enough.

Another likely biochemical cause of diabetic sequelae relates to the existence of tissues that can accumulate glucose even in the absence of insulin. These include the lens of the eye, neurons, Schwann cells, renal mesangial cells and vascular pericytes. All these tissues contain the enzyme aldose reductase, which rapidly converts glucose to its alcohol sorbitol. Sorbitol is

then slowly (over weeks) is converted to fructose, which can diffuse out of the cell. In the meanwhile, however, the sorbitol cannot leave the cell. There it acts as an osmotic agent drawing water into the cell. The excess water can, at the very least, interfere with cellular function. If enough is accumulated, the cell bursts.

If BG is normalized before the cell bursts, it can recover. Thus neuropathies, for example, have two components – the metabolic and the anatomic. In the former, symptoms can rapidly reverse (hours to weeks) with near normalization of BG. In the latter, it may take years for neurons to re-grow, at a rate of about one millimeter per day.

In this chapter we will discuss the diagnosis and treatment of a few of probably more than fifty known long-term complications of diabetes that can cause distress or disability but which are frequently undiagnosed, misdiagnosed or mistreated. We will focus on approaches accessible to the primary care physician or to the psychiatrist. Some of these approaches to treating and diagnosing such complications are not described in the scientific literature and are probably unique to my practice.

NEUROPATHIES

Elevated BG probably inflicts at least minor damage to every nerve in the body. The severity and reversibility of such damage is likely related to the amount of such elevation and the time frame over which it has existed. Neuropathies can be classified by the types of neurons involved, such as autonomic, sensory, motor and even central nervous system (brain). It is well known that the more distal a neuron extends from the brain, the sooner it will be affected by diabetic neuropathy. Thus tall diabetics tend to develop various neuropathies of the feet earlier than short people with diabetes.

The Intrinsic Minus Foot

Virtually all individuals with more than ten years of elevated BG will demonstrate this foot deformity. It is caused by a combination of motor neuropathy and likely glycosylation of the collagen in the plantar fascia. The plantar fascia acts like a bowstring. When glycosylated it shrinks, increasing the curvature of the arch. This in turn makes for prominence of the plantar metatarsal heads at the bases of the toes, potentially subjecting them to excessive pressure when standing or walking.

The lumbricals are called the intrinsic muscles of the foot because their origins and insertions lie within it. They straighten the toes by extending the interphalangeal (i-p) joints and flexing the metatarsal-phalangeal (m-p) joints. The nerves that innervate the lumbricals are the longest motor nerves of the body and therefore are usually the first to suffer neuropathy. When lumbricals are partially denervated, the m-p joints will extend, raising the toes above the dorsum of the forefoot. The i-p joints will flex creating the claw-like appearance called hammertoes. The great toes will lose strength on extension, extend at their m-p joints above the other toes and display a prominent extensor tendon (cock-up deformity of the hallux). The plane of the forefoot will be rotated upward so that a straight edge placed along the forefoot will no longer contact the heel ("Bernstein Test"). As the denervation of the lumbricals proceeds, they will waste, leaving dorsal channels between the metatarsal bones, radiating proximally.

The hazard of this deformity lies in the creation of pressure points where skin can readily break down. These points occur at the heels, the plantar m-p heads, the downward pointing tips of toes and the knuckles (proximal i-p joints) of the toes.

The goal of treatment should be to off-load pressure thereby preventing skin breakdown (ulceration). Mild cases can be treated with modern sneakers or walking shoes having a deep

rise (to accommodate orthotics and raised toes), and a wide, non-pointed toe box. Orthotics inserted into shoes, serve to off-load the heels and the prominent m-p heads by shifting plantar pressure to the arch. It is essential that they are comfortable and to this end, they may have to be modified or custom fabricated. For progressively more serious intrinsic-minus deformities the shoe choice would begin with extra depth orthopedic oxfords and continue through custom orthopedic oxfords. Then the addition of a Denver heel and in extreme cases, the use of a metatarsal bar to transfer even more weight bearing to the arch from the heels and m-p heads by preventing the rolling motion of normal gait.

The intrinsic-minus foot is not unique to diabetes. It can be found in neurosyphilis and Hansen's disease and even appears at birth in many individuals.

In the diabetic, this deformity can be prevented by maintaining essentially normal BG's. It cannot be reversed as it involves loss of musculature.

Xerotic Skin

Damage to sympathetic nerves of the lower extremities can cause several problems, including partial or total loss of perspiration (xerosis). The resultant dry skin may become cracked, facilitating the entry of pathogenic organisms into subcutaneous tissue. Dry skin is more susceptible to injuries and can experience slow healing when injured.

Again, prevention is normalization of BG. Treatment is lubrication with any animal or vegetable oil. Petroleum based lubricants are not absorbed into the skin and therefore are inappropriate in spite of widespread advocacy by "authorities." Likewise, urea-based products serve as extolians and are of no value for lubrication. Alcohols and glycols tend to dry the skin and should not ordinarily be used on the feet. In our clinic, which caters to the indigent, we have had outstanding results when we prescribe olive oil, which is inexpensive. Depending upon the

degree of dryness, we will suggest that it be rubbed in once or twice daily. The excess can be rubbed off with a towel if it bothers the patient. Many products with more elegant aromas are available in “health food” stores and some drugstores. Other products that are perhaps marginally better than olive oil are vitamin E oil and highly purified mink and emu oils. Full strength Vitamin E oil, as obtained by cutting an oral capsule, is especially helpful for facilitating the healing of painful cracks in the skin.

Orthostatic Hypotension/Syncope/Near Syncope

Upon standing from a seated or supine position, it is normal for the muscular tunica media of arterial walls in the legs, to contract. This sympathetic, autonomic reflex is necessary to prevent the pooling of blood in the legs, that might otherwise diminish circulation to the brain. It is in fact normal, for central blood pressure (BP) to actually increase upon standing. Patients with longstanding BG elevation frequently display a form of sympathetic neuropathy wherein this reflex is diminished or absent. As this form of neuropathy progresses, one finds initially, upon standing or one minute thereafter, a drop or lack of increase in brachial BP together with a partially compensatory increase in pulse rate. If BG elevation continues, the patient will eventually experience upon standing, light-headedness that can progress to near syncope, and eventually to syncope.

Upon first encountering a patient with diabetes, it is appropriate to test BP after about fifteen minutes of supination and then upon standing and one and two minutes thereafter. I define mild orthostasis (postural hypotension) as failure of BP to increase. Severe orthostasis would entail a combination of syncopal history or light-headedness on standing, with a drop in systolic BP greater than 20mm Hg upon standing.

Many non-diabetic (and diabetic) chronically hypotensive individuals can experience symptoms such as those mentioned above, usually due to reduced pulse pressure (systolic minus diastolic <35 mm Hg). This problem is very common amongst the hypotensive elderly during warm weather. It is best treated with restoration of blood volume by consumption of water or fluids containing one level teaspoon of table salt per quart. Treatments recommended elsewhere, such as glycyric acid, NSAID's, SSRI's, fludrocortisone acetate and midodrine, are usually not necessary.

The following measures to prevent syncope or near syncope are recommended for diabetic neuropathic orthostasis. They are usually quite effective for individuals with adequate pulse pressures when seated or supine:

- 1) Do not arise suddenly from a supine or squatting position. If lying in bed, dangle feet over the side for 2-5 minutes before standing.
- 2) Men who become symptomatic while voiding from the upright position should sit to void.
- 3) When symptoms impair standing and ambulating in spite of the above precautions, high quality compression stockings should be prescribed to prevent pooling of blood in the legs. These can either be ready made (30-40 mm Hg compression) or custom woven. The custom woven hose is easier to apply but is much heavier and therefore warm and unsightly. Depending upon severity of symptoms one prescribes calf length, thigh length or panty hose. Above the knee hosiery can impede flexion of the knee. Difficulty in removing the panty hose can impede use of a toilet. It therefore is wise to try the calf length stockings first.
- 4) If blood pressure is usually <100/70, when the weather is warm, affected individuals should drink at least one glass of water with a pinch of salt at each meal.

Why should this chapter devote so much space to this superficially benign complication of diabetes? My reasons stem from personal experience.

During medical school (1983) I spent several months on the medical service of a prominent university hospital. Our team encountered at least two patients per week who were admitted for “syncope work-up”. Virtually all had poorly controlled diabetes. They were all subjected to numerous costly cardiac and CNS work-ups. Their stays lasted 2-5 days. Virtually all were released without a positive diagnosis but were given cardiac or anti-seizure medications. Not one had been tested for supine vs. standing BP.

I was in private practice but a few years when I encountered Gene, a 78-year-old normotensive man with a long history of poorly controlled type 2 diabetes, treated with insulin. He was very alert, drove a car and played golf. At his initial work-up he displayed several symptoms of severe autonomic neuropathy:

- 1) Very dry cracked pedal skin (sympathetic deficit).
- 2) A heart rate variation upon deep breathing of only 7% (normal for age = 30%).

This is now a widely used diagnostic test for parasympathetic neuropathy.

- 3) An orthostatic drop in systolic BP > 30 mm Hg (supine to standing) with mild discomfort.

I warned Gene and his wife that he should sit for five minutes with legs dangling before arising from bed and that he should sit when voiding. He was a very cooperative patient. We were rapidly able to normalize his BG's and lipids by using a very low carbohydrate diet, BG self monitoring and at least five daily low dose insulin injections. About two years later his wife phoned me after midnight in a panic. He had fallen without losing consciousness. His BG was normal. He admitted that he had forgotten to dangle his legs and felt light-headed on arising to void. I repeated my earlier warnings to both of them. Over my objections, his wife pushed him

to see a neurologist who found approximately 70% stenoses of both carotid arteries. The neurologist did not check for orthostasis and ignored my suggestion that he do so. As far as I was concerned, the carotid artery disease was asymptomatic.* Nevertheless, an endarterectomy of the more severely stenosed carotid was scheduled over my pleas to his family and physicians. While in the hospital awaiting surgery he was put on a high carbohydrate ADA (American Diabetes Association) diet with resultant BG's suddenly above 400 mg/dl. During surgery he suffered a mild ipsilateral stroke. On his next visit to my office he had a unilateral lip droop and slightly slurred speech. I repeated my prior warnings about leg dangling and the hazards of surgery. About nine months later, a similar nocturnal incident (with normal BG) occurred, but this time he struck his nose on falling and suffered epistaxis. His terrified wife promptly took him to his vascular surgeon – again over my objections. He suffered another stroke during surgery and remained in a coma for six months until he expired. I have since told his story to every patient (and family) for whom I diagnose orthostasis. I also warn patients to sit when voiding and to avoid warm or hot showers or baths that can lower blood pressure by peripheral vasodilation. Similarly, potent vasodilating medications such as minoxidil or alpha₁ adrenergic blocking agents should also be avoided.

Painful Pedal Neuropathy

Pharmacologic treatments for painful pedal neuropathy have been widely discussed in the scientific literature. The interest in this subject probably stems from the fact that it is so common and from the sympathy that even many physicians have for the anguish of its sufferers.

*A study published about ten years later in LANCET, 345:209-12, demonstrated that asymptomatic carotid stenosis confers an insignificant risk for disabling stroke or death.

The pain is usually much more severe when the patient is supine (as when attempting to sleep) and therefore frequently causes insomnia. The most common sensation is burning. Frequently, the sufferer cannot tolerate the pressure from even a sheet upon the feet. Inevitably most patients find that standing or sitting brings considerable relief, so they treat the symptoms by sleeping in a chair. If elevated BG's continue, the pain is eventually replaced by total numbness of the feet due to death of the affected nerve fibers.

It is likely that this condition is due to metabolic neuropathy combined with infarcts or stenoses of the vasa nervorum, with emphasis on the latter. This hypothesis is supported by the improvement when legs are dependent so that gravity aids blood flow to the affected nerves. This condition is therefore often called ischemic neuropathy.

Many treatments have been used with partial success to treat symptoms until the nerves finally die. These include acupuncture with electrical stimulation, mexilitene (an anti-arrhythmic agent that is chemically similar to the anesthetic lidocaine), tricyclic antidepressants, gabapentin (an antiepileptic) and pentoxifylline (which can temporarily improve microcirculation). Recently, much relief has been obtained with injections of NGF (nerve growth factor). My approach is to attempt normalization of blood sugars. This always works but takes a few weeks to achieve and many months to affect a cure. While waiting, I instruct patients to put 6" x 6" x 6" wood blocks on the floor under the bedposts at the head of the bed. This places the head above the feet and brings about dramatic reduction in pain. If total relief is not attained, I first prescribe alpha-lipoic acid (600 mg three times daily). This is a benign but powerful antioxidant that accelerates nerve healing, inhibits glycosylation of proteins, possibly improves microcirculation and even enhances insulin sensitivity. It is rarely necessary for me to go beyond these treatments, but when necessary I will prescribe mexilitene (thus far without adverse effects) or gabapentin.

The Insensate Foot

In my experience, diminished or lost pedal sensation is far more common than pedal pain, possibly because the vasa nervorum are not stenosed. This condition is not unique to diabetes. It is also found in tertiary syphilis and Hansen's disease. The classic woodcut illustrations of a leper on crutches with a bandaged knee stump illustrate the end result of this problem.

In diabetes, metabolic neuropathy leads to early diminution of sensation. As sensory loss proceeds, more nerve fibers die and anatomic neuropathy predominates. Although ischemic neuropathy may be initially painful, the eventual loss of nerve fibers likewise proceeds to total loss of sensation. The resultant numb or insensate foot renders the sufferer unable to perceive injury. Thus an affected individual may be unaware of shoes that are chronically pressing upon or rubbing the skin of the feet. Even stepping upon a nail or into very hot water may bring no pain. This loss of sensation is the principle cause of both "diabetic" ulcers that affect about 7% of diabetics, and of "Charcot's foot."

Jean Martin Charcot observed more than one hundred years ago that a certain deformity of the foot was always associated with systemic disease. In an advanced stage it is characterized by a "rocker bottom" in place of a raised arch, and total loss of anatomical landmarks. Although much less common than foot ulcers, it is the ultimate example of how a foot, unprotected by sensations of pain, pressure or proprioception, can be battered by poorly controlled ambulation until it resembles a bag of broken bones.

Early in my private medical practice, I was visited by a man whose wife wanted his diabetes "controlled". On routine physical examination, I discovered a deep 2x3 cm ulcer in the sole of one foot. It was filled with white vegetation. When I asked if he was aware of the hole in

his foot, he replied, “Oh, that must be where the smell is coming from.” He was unaware of the fact that he felt no pain until I demonstrated his impaired sensation.

By the time a patient discovers sensory loss, great danger is already present. It therefore is imperative that every diabetic be carefully examined for early peripheral sensory neuropathy, before it becomes evident to the patient. My protocol, which follows, is first performed on the cheek for comparison, and then on the dorsum of the distal phalanx of the second toe of each foot – just proximal to the nail:

- 1) Light touch – Use a semi-rigid plastic fiber of continuously variable length manufactured by Rowan Products, Inc. The length is calibrated from 300 to 2,000 mg. Such a product is sold by most biological supply houses but not by surgical dealers. It is not the same as the fixed length “Semmes-Weinstein monofilament” recommended by the American Diabetes Association. The latter, produces a fixed force of 10,000 mg and thus can only detect advanced disease. The variable length fiber can detect normal sensation (300 mg). Perception of light touch is abnormal if a force greater than 400 mg is required.
- 2) Vibration – Activate a standard 128Hz tuning fork and immediately start a digital timer. Apply the base of the fork to the test site. The patient must then identify the instant at which vibration sensation has vanished? The time is recorded. Normally, expired time until loss of sensation is 20 seconds but 15 seconds may be considered acceptable.
- 3) Sharp versus dull – A reasonable comparison is the sharpened point of a pencil versus the eraser. Apply gently.
- 4) Warmer versus cooler – Although it is normal to distinguish a temperature difference of 1.5°C, the cost of providing such a precise temperature differential is prohibitive.

The following crude test, however, can be very informative. It requires but a pair of stainless steel or aluminum test tube shields, used in centrifuges. Hold one shield under warm water for an instant or put it under your arm for about 30 seconds.

Compare sequentially the temperatures of the two tubes on your own cheek. If a slight differential is perceived, apply the tubes to the patient's cheek. If the cooler one can be identified, try the tubes in a changed sequence to the dorsum of the distal phalanx of the second toes or to any other dorsal site of your choosing. In the absence of sensory neuropathy, it should be possible to perceive the same temperature difference by the foot that can be perceived by the cheek.

- 5) Joint Position – Hold fixed with one hand, the middle phalanx of one toe (I use the second toe). With the other hand move the distal phalanx into the dorsal (up) and plantar (down) directions. Identify “up” and “down” verbally to the patient. Then move the phalanx up and down several times at random and ask the patient to positively identify the directions – without guessing.
- 6) Pain – This test does not involve the toes or using the cheek as a control. While observing the patient's face, briefly squeeze the Achilles tendon of the test foot, as hard as you can. In the absence of neuropathy this test can be as painful as touching the cornea or squeezing the testes. A normal response is a combination of grimace, shout and withdrawal. Record the results by drawing 0-4 downward pointing arrows on your report or writing “0” for no pain sensation whatever. Such a result suggests great risk for the development of trophic ulcers.

As previously indicated the insensate foot will slowly respond to near normalization of blood sugars. As nerves sprout new fibers severe pain may ensue for several weeks or months. This symptom should be encouraging. It may, however, take years for full recovery as

nerves re-grow no faster than 1 mm daily.* Furthermore, there are very few medical facilities where blood sugar normalization is even attempted. So what can we do to prevent Charcot's foot, infected ulcers and eventually amputation. One way to possibly prevent the fractures that constitute Charcot's foot is a combination of slow cautious gait with custom shoes containing a metatarsal bar. Ulcers do not occur spontaneously. They are always preceded by an injury. Ulcer prevention thus boils down to immaculate care for the skin of the feet. Although I examine feet at every routine office visit of a diabetic, ultimate care is in the hands of the patient and family. To facilitate this, I routinely distribute to patients a handout entitled, "Prevention is the Best Cure for Diabetic Foot Ulcers." It appears at the end of this chapter. You should feel free to photocopy it for your own patients.

Gastroparesis Diabeticorum

This condition is a paresis or even virtual paralysis of stomach emptying, secondary to neuropathy of the vagus nerve. It is almost ubiquitous in longstanding diabetes. In advanced stages it extends to the entire gastrointestinal tract and can cause constipation, early satiety, bloating, belching, retrosternal burning and even vomiting. It is rarely diagnosed and more rarely adequately treated. In type 1 diabetics it can render BG control impossible (unless the gastroparesis is properly treated) since it causes the stomach to empty in an unpredictable fashion. Thus even if intensive insulin therapy is attempted, BG's may become too low after a meal on one day, and fine after the same meal on another day. If a postprandial blood sugar is too low it is sure to become very elevated many hours later when the stomach finally empties. Although type 2 diabetics may experience the aforementioned physical symptoms, their BG's

*Some oral treatments that have been shown to accelerate nerve growth include alpha lipoic acid (600 mg, tid), gamma linoleic acid (evening primrose oil, 8 mg/d), fish oil (several grams daily) and magnesium (300 mg/d).

may be relatively stable because many still make insulin and can turn it on or off as needed.

Since the treatment of this disorder is too complex to fit into this chapter, I refer you to Chapter 21 of my latest book *DIABETES SOLUTION*, Little Brown, 1997, which is still in print and will probably be available for a number of years. If a patient does not produce endogenous insulin, treatment of this condition is essential for even a semblance of blood sugar control.

Ulcers of the Feet

If even the faintest pulse can be found in any of the pedal arteries most ulcers can be healed – even in diabetics with high blood sugars.* Unfortunately, the usual combination of debridement, antibiotics, and whirlpool baths can do more harm than good. Our clinic treats foot ulcers in poorly controlled indigent diabetic patients at a large New York City owned hospital, yet our cure rate in the absence of pre-existing osteomyelitis is essentially one hundred percent.

Let's take a look at our techniques:

- 1) Check circulation to determine if it is adequate for healing. This can be done in only five minutes with the help of an inexpensive instrument – the oscillometer. This device is the poor man's version of plethysmography – a costly but usually unnecessary technique. Although readings in the ankle of 2-5.5 “oscillometric units” are normal, a reading as low as 1/4-1/2 unit is frequently adequate for healing.

Conservative attempts at healing may nevertheless be tried briefly for patients with even “trace” readings before referring a patient for by-pass grafting.

- 2) If the wound appears deep or if fat or muscle are visible, the wound should be probed

*Provided that doppler blood pressure measurements are greater than or equal to 20 mm. Hg in toes or >40 mm. Hg in ankles

with the wooden tip of a cotton applicator stick. If bone can be touched, one is obliged to assume that osteomyelitis is present. This condition mandates hospital or outpatient treatment with intravenous antibiotics and frequently surgical debridement of infected bone. If this approach is unsuccessful and infection ascends, amputation may be necessary.

- 3) Since even benign-looking “diabetic” ulcers contain some infection, wounds should be swabbed for culture before and after debridement. Culture specimens should be obtained from the deepest part of the wound. If there is a flap of overlying tissue at the wound margin, a specimen should also be obtained from as far under the flap as can be reached. Specimen collection should include aerobic, anaerobic and fungal media. Most infected “diabetic” ulcers contain polymicrobial flora. Since anaerobes are usually present but may not always appear on culture, treatment should include antibiotics for anaerobes as well as for whatever common gram positive and gram negative organisms may be present. Always palpate the wound area for crepitation and sniff for foul smell. If there is a green exudate (usually foul smelling) assume that pseudomonas is present. This organism cannot tolerate an acid environment, so in addition to the appropriate oral antibiotic, topical moist (not wet) to dry acid containing dressings all day long may be of great value. We usually use aluminum acetate powder, one 2.5 gm packet dissolved in 200 ml of warm water, which is then allowed to cool. Alternately one tablespoon of white vinegar in 200 ml of water should also be effective.
- 4) The usual indicators of cellulitis (rubor, dolor, calor) may not be present in a diabetic because of neuropathy or poor circulation. It therefore is wise to also check body temperature and inguinal lymph nodes in addition to seeking the above three signs.

Many poorly controlled diabetics, however, are immuno-compromised and won't have fevers. If cellulitis or any infection is suspected, broad spectrum antibiotics should be started immediately while awaiting culture results. If the infection is accompanied by ascending lymphangitis (red streaks), the patient must be hospitalized for intravenous antibiotics and the affected leg must be kept level with the heart – not elevated as in common practice.

- 5) All diabetics with foot ulcers should be examined for phlegmons, ascending infections along tendon sheaths. This is achieved by palpating the deep flexor tendons along the metatarsal area for tender cords or crepitation. Even diabetics with sensory neuropathy will usually perceive an unpleasant sensation during palpation if a phlegmon is present. If a phlegmon is palpated in a toe, it is likely that infection has already spread to the entire foot. Treatment is surgical incision and drainage with radical debridement of affected fascia. The causative organism is often streptococcus pyogenes.
- 6) The purpose of routine debridement should be threefold:
 - Removal of necrotic material.
 - Removal of dead skin or surrounding callus.
 - Removal of overhanging flaps that prevent drainage from the wound periphery or hide tracts, fistulas or other extensions of the wound.

Debridement should not be performed without one of the above justifications.

Debridement should be down to pink skin but should not be so extensive as to cause bleeding, since opening intact vasculature can spread an infection.

- 7) We will swab a wound and its surrounding skin with providone iodine solution prior debridement, as with any minor surgical procedure. Contrary to common practice,

- however, we never use providone iodine or hydrogen peroxide as wound dressings. The iodine inhibits healing by preventing fibroblast activity while the peroxide actually destroys exposed tissue. When we suspect infection or contamination with staphylococcus we will frequently apply aqueous (not tincture) gentian violet solution which is staphylocidal. Although bacitracin ointment has very little antimicrobial effect, its base is less likely than other petroleum jellies to cause irritation or allergic reaction. We therefore ask patients to apply it daily with a gauze dressing to dry or nearly dry wounds in order to keep them soft and draining. Mupiricin ointment is a broad spectrum antibiotic that we find very effective for treating infected wounds. It should usually not be used longer than two weeks as resistant organisms can develop.
- 8) Again contrary to common practice, we do not debride eschar (scabs). They protect the wound and facilitate healing. If eschar is loose and likely to come off on its own, it will move when rubbed with the cotton end of an applicator stick. If it moves, we apply a gauze pad saturated with mineral oil and let it sit on the eschar for at least five minutes. We then gently rub the scab with the saturated gauze. If it is ready to come off, it will. If not, we do not attempt to remove it.
- 9) The common practices of soaking of feet in saline, water or medicated solutions or using wet dressings are downright dangerous. The two exceptions would be a 5-10 minute soak in cool potassium permanganate solution for treatment of fungal infections and the use of moist to dry mildly acidic dressings mentioned above for killing pseudomonas. Prolonged exposure to water or aqueous solutions macerates the skin. Macerated skin is more susceptible to injury than normal skin and macerated wounds do not heal readily. Furthermore, water temperatures of only 92° F can burn the skin if circulation is so impaired that the heat cannot be conducted

away. This was discovered many years ago when diabetics treated in whirlpool baths set at 92° F were found to experience burns. The burns were painless because of sensory neuropathy. We have reversed the downhill course of many ulcers by merely insisting upon termination of foot soaks and whirlpool baths prescribed elsewhere and off-loading pressure.

- 10) Since many foot ulcers are initiated by pressure from ill-fitting shoes or bony prominences, one cannot expect an ulcer to heal if the pressure is allowed to continue. The most important single technique for healing a foot ulcer of any etiology is to off-load pressure. Thus if the ulcer is on the dorsum or side of a foot, an appropriate cutout must be made in the patient's shoe, sneaker or in a surgical shoe. Cutouts should be "U" or "C" shaped, not Circular. A circular cutout around a wound will act as a tourniquet thereby rendering it ischemic. If the ulcer is on the plantar surface, the patient should be non-ambulatory. Since this may be impractical in the real world, a less than ideal substitute would be the use of crutches combined with specially modified shoes. Special surgical shoes are available* that take all weight off the forefoot and other shoes that take all weight off the heel. Recently, the Diabetic Pressure Relief Shoe* with thick insoles has become available wherein removable pieces of insole can be removed to create a "U" or "C" shaped hole under the ulcer. Because insurance does not usually pay for such products, we cut insoles for standard canvas or fabric surgical shoes, from self-adhering ¼ or 3/16 inch thick self-adhering felt. Sometimes two thicknesses are necessary. We then cut out "U" or "C" shaped holes to fit under plantar ulcers. The open end of the "U" or "C" is extended to the outer edge of the insole. When toes override or are pressed together by pointed toe

*Ali Med®, Dedham, MA 02026

shoes, “kissing ulcers” on adjoining toes may occur. Downloading in this case consists of using open toe surgical boots and separating the affected toes with several thicknesses of gauze. Again, many longstanding non-healing ulcers referred by surgeons, podiatrists, etc., have been rapidly healed, merely by off-loading.

- 11) If the use of the above techniques fails to bring about rapid reduction in ulcer dimensions or if the ulcer has a depth greater than 3mm, suspect osteomyelitis – even if cultures yield only “normal skin flora” and bone cannot be touched with a probe. This condition can readily be diagnosed by means of an indium tagged leukocyte scan – or magnetic resonance imaging (MRI), both of which insurance will usually reimburse. If the leukocyte scan is negative, we have had success using hydrocolloid plasters to accelerate healing of otherwise slow healing wounds. We cut out a piece of the hydrocolloid to fit inside the wound and hold it in place with roll gauze. Never apply adhesive tape to a “diabetic” foot as it can rip off skin when removed. We have also had excellent results using a gel called Derma-Fine, produced by Bryce Laboratories in Hawthorne, NY. Unfortunately, this product is not covered by most insurers. It should be covered with a gauze pad that is held in place by roll gauze. The hydrocolloid should be changed when it starts to ooze and the Derma-Fine should be reapplied daily.
- 12) Although we have an excellent track record of healing ulcers even when blood sugars are poorly controlled, it would speed things up if near normal blood sugars were attained. This is an important goal in my private medical practice but our clinic is not permitted to address it. This is in the domain of other clinics in our medical center that have neither the time nor the know-how to achieve.

13) High blood levels of Vitamin E have been shown to enhance wound granulation, reduce glycosylation of proteins (in diabetics) and improve insulin sensitivity in type 2 diabetics. When a patient can afford it, we therefore prescribe 400 i.u. of alpha or mixed tocopherols three times daily.

14) Prevention is the best treatment for diabetic foot ulcers. See the last two pages of this chapter for preventive guidelines. Several of our guidelines challenge common practice.

A full dissertation on the treatment of foot ulcers in diabetics would require at least a long chapter or possibly an entire book. The above guidelines, however, should encompass most situations that you may encounter.

Diabetic Diarrhea

About 5% of my first encounters with diabetic patients include complaints of frequent sudden episodes of massive loose bowel movements. These may occur several times a month to several times daily. The episodes come without warning and are totally beyond the patient's control. Many fear leaving home and although they station themselves near the toilet, "accidents" are frequent. A number of speculations have been made regarding etiology but to my knowledge, no hard data supporting underlying mechanisms has been reported. One theory relates autonomic neuropathy to impaired absorption of electrolytes and water by the gut. A neuropathically incompetent anal sphincter may be involved, but this would not account for the large stool volume usually encountered. Whatever the cause, this problem is a disaster to those who must endure it.

None of the affected diabetics I have seen had ever been told that this condition is both treatable (short term) and curable (longer term). The short term treatment is simply "off label"

use of clonidine which is marketed as an antihypertensive agent. Although available in oral tablets, I prefer to use the skin patches because they need be changed only once weekly. Furthermore, sudden discontinuation of the patches is not associated with rebound hypertension as with the tablets. For some the diarrhea returns in less than a week, obliging twice weekly use. The skin patches come in three sizes – 0.1, 0.2 and 0.3 mg. A common adverse effect is tiredness, which is more pronounced at higher doses. The somnolence vanishes within one day of removing a patch. It is wise to give the patient a supply of 0.1 mg patches with instruction to add one or two more patches if necessary to control the diarrhea. If two or three 0.1 mg patches bring about resolution of the diarrhea, then we prescribe single 0.2 mg or 0.3 mg patches, respectively, thereafter. A very obese individual may require two 0.3 mg patches for full efficacy. Although I warn patients of the possibility of postural hypotension, I have yet to encounter it. Severe somnolence may sometimes be averted by replacing the clonidine with guanfacine (a similar antihypertensive agent) tablets. In my experience, these agents always work but both can occasionally cause fatigue.

Clonidine skin patches inevitably cause severe skin inflammation in redheads and sometimes in blondes or other very fair-skinned individuals. It is often possible to prevent this untoward effect by first rubbing a potent steroid cream into the skin at the application site.

INFECTIONS

Infections can be two-edged swords for people with diabetes. High glucose levels in blood or tissue can serve as excellent culture media for bacteria. The impairment of immune function that accompanies chronic blood sugar elevation predisposes for infestations by bacterial, viral, and fungal pathogens. Recurrent vaginal candidiasis, for example, is a prime

warning sign of possible type 2 diabetes. We shall discuss below only two particular conditions – pedal onychomycosis and endodontitis/periodontitis. The reasons for these selections will be apparent.

Onychomycosis Pedis or Fungal Toenails

Pedal onychomycosis, although not unique to diabetics, is virtually ubiquitous amongst diabetics with poorly controlled blood sugars. I estimate that, at their first visits, nearly one hundred percent of my diabetic patients at clinic and fifty percent of my private patients have this condition.

Onychomycosis is readily diagnosed by its visual appearance – a thickened nail plate, usually with yellow discoloration. Frequently the nail plate is slightly raised from the nail bed distally. Under the raised nail, loose material (detritus) can be removed with the end of an applicator stick, although there is no reason to remove it. Sometimes the nail is soft and crumbling, at other times it may be too hard and thick to cut with a nail clipper. If diagnosis is uncertain, nail parings can be sent for fungal culture. I discuss onychomycosis pedis in this chapter for two reasons: It is very common and my treatments for it are quite unconventional.

Nowadays, physicians prescribe oral antifungal agents for treating this condition. Several such agents are marketed in this country. They all, however, pose such problems as very high cost, potential adverse side effects and competition for hepatic cytochrome P-450 enzymes that can potentiate or clear other medications. These effects may lead to inappropriate blood levels of other drugs that a patient may be using.

Our principal tool for treating onychomycosis is Tincture of Fungoid. This is a pre-1938 topical liquid containing cetylpyridinium chloride, chloroxlenol and triacetin. It is available without a prescription, inexpensive and is also the most effective drug I know of for the rapid

treatment of tinea pedis (athlete's foot). The liquid is applied twice daily by the patient to the nail plate, cuticle and under the distal end of the nail if it is raised. It should be applied every day until the nail fully grows out. This may require a full year in the elderly. If it is applied only once daily, the condition usually will not worsen but it will not improve. Progress can be tracked by observing the line of demarcation between infected and uninfected nail over time. Sometimes the nail plate will come off during treatment. If this occurs, this medication should be applied to the nail bed and to the new nail as it grows, to insure that it does not become infected.

Oftimes, the infected nail plate is so thick (greater than 2 mm) and hard, that the medication will be ineffective. In such cases it can be softened with Desitin ointment until it can be pared down or even removed with a nail clipper (H.I. Lippman, MD, personal communication). Desitin is a non-prescription white ointment sold for the treatment of diaper rash. It should be rubbed into the nail plate twice daily by the patient or family. This pretreatment is usually completed within 1-2 months.

Although onychomycosis does not cause elevation of diabetic blood sugars, the pressure of shoes upon a thickened nail can cause ulceration and infection of the nail bed.

Endodontal and Periodontal Disease

I believe that people with diabetes are entitled to essentially the same blood sugars as those without diabetes and should therefore not have to endure the grave long term complications of this disease. This goal is attainable for most, using the methods described in my book *DIABETES SOLUTION*. When a patient with prior well controlled blood glucose complains of new onset unexplained blood sugar elevation, I think of two likely causes – deterioration of pharmaceutical insulin preparations (for those who use insulin) and infection. It's easy enough to try new vials of insulin and infections can usually be identified by history and physical

examination. Almost every month, I will encounter an individual using oral hypoglycemic agents or new insulin vials who exhibits none of the usual signs of infection. Then I look in the mouth for swollen or inflamed gums and tap on the distal surface of the teeth with the blunt end of a metal probe to elicit pain. If I secure no positive findings, I will send the patient to a dentist for x-rays of the jaws. Usually, endodontitis (osteomyelitis) is present and sometimes soft tissue infection (peridontitis) is found. Occasionally, I encounter a new patient with very high blood sugars for years, while taking over 100 units of insulin daily. Many of these people have been under the care of diabetologists. The reason I discuss these conditions here is because they are rarely suspected by the physicians in charge, yet they are readily treatable. A previously treated endodontitis can leave a quiet small pocket of infection for years that suddenly explodes with dramatic effects upon blood sugar.

About fifty percent of my new patients, older than forty years, with long standing diabetes have lost at least one tooth, attesting to the frequency of this problem. There is no excuse for missing it! I advise all diabetics to visit their dentists every three months for examination and ultrasonic scraping of tartar below the gum line.

DISEASES AFFECTING THE TENDONS

Virtually all of my new patients with longstanding poorly controlled diabetes display evidence of damage to (likely glycosylation of collagen) tendons or tendonous insertions into muscle or bone. These problems are usually either misdiagnosed, mistreated or not recognized as relating to high blood sugars.

Carpal Tunnel Syndrome (CTS)

Physiatrists are well aware of this condition and its relation to certain activities such as typing and computer use. What they do not usually know is that this condition is a common complication of diabetes. There are several diagnostic indicators of CTS (such as Tinel's sign and Phalen's sign) that are so well known that we need not describe them here.

What disturbs me about this condition is its treatment. About half of the patients I encounter who have had a prior diagnosis of CTS have already been treated surgically and have never been apprised of the alternative treatment – cock-up wrist splints. These may be used only at night or in more severe cases all day long, and are quite effective if the condition is caught early. One catch to any treatment is the likely return of the problem if blood sugars are permitted to remain elevated.

Dupetryn's Contracture (DC)

Dupetryn's Contracture is so common in diabetics that my late mentor, Professor Heinz I. Lippman, insisted that every case he had seen was associated with diabetes. Of the many cases that I have diagnosed, only three involved people with non-diabetic levels of glycosylated hemoglobin. As with CTS, many of the patients I have seen, had already experienced unnecessary "corrective" surgery and were never told about finger extension splints.

DC usually presents early on with a "V" shaped denting of the skin on the palmar surface of the hand over the fourth metacarpal-phalangeal joint. At the apex of the "V" is usually a small dimple. The flexor tendon of the finger extends proximally from the dimple and is inevitably swollen and even nodular. As DC progresses, the finger flexes and can only be straightened passively. Oft times, the flexor tendon is painful. Many of the diabetics I have examined have DC of all fingers but the thumb.

What is special about this condition is the simplicity of treatment. Although many mechanical springloaded finger extension devices are available, I prescribe one product exclusively – the Dynamic Digit Extension Tube, sold by AliMed, Inc. of Dedham, Massachusetts, USA. This product, available in five sizes, is a fabric-covered rubber tube that is merely slipped over the finger in such a fashion that its curvature stretches and reverses the contracture. It can be cut with a scissor to fit any finger. It also keeps the finger warm, facilitating pain relief. In my experience, it always works. As with CTS, Dupetryn's Contracture will reappear if blood sugars remain elevated.

Frozen Shoulder or Diabetic Capsulitis

Yet another common condition that is probably associated with glycosylation of tendonous or even muscular tissue, diabetic capsulitis is mentioned with some frequency in the scientific literature. What has not been described are the early signs and successful treatment.

Frozen shoulder is the end stage of many types of shoulder injury and is well known to physiatrists. The most common presenting signs for moderately severe cases are pain and limited range of motion upon abduction and internal rotation. Typical complaints include, “I can’t put on a t-shirt or reach for something in the back seat when I drive my car.” As the affliction progresses the patient has difficulty putting on a jacket and may require assistance in this task. Eventually, pain may be present even when the arm is at rest – especially if the affected side is adjacent to a cold window – as on a train or bus. Sleeping may even be impaired because of the pain.

My physical examination of diabetic patients always includes checking for capsulitis. When present, the dominant side inevitably is more severely affected than the non-dominant

side. Out of hundreds of cases with positive findings, I have seen only one case where the non-dominant side was more disabled.

This condition can be elucidated in nearly all long term diabetics even if they deny any of the usual symptoms. My examination consists of comparing both shoulders for range of motion on internal rotation. I do not use goniometry because I find angle measurement to be somewhat subjective. Instead I ask the patient to try to scratch his/her back from below, along the midline and as high as possible. We usually start with the dominant side and I put a small piece of tape on the highest point that can be reached with any finger. We then repeat the test with the non-dominant shoulder and I measure and record the distance between the two pieces of tape. If this distance is greater than 5 cm, I consider it a positive diagnosis. Frequently, I will test the non-diabetic spouse and find the ranges of motion for both shoulders to be equal.

What about treatment? Years ago I tried stretching exercises, heat, cold, diathermy, ultrasound and differential electrical stimulation without long term improvement. Even near normalization of blood sugar does not work. What does work is deep trigger-point massage. Frequently tender trigger points can be found in the supraspinatus, infraspinatus, teres major/minor, deltoid and trapezius muscles – usually at insertions of tendon into bone. Other trigger points can be found in the joint capsule and the biceps tendon. These trigger points are usually tender spots that feel like knots to the palpating finger.

Deep trigger point massage by a competent physiotherapist inevitably cures the condition. The catch again is that symptoms will return if blood sugars are not kept meticulously controlled.

Iliotibial Band/Tensor Fascia Lata (ITB/TFL) Syndrome

“Low back pain” is ubiquitous in the general population of adults. In my experience it is especially prevalent in diabetics. I interview and thoroughly examine for the first time, about two diabetic patients every week. At least one of these new patients every month will admit to chronic low back pain that began years after the onset of their diabetes. Most of these patients will have seen chiropractors, orthopedists, rheumatologists, or neurologists and will have received a variety of diagnoses, the most common being “sciatica.” Many have been treated surgically for “slipped discs,” “spinal stenosis,” etc. In virtually all surgical interventions, the symptoms have not been relieved and in many, new symptoms such as paresis or paralysis have been created. A minority of diabetic patients complaining of low back pain are so disabled that they use crutches, wheelchairs or must be carried into my office.

The readers of this volume, mostly specialists in physical medicine, are probably more aware than other physicians that low back pain is usually a musculoskeletal problem. Inevitably this is what I encounter in my diabetic patients.

The usual complaint describes intermittent (rarely constant) pain that radiates from the upper buttocks along the lateral leg to the knee – where it terminates. The absence of extension below the knee is evidence that the sciatic nerve is not involved. As a rule, both legs are affected with pain, in one more severely than in the other. Pain may be exacerbated by driving a car or by lying on the affected side.

Physical examination discloses “knots” or trigger points that are tender to deep palpation. Since these trigger points encompass the iliotibial band and/or the tensor fascia lata, I’ve used the diagnosis “iliotibial band/tensor fascia lata syndrome”. To my knowledge, the association of this syndrome with diabetes has not been heretofore disclosed in the scientific literature.

The fascia investing the muscles of the thigh and hip is called the fascia lata. It merges proximally with the gluteal fascia and distally with the iliotibial tract or band. The latter extends along the lateral leg where it inserts distally into the lateral femoral epicondyle. About two-thirds along its proximal course, the more anterior aspect of the iliotibial tract bifurcates to merge with the distal end of the tensor muscle of the fascia lata. I speculate that in poorly controlled diabetes, collagen in any or all of the aforementioned fascial structures can become glycosylated.

The Trandenberg Test is used by physiatrists to diagnose the proximal end of this syndrome. The supine patient is asked to flex both hips and knees. The examiner then presses downward on both lower legs to fully flex hips and knees. A positive diagnosis is obtained if the buttocks rise above the examining table. Although this test detects tight proximal fascial structures, I find it to be frequently positive in patients without complaints of pain and without tender trigger points. I therefore prefer to use Noble's Compression Test which I find is always positive when complaints and trigger points are present and negative when they are absent. For this test the patient must be seated at the end of the examining table with the legs dangling so that the knees are flexed at 90° . The examiner grabs the affected knee so that her thumb presses on the iliotibial band about 1.5 cm proximal to the lateral femoral epicondyle. The thickened band is found as a cord that can be readily palpated. While pressure is being applied by the thumb, the knee is slowly extended passively. When the leg makes an angle of about 30° from the vertical, pain under the thumb is maximal.

My diagnosis is therefore based upon a combination of appropriate history plus tender trigger points along the ITB or TFL and a positive Noble's Compression Test.

The treatments that I have used with partial success include:

- 1) Application of a suspension of ibuprofen in 99% dimethylsulfoxide (DMSO). This treatment may be rapidly palliative but pain returns within hours.

- 2) Application of differential electric currents with rotating summation vector and varying frequencies (Nemectron). This approach can relieve pain for several days. Equipment is costly and some operator skill is required. It is not a long term cure.
- 3) Deep massage of tender trigger points. This form of therapy can actually cure the condition. Depending upon the number of trigger points, a single treatment might take 20-30 minutes of strenuous work by the therapist and pain for the patient. Most patients are willing to endure the pain because of the progressive improvement in their symptoms. Although physical therapists who spend their lives doing trigger point massage may find this work non-strenuous, I much prefer the assistance of one of the many vibrating or thumping electric “fingers” that are widely available. Treatments should be rendered every 10-14 days and may require many months to achieve a cure.

By far, a preferred mode of therapy is vacuum stretching of the entire affected length of the ITB/TFL. This technique requires a relatively inexpensive vacuum pump, available new or used from many suppliers of physiotherapy equipment. Since the pumps are sold for use with vacuum electrodes, they must be provided with a length of flexible tubing and a plexiglas suction cup. The cup I use has a handle (11-1/2 cm long) and a 4-1/2 x 6 cm opening with 0.4 cm thick rounded edges. Palpable trigger points are first marked on the skin to illustrate the area of treatment. After lubricating the skin and turning on the vacuum, the cup is moved along the affected area while being pulled away from the body. This actually lifts the ITB/TFL causing it to stretch. Vacuum should be adjusted to minimize bruising while not losing contact. The procedure is painful and can cause mild eccymoses. Pain is less than with trigger point massage and cures can usually be achieved with 5-20 treatments spaced two weeks apart (to allow

bruising to resolve). The success of vacuum stretching after months or years of chronic pain seems miraculous to the patient and continues to impress me.

Like the other “cures” mentioned in this chapter, vacuum stretching does not prevent recurrence if blood sugars remain elevated.

DYSLIPIDEMIA

The dyslipidemias frequently found in poorly controlled diabetics have been traditionally attributed to excessive consumption of dietary fats. Although not a long term complication of diabetes, I mention it here because it is universally (except in India) misunderstood and mistreated. I’ve seen more than one thousand patients whose dyslipidemia was caused or exacerbated by conventional low fat/high carbohydrate diets (such as those recommended by the American Diabetes Association, the American Heart Association and the U. S. Department of Agriculture). In my experience the improvements in lipid profiles achieved by the common prescription of coenzyme A reductase inhibitors is real but marginal for most diabetics.

The one treatment that truly works for diabetic dyslipidemia is near normalization of blood sugars. This is only possible with a very low carbohydrate diet. I prescribe for diabetics no more than 6 grams of carbohydrate at breakfast, 12 grams at lunch and 12 grams at dinner. I use these amounts instead of no carbohydrate at all, so that patients will be able to consume a reasonable amount of vegetables. I have even found significant improvements of dyslipidemias in non-diabetics with this diet. It also is essential for weight loss in obese patients. I have been following such a diet myself for more than 25 years.

Table 1 lists changes in cardiac risk factors for two diabetic men who experienced cardiac events at relatively young ages. Each was subsequently transferred from a low fat diet to a very

low carbohydrate diet. I have flow sheets for about one thousand other cases with similar results.*

There are perhaps fifty or more long-term complications of elevated blood sugars in diabetes that are frequently unrecognized or inadequately treated. Many of these respond to blood sugar normalization. This is usually easy to achieve but rarely attempted.

I learned many of the diagnostic and treatment techniques described herein for the diabetic foot from the late University Professor Heinz I. Lippman, M.D. of the Albert Einstein College of Medicine, under whom I served for 15 years. Dr. Lippman was the world's foremost authority on the diabetic foot.

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The above chapter will appear in the book ***ALTERNATIVE MEDICINE AND REHABILITATION: A GUIDE FOR PRACTITIONERS***, edited by Stanley F. Wainapel, M.D., MPH, and Avital Fast, M.D., Demos Medical Publishing, 2000. © 1999.

*Because my records are not computerized, statistical analysis would be a prohibitive undertaking. Nevertheless, since my flow sheets identify patients by number instead of by name, they are available for inspection by physicians and legitimate researchers.

<u>Patient Number</u>	<u>Age at First Cardiac Event</u>	<u>Hemoglobin A_{1c} Lo Fat/Lo Carbo</u>	<u>Triglycerides Lo Fat/Lo Carbo</u>	<u>Total Cholesterol Lo Fat/Lo Carbo</u>	<u>HDL Lo Fat/Lo Carbo</u>	<u>Cholesterol ÷ HDL Lo Fat/Lo Carbo</u>	<u>LDL Lo Fat/Lo Carbo</u>	<u>Fibrinogen Lo Fat/Lo Carbo</u>	<u>Lipoprotein (a) Lo Fat/Lo Carbo</u>	<u>Body Weight (lbs) Lo Fat/Lo Carbo</u>
97055	39	6.3/5.9	225/55	195/116	41/43	3.5/2.7	120/64	316/166	113/15	225/193
97005	55	11.2/6.7	202/59	331/172	30/49	11.0/3.5	271/111	465/449	71/55	137/142

TABLE 1