

The musculoskeletal effects of diabetes mellitus

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Diabetes mellitus (DM) is a multi-system disease characterized by persistent hyperglycemia that has both acute and chronic biochemical and anatomical sequelae, with Type-2 DM representing the most common form of the disease. Neuromusculoskeletal sequelae of DM are common and the practicing chiropractor should be alert to these conditions, as some are manageable in a chiropractic office, while others are life and/or limb threatening. This paper reviews the effects of DM on the musculoskeletal system so as assist the chiropractor in making appropriate clinical decisions regarding therapy, understanding contraindications to therapy, referring patients to medical physicians when appropriate and understanding the impact that DM may have on the prognosis for their patients suffering from the myriad musculoskeletal conditions associated with this disease. (JCCA 2006; 50(1):43-50)

KEY WORDS: diabetes, musculoskeletal, chiropractic.

Introduction

Diabetes mellitus (DM) is a multi-system disease characterized by persistent hyperglycemia that has both acute and chronic biochemical and anatomical sequelae. It is thought to affect almost 17 million Americans, only 11

Le diabète sucré (DS) est une maladie multi-système qui se caractérise par une hyperglycémie persistante, qui présente, à la fois des séquelles aiguës et biochimiques, de même, que des séquelles anatomiques avec un DS de Type-2. Ce qui représente la forme la plus commune de cette maladie. Les séquelles neuromusculosquelliques du DS sont habituelles et le chiropraticien qui pratique devrait être avisé de ces conditions, car même si certaines sont traitables dans un établissement de chiropraxie, d'autres constituent un danger de mort et/ou la perte d'un membre. Cet article révisé les effets du DS sur le système musculosquellique pour aider le chiropraticien à prendre les décisions cliniques appropriées, relativement à la thérapie, comprendre les contre-indications de la thérapie, référer les patients à des praticiens lorsque nécessaire, ainsi que saisir l'impact que le DS peut avoir sur le pronostic de leurs patients, souffrant d'une myriade de conditions musculosquelliques, reliées à cette maladie. (JACC 2006; 50(1):43-50)

MOTS CLÉS : diabète, musculosquellique, chiropratique.

million of whom have been diagnosed according to the American Diabetes Association.

In type 1 diabetes, a lack of insulin results in poor carbohydrate, fat, and protein metabolism. Insulin is functionally absent, typically due to immune-mediated

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destruction of the beta cells of the pancreas, though other etiologies of beta cell destruction have also been implicated, including drugs, chemicals, viruses, mitochondrial gene defects, pancreatectomy and ionizing radiation.¹ Type 1 DM (DM1) occurs most commonly in juveniles. It can occur in adults, especially in those in their late 30s and early 40s. Unlike people with Type 2 DM (DM2), those with Type 1 DM are usually not obese and they may initially present to the clinician in physiologic crises with diabetic ketoacidosis (DKA). Symptoms typically do not become apparent until 80–85% of the beta cells have been lost. Although diabetic concordance among first degree relatives is relatively low (6–10%), there does appear to be a genetic disposition toward diabetes mellitus type II, mainly determined by genes in the major histocompatibility complex (i.e. human leukocyte antigen [HLA] region located on the short arm of chromosome 6).²

Type 2 DM represents approximately 90% of all cases of diabetes. It usually occurs in older overweight individuals and does not often present initially with DKA. It is thought that while the primary defect may be insulin resistance, many of these patients also have poor insulin production, particularly for their level of glycemia. There is a suggested genetic predisposition as well, and the prevalence varies widely by ethnicity, from a high of 18% among Native Americans and Alaska natives to a low of approximately 7% among non-Hispanic Caucasians.³ Many patients with DM 2 will ultimately require insulin treatment for good glycemic control. Presumably, the defects of type 2 diabetes mellitus occur in patients who live a diabetogenic lifestyle. Excessive caloric intake, inadequate caloric expenditure, and obesity are suspected to be superimposed upon a susceptible genotype.

There are four basic categories within the American Diabetes Association's classification system for DM. These are "Type I DM," "Type II DM," "Gestational Diabetes Mellitus"(GDM) and "other specific types." It should be noted that the terms "insulin-dependent diabetes mellitus" and "non-insulin-dependent diabetes mellitus" have been eliminated because of confusion created by these terms. These terms focus on the treatment of DM rather than the etiology of the disease. "Pre-diabetes," a condition between normoglycemia and diabetes is also recognized. These patients typically have normal or near normal glucose levels, but with high levels of circulating insulin and relative insulin-resistance.⁴

The purpose of this paper is two-fold. Chiropractors see patients with both types of DM. It is important for the practicing chiropractic doctor to recognize the effects of DM on the musculoskeletal system so as to make more appropriate clinical decisions regarding therapy in these patients, including understanding contraindications to therapy and referring patients to medical physicians when appropriate. It is also important for the DC to understand the impact that DM may have on the prognosis for their patients suffering from myriad musculoskeletal conditions associated with this disease.

In addition, it has been suggested that health care providers offer their patients counseling to promote physical activity, a healthy diet, and smoking cessation as part of the preventive health examination.⁵ It is also in this light that the musculoskeletal effects of DM are discussed in this manuscript, as most patients visiting chiropractors have musculoskeletal complaints.^{6,7} It is hoped that through appropriate counseling regarding a healthy lifestyle, the chiropractor may help to prevent some cases of

Table 1 Criteria for the Diagnosis of Diabetes Mellitus¹

<ul style="list-style-type: none"> • Classic symptoms of polydipsia, polyphagia, polyuria and weight loss with a random serum glucose >200 mg/dl • Fasting serum glucose >126 mg/dl on at least two occasions • 2 hour serum glucose 200 mg/dl during an glucose tolerance test
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Table 2 Musculoskeletal Effects of Diabetes Mellitus

<p>Muscle cramps Muscle infarction Loss of deep tendon reflexes Peripheral neuropathy Reflex Sympathetic Dystrophy Syndrome Stiff Hands Syndrome Neuropathic joints Carpal tunnel syndrome Adhesive capsulitis of the shoulder Tenosynovitis Diffuse Idiopathic Skeletal Hyperostosis Dupuytren's contracture</p>
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Type 2 DM and that the incidence of the musculoskeletal effects of DM can be reduced.

The American Diabetes Association released criteria in 2003 regarding the diagnosis of DM. (Table 1)

This manuscript will discuss some of the more common musculoskeletal manifestations of diabetes mellitus. Table 2 lists the more common musculoskeletal effects of DM.

Muscle Cramps

Muscle cramping is a relatively common manifestation of DM. It can be the result of electrolyte imbalances, hypoglycemia, peripheral vascular disease with arterial insufficiency, and/or peripheral neuropathies. The cramps tend to be more common in the lower extremities and may be seen more commonly at night. Symptoms include cramping muscle pain and, at times, fasciculations secondary to lower motor neuron lesions. These cramps may be confused with hypocalcemic cramps and the Restless Legs Syndrome.

Muscle Infarction

Diabetic muscle infarction is a rare, but potentially disabling condition. The infarction tends to be spontaneous, without a history of trauma. It affects patients with a long history of poorly controlled diabetes and is most common in diabetic patients who require insulin. Most patients affected with infarctions have multiple micro-vascular complications typical of DM including peripheral neuropathy, nephropathy, and retinopathy. Muscle infarction in this instance is mostly the result of ischemia. It can, however, been seen during episodes of diabetic ketoacidosis, especially while the patient is being treated in the intensive care unit.⁸

It should also be kept in mind that many patients with DM also have dyslipidemias, either secondary to or in addition to their DM. Therefore, in addition to their DM medication regimen, they may also be taking an HMG-coA reductase inhibitor (statin medication) for lipidemic control. Statins are, unfortunately, rather well known for their ability to cause rhabdomyolysis in some patients.⁹

The clinical presentation of muscle infarction is that of an acute onset of pain and swelling over days to weeks in the affected muscle groups along with varying degrees of tenderness. The most often affected region is the thigh or calf. Creatine phosphokinase (CPK) levels may be nor-

mal or elevated, depending upon the degree of muscular involvement. The muscle isoenzyme of CPK, CPK-MM helps to confirm the diagnosis. Other laboratory investigations are done to exclude other muscular conditions, such as tumor, infectious myositis, thrombophlebitis/thrombosis, localized myositis, or osteomyelitis. Muscle biopsy may be needed to confirm the diagnosis. The primary findings on biopsy are muscle edema and necrosis.

Rest and analgesia are the hallmarks of therapeutic management. Normal activities of daily living are not deleterious to the condition, but some physical therapy modalities may cause exacerbation. In most cases, spontaneous diabetic muscle infarction tends to resolve over a period of weeks to months.

Complex Regional Pain Syndrome

Patients with complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy syndrome and Sudek's atrophy, characteristically present with localized or diffuse pain in the upper or lower extremity usually associated with swelling, vasomotor disturbances and trophic changes including loss of hair, skin color changes, temperature changes and skin thickening.^(X) The pathogenesis of this disease is poorly understood although recent evidence suggests elevated levels of IgG in the affected extremities and impairments in phosphate metabolism. It may occur after minimal trauma to the spine or portion of an extremity, or it may be spontaneous in onset.

Treatment effectiveness is anecdotal. Purportedly effective treatments include physical therapy, analgesics, sympathetic ganglion blocks and pharmaceutical therapy.¹⁰ Some patients have recalcitrant disease that may eventually result in limb amputation.

Hydroxyapatite Deposition Disease (HADD)

Hydroxyapatite deposition disease is seen in diabetic patients at an incidence rate three times that of the general population.⁹ It is also known as calcific tendonitis and calcific periarthritis. Deposition of calcium hydroxyapatite crystals in the tendons around the shoulder is most common. These patients can present with symptoms of pain and decreased range of motion of the shoulder. Secondary to loss of sensation, some of the patients may have no pain with this condition which confounds diagnosis in some cases.

Treatment is directed at increasing range of motion and decreasing pain through the use of mobilization, physical therapy modalities and therapeutic exercises.¹⁰

Limited Joint Mobility(LJM)

A condition seen in both Type I and Type II diabetics has been described as limited joint mobility of the hand (LJMH). This is a very common condition seen in a majority of diabetic patients, although most of these patients interestingly had no overt signs of arthritis, although osteopenia was present in some.

Limited joint mobility in the foot is a common condition owing to increased foot pressure and foot ulceration.

Diabetic Stiff Hands Syndrome(DSHS)/ Cheiroarthropathy

The hands are the target for several diabetes-related complications. DSHS, also known as diabetic cheiroarthropathy or limited joint mobility, affects up to 50% of all people with type 1 diabetes and is also seen in those with type 2 diabetes.¹¹ The prevalence of this condition increases with the duration of diabetes. DSHS is also associated with and predictive of, other complications of diabetes.

This syndrome is characterized by tight, thick, waxy skin. Some suggest that this presentation is reminiscent of progressive systemic sclerosis(scleroderma). Sclerosis of tendon sheaths and limited joint range of motion are also present. It has been suggested that the underlying cause is multi-factorial. Increased glycosylation of collagen in the skin and periarticular tissues, increased collagen degradation, diabetic microangiopathy, and even diabetic neuropathy have been implicated as contributing factors.¹² Flexion contractures of the fingers may develop in the advanced stages of the condition. One indication of the presence of DSHS is known as the “prayer sign”. The patient is unable to press their palms together completely, as if praying, without a gap remaining between opposed palms and fingers. There is no specific treatment for DSHS, although maintaining as much pain free range of motion as is possible is the goal of therapy.

Neuropathic Joints

Neuropathic arthropathy, also known as Charcot joint or diabetic osteoarthropathy, is a condition causing severe destruction of joints, particularly in the feet. It occurs as a

result of a loss of sensation in the involved joints secondary to the micro-neuropathy associated with DM. This loss of sensation leads to inadvertent and often unnoticed repeated micro-trauma to the joints which leads to the degenerative changes. The condition is quite rare, affecting less than 1% of diabetic patients. It is seen in both type 1 and type 2 diabetes and the average duration of the disease in affected persons is 15 years.

The diagnosis is made based on radiographic findings, with symptoms often milder than would be expected from the degree of destruction noted on radiographs. A history of overt trauma is usually absent. Depending on the stage and severity of the arthropathy, radiographs can show degenerative changes with subluxation, bone sclerosis and fragmentation, osteolysis, periosteal reaction, deformity, and/or ankylosis. These changes have been referred to as “degenerative joint disease with a vengeance.” Diabetic peripheral neuropathy is thought to play the greatest pathogenic role in diabetic osteoarthropathy.

Treatment is generally conservative and often unsatisfactory. Both splinting/bracing to protect the area from weight bearing, and good glycemic control are oft used therapies. Sometimes a total-contact cast is applied for neuropathic joints in the foot. This should be applied by an experienced physician, and monitored and changed frequently. Unfortunately, it carries a fairly high risk of causing new injuries and ulceration secondary to the tight fit of the cast and the patient’s underlying neuropathy. Broad-spectrum antibiotics are also frequently used when skin ulcers accompany the arthropathy.

Carpal Tunnel Syndrome

Carpal tunnel syndrome (CTS) can be seen in up to one-third of diabetic patients and its prevalence generally increases with duration of the disease.¹³ A specific relationship to diabetes is thought to be the result of median nerve entrapment caused by diabetes-induced connective tissue changes, including sclerosis and collagen degradation.

CTS is typically diagnosed based on history and clinical findings. Classically, patients complain of burning, paresthesias, or sensory loss in the median nerve distribution. They may also complain of pain in the same area, often with radiation proximally into the forearm and elbow. The pain may awaken people from sleep and is aggravated by activities involving wrist flexion or extension.

It is important to examine patients for possible motor

weakness from median nerve compression. Assessment of thenar muscle strength and examination of the hand for the presence of the muscle atrophy help accomplish this task. It is important that clinicians intercede in CTS before the development of this type of atrophy.

Diabetic patients may have paresthesias secondary to peripheral neuropathy and this condition must be differentiated from CTS. Electromyography/nerve conduction velocity (EMG/NCV) testing can confirm the diagnosis of CTS in uncertain cases and can also help to localize the site of entrapment.

Management of CTS is the same for diabetic patients as for non-diabetic patients, with the exception of glycemia control in diabetics. Conservative treatment involves the use of volar wrist splints, particularly at night, with or without adjunct non-steroidal anti-inflammatory drugs (NSAIDs) in early uncomplicated cases of CTS. Changing the ergonomic work and home environments should be made when appropriate. Local corticosteroid injection of the carpal tunnel may prove helpful in some cases, as may joint mobilization. Patients with severe or refractory cases, should be referred for possible surgical correction.

Adhesive Capsulitis of the Shoulder

Adhesive capsulitis, or frozen shoulder, has been reported in approximately 20% of diabetic patients. This term refers to a stiffened glenohumeral joint usually caused by thickening and contraction of the joint capsule which results in a substantial decrease in capsular volume capacity. Patients report shoulder stiffness, along with decreased range of motion and pain, although the pain of this conditions in diabetics is typically less than that of the general population. The decreased range of motion is worst in abduction and external rotation. Internal rotation is affected least. It appears to be twice as common in diabetic patients. Therapy is largely conservative and involves minimizing progress of the adhesions, mobilization of the shoulder including gentle stretching and range of motion exercises, and the use of analgesics and/or intra-articular injections.

Tenosynovitis

Flexor tenosynovitis, also know as trigger finger, is a frequent complication in the hands of diabetic patients. People complain of a “catching” or “locking” sensation that

may be associated with pain in the affected fingers. Examination shows a palpable nodule and thickening along the affected flexor tendon sheath overlying palmar aspect of the metacarpophalangeal joint. Occasionally, the locking phenomenon may be reproduced with active or passive finger flexion. This complication is thought to have the same pathogenesis as DSHS, and its incidence is similarly related to the duration of diabetes.

Initial treatment involves injecting corticosteroids into the tendon sheath. If this is unsuccessful, patients will most likely need to be seen by an orthopedic hand surgeon.

Dupuytren’s Contracture

Thickening, shortening, and fibrosis and nodule formation of the palmar fascia is termed Dupuytren’s contracture(DC). These pathologic changes result in flexion contractures of the fingers. The fourth finger is most often affected, but any the second through fifth digits may be involved. DC has been reported in over 1/3 of diabetic patients. Its pathogenesis is thought to be the same as that for DSHS. Like DSHS, the prevalence of this condition increases with disease duration. Occasionally, it may also be seen early in the course of diabetes. This condition is the most commonly seen musculoskeletal complication of diabetes seen in the hand. Varied success has been reported with local cortico-steroid injections. Surgical intervention may be needed for severe cases.

Osteoporosis

Whether or not DM is associated with an increased risk of osteopenia or osteoporosis is a topic of much debate in the current literature. There are some studies that suggest that patients with DM, especially DM 1, do have some loss of bone mineral density (BMD). There is biological plausibility in this, given that DM 1 patients have excessive renal calcium losses related to an osmotic diuresis with glycosuria, and they have deficiencies in both insulin and insulin-like growth factor 1 (IGF-1) which are important factors for bone growth and development. Postmenopausal women with diabetes are at greater risk of hip fracture than age-matched controls.¹¹

DM 2, however, has a scattering of inconsistent studies, some showing decreased BMD, and some showing either no change, or actually an increase in BMD. The only thing that seems clear is that morbidity is greater in diabetic patients vs non-diabetic patients after a skeletal

fracture, and therefore increased vigilance is in order.

Osteomyelitis/Septic Arthritis

Osteomyelitis and septic arthritis are rare but serious infections by pyogenic bacteria invading the cortex of bone or the joint. Upon presentation, most affected patients will report vague and nonspecific constitutional symptoms such as fevers, chills, lethargy or malaise. Local pain, swelling and erythema may also be present, though are commonly nonspecific. Diagnosis can often be made by plain film x-rays, but occasionally more sophisticated imagery such as nuclear medicine bone scans or magnetic resonance imaging (MRI) may be necessary.

The pathological sequelae of DM leads toward increased risk of infections in general, but of osteomyelitis in particular among diabetic patients. Long-standing diabetes is associated with neuropathic and microvascular changes that can predispose to an infection.¹² A lack of adequate blood supply decreases the transport of parenteral antibiotics to the site of the infection, and a lack of tight glycemic control impairs neutrophil function, decreasing the body's ability to respond adequately to the infection.

Diffuse Idiopathic Skeletal Hyperostosis

Diffuse idiopathic skeletal hyperostosis (DISH) is a disease characterized by flowing calcification of paraspinal ligaments. The intervertebral discs, facet joints, and sacroiliac joints are most often unaffected. The disease is most common in the thoracic spine, followed by the cervical spine and finally the lumbar region. It may demonstrate calcification of extra-axial ligaments and tendons as well.

The underlying pathophysiology is not understood. DISH has a higher prevalence among diabetic patients than among people without diabetes. In fact, approximately 26% of patients with DM may eventually develop DISH.¹⁴ More specifically, it is commonly seen in association with type 2 diabetes, particularly in obese patients. It is thought by many to be exacerbated by hyperinsulinism and elevated growth hormone levels.

Patients complain of stiffness in the neck and back, with decreased range of motion. Pain is generally not a prominent symptom. Treatment consists of physical therapy and therapeutic exercise. There is no convincing evidence that adequate glycemic control delays the onset or

improves the symptoms of this condition.

Ossification of the Posterior Longitudinal Ligament

Ossification of the posterior longitudinal ligament in the cervical spine is more common in diabetic patients¹⁵ and is more common in the Japanese population. The ligament may ossify in these patients and may lead to narrowing of the cervical spinal canal with resultant canal stenosis in some patients. It has also been seen in patients with DISH and in patients who consume high-salt levels and in patients who consume a great deal of meat products as well.

Patients often complain of a stiff neck and progressive reduction in neck movement over time. Management is directed at maintaining mobility with compromising the spinal canal. In severe cases, decompressive surgery is necessary, although this is unusual.

Clinical Pearls

- Diabetes Mellitus is a common disease affecting a relatively large portion of the population.
- Signs and symptoms of DM do not become evident until approximately 80% of the beta cells are destroyed.
- Muscle infarction (acute pain, swelling, elevated CPK-MM levels) is a rare but life-threatening condition that requires immediate medical management.
- HADD is a condition commonly seen in diabetics and managed well with conservative measures in most cases.
- DSHS is common in diabetics and although no definitive therapy exists, the goal of management is to maintain as much pain free range of motion as possible.
- Neuropathic joints, most commonly seen in the foot and ankle in diabetics, are a rare but important complication of DM.
- CTS is a common diabetic sequela and is often managed successfully with conservative measures.
- Joint and/or bone pain and a fever in a diabetic should raise strong suspicion of osteomyelitis/septic arthritis.
- DISH and OPLL are relatively commonly seen in diabetics and no long-term routinely effective therapy has been developed, although the goal of any treatment should be to maintain as much pain free mobility of the affected joints as possible.

Summary

Diabetes is a common condition which is becoming even more common with the passage of time. Chiropractors have an opportunity to intervene at several different points in the diabetes time line. By emphasizing and recommending healthy lifestyle choices to their patients, they can hopefully help to decrease the incidence of obesity, alcohol abuse and dietary indiscretions that can predispose to diabetes, especially in Native American, African-American and Hispanic populations, in which the inherent risk of diabetes seems to be even greater than it is within the non-Hispanic Caucasian population.

By concentrating upon secondary prevention in those patients who already show signs of glucose intolerance or who are already in a diabetic state, complication rates can be reduced, or the amount of time before complications arise can be lengthened. Although there is little specific data about the progression of the discussed musculoskeletal complications of diabetes, several studies, including the United Kingdom Prospective Diabetes Study (UKPDS), the Diabetes Control and Complications Trial (DCCT), and the Japanese Kumamoto study showed that aggressive control of serum glucose in diabetics slowed the progression of microvascular disease, including retinopathy, nephropathy and neuropathy. If microvascular disease progression is slowed, it can likely be assumed that the sequelae of microvascular disease would also be slowed.¹⁸⁻²¹

By recognizing the musculoskeletal effects and complications of diabetes, chiropractors can better manage, and help to manage, many of the pathologies that are currently seen as a natural consequence of the high glucose state.

In making the proper diagnosis and offering the appropriate treatment and/or referral, the chiropractor then distinguishes him or herself as an integral and cooperating member of the total healthcare team.

References

- Behrman: Nelson Textbook of Pediatrics, 17th ed. p1947. Elsevier 2004.
- Veijola R, Reijonen H, Vahasalo P, Sabbah E, Kulmala P, Ilonen J, Akerblom JK, Knim M. The childhood diabetes in Finland study group. HLAQB1-defined genetic susceptibility, β -cell autoimmunity, and metabolic characteristics in familial and nonfamilial insulin-dependent diabetes mellitus. 1996. *J Clin Invest* 98: 2489–2495.
- 1999–2001 National Health Interview Survey.
- Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 2003. *Diabetes Care* 26:S5-S20.
- Missed opportunities in preventive counseling for cardiovascular disease—United States, 1995. *Morb Mortal Wkly Rep* 1998; 47:91–95.
- Coulter et al. Patients Using Chiropractors in NA Spine 2002; 27(3):291–298.
- Hawk C, Long C, Boulanger K. Prevalence of non-musculoskeletal complaints in chiropractic practice : report from a practice-based research program. *JMPT* 2001; 24(3):157–169.
- Casteels K. Rhabdomyolysis in diabetic ketoscidosis. *Pediatr Diabetes*. 2003; 4(1):29–31.
- Bottorff M, Hansten P. Long-term safety of hepatic hydroxymethyl glutaryl coenzyme A reductase inhibitors: the role of metabolism-monograph for physicians. *Arch Intern Med* 2000; 160:2273–2280.
- Teasdall R, Smith B, Koman L. Complex regional pain syndrome (reflex sympathetic dystrophy). *Clin Sports Med* 23 (2004); 145–155.
- Mavrikakis ME, Drimis S, Kontoyannis DA, Rasidakis A, Mouloupoulou ES, Kontoyannis S. Calcific shoulder periarthritis (tendinitis) in adult onset diabetes mellitus: a controlled study. *Ann Rheum Dis*. 1989 Mar; 48(3): 211–214.
- Garcia GM, McCord GC, Kumar R. Hydroxyapatite crystal deposition disease. *Semin Musculoskelet Radiol*. 2003 Sep; 7(3):187–193.
- Aljahlan M, Lee KC, Toth E. Limited joint mobility in diabetes. *Postgrad Med*. 1999 Feb; 105(2):99–101, 105–106.
- Wilbourn AJ. Diabetic entrapment and compression neuropathies. In: Dyck PJ, Thomas PK, editors. *Diabetic neuropathy*. Philadelphia: WB Saunders; 1999. p 481–508.
- Nicodemus KK, Folsom AR. Type 1 and Type 2 diabetes and incident hip fractures in postmenopausal women. *Diabetes Care*. 2001; 24:1192–1197.
- Tice AD. Outpatient parenteral antimicrobial therapy for osteomyelitis. *Infect Dis Clin North Am*. 1998; 12: 903–919.
- Kobashi G, Washio M, Okamoto K, Sasaki S, Yokoyama T, Miyake Y, Sakamoto N, Ohta K, Inaba Y, Tanaka H; High body mass index after age 20 and diabetes mellitus are independent risk factors for ossification of the posterior longitudinal ligament of the spine in Japanese subjects: a case-control study in multiple hospitals. *Spine*. 2004 Apr 23; 29(9):1006–1010.

- 18 The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and the progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993; 329:977–986.
- 19 UK Prospective Diabetes Study Group. Intensive blood glucose control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; 352:837–853.
- 20 UK Prospective Diabetes Study Group. Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998; 352:854–865.
- 21 Ohkubo Y, Kishikawa H, Araki E et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract* 1995; 28:103–117.

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