CHAPTER **56**

CIGARETTE SMOKING AND ITS EFFECT ON THE MUSCULOSKELETAL SYSTEM

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Cigarette smoking carries with it many detrimental effects to the human body. Many are common knowledge and many are not. Smoking remains an epidemic in the industrialized world with 26.2 million men and 20.9 million women smokers in the US alone. Around 15 billion cigarettes are sold daily, which is approximately 10 million every minute. Smoking related diseases have been linked with deaths in 1 in 10 people. About 1 in 5 young teens smoke and this is the common time in life that one begins smoking.[1]

Cigarette smoking is known to have 2 phases, the volatile and the particulate phases. The volatile phase is longer in length and accounts for around 95% of the cigarette smoke. There are almost 500 different gases released during this phase and include nitrogen, carbon monoxide and many others. During the particulate phase there are almost 3,500 gases released including nicotine, nornicotine, and anatabine. The majority of the carcinogens that exist in the cigarette smoke are in the particulate matter.[2,3] Nicotine is the ingredient that leads to the addictive properties of cigarette smoking. Nicotine has been shown to increase platelet aggregation and decrease microvascular prostacyclin levels. Nicotine also has been shown to inhibit the function of fibroblasts, red blood cells, and macrophages.[3,4] Carbon monoxide has many detrimental effects on the body due to its higher affinity for hemoglobin than does oxygen. This higher affinity leads to displacement of oxygen from the hemoglobin and therefore lower oxygen tension in the tissues.[5] This review will discuss some of the many effects cigarette smoking has on the musculoskeletal system in order to educate the podiatric surgeon as to the impact smoking may have on their daily practice.

Bone healing occurs in 3 distinct phases, the initial inflammatory phase, followed by the reparative phase, and lastly the remodeling phase. The initial inflammatory phase consists of a hematoma formation caused by the bleeding of bone and periosteal vessels. Local vasoconstriction then occurs secondary to the injury. The coagulation system then releases potent vasoactive mediators. The oxygen tension then subsequently drops at the fracture or osteotomy site. Local vasodilatation then occurs, which allows an influx of reparative cells. This initial phase lasts approximately 3-7 days and clinically is characterized by pain, swelling, erythema, and muscle splinting. The reparative phase consists of necrotic bone resorption by osteoclasts. The fibrin within the fracture hematoma is then replaced by cartilage forming the soft callus. Bone then gradually replaces the cartilage through the process of endochondral ossification resulting in a hard callus formation. This initial bone formed is immature woven bone. The final remodeling phase is when the immature woven bone is converted to lamellar bone and the remaining callus is resorbed. This bone healing process is usually complete in approximately 20 weeks, but remodeling can occur from weeks to years.

Primary bone healing is possible with rigid internal fixation and the hard callus formation is not necessary due to a lack of motion at the fracture or osteotomy site. In this form of bone healing, the bone ends are in direct contact with each other and lamellar bone forms by direct extension of the osteons. A cutting cone of a cluster of osteoclasts is formed and cuts across the fracture line and are followed by osteoblasts, which lay down new bone.

Delayed or nonunion of bone has been defined by the Food and Drug Administration as a fracture that is at least 9 months old and has not shown any progressive signs of healing for 3 consecutive months. Cigarette smoking and its constituents have been shown to directly impair multiple aspects of these phases of bone healing. Nicotine releases adrenal catecholamines, which results in vasoconstriction and decreased tissue perfusion. Fibroblasts have been shown to nonspecifically bind to and rapidly internalize nicotine, which results in an alteration of cell metabolism, including protein secretion and collagen synthesis. Nicotine decreases prostacyclin production. Prostacyclin is a vasodilator that aids

in healing processes. Prostoglandin I2 production is decreased by nicotine, which delays healing of endothelia. Carbon monoxide binds to hemoglobin forming carboxyhemoglobin. Normally one has levels of carboxyhemoglobin of 0.5-1%. Smokers can have levels of 1-20% on average. The presence of carboxyhemoglobin causes a left shift of the oxygen-hemoglobin saturation curve, which results in tissue hypoxia. Hydrogen cyanide, found in cigarette smoke, has been shown to inhibit cellular respiratory enzymes.[6]

Cigarette smoking has been correlated with delayed fracture healing. Hossam et al displayed in a mouse model that chondrogenesis was delayed in the smoke exposed group. They found that at day 7, the mice exposed to the smoke had a smaller fracture callus. At day 14 the smoking group had more chondrogenesis occurring while the non-smoking group had more active bone proliferation.[7] Lau et al used rabbits with an osteotomy created in the mid fibula and found the incidence of delayed or nonunion was twice as high in the rabbits exposed to cigarette smoke.[8] Daftari et al showed decreased revascularization within cancellous bone grafts implanted in a rabbits eye in those rabbits that received nicotine subcutaneously. They were able to conclude that this inhibition in graft revascularization was the pathophysiological mechanism of adverse bone healing in spinal fusion procedures.[9] Ueng et al demonstrated that rabbits receiving tibial lengthening that were exposed to cigarette smoke had a delay in granulation tissue resorption, bone formation, and remodeling.[10] Reibel at al demonstrated in rabbit models that nicotine decreased the vascular ingrowth into the autogenous cancellous bone graft.[11] Silcox et al showed a 0% solid fusion rate compared with 56% fusion rate in the spine of rabbits exposed and not exposed to nicotine, respectively.[12] Brown et al found a surgical nonunion rate of 40% in smokers compared with 4% in nonsmokers undergoing a two-level laminectomy and fusion.[13] Kyro et al found a 50% nonunion rate in smokers compared with 32% in nonsmokers who had a tibial shaft fracture.[14] Gualdrini et al observed a 33% shorter healing time from septic pseudarthrosis of the tibia as compared with smokers.[15] Cobb et al in a case control study found a 3.75 times higher relative risk of nonunion of ankle arthrodesis in smokers.[16]

Raikin et al evaluated long bone healing in a rabbit model. They plated 40 midshaft tibial osteotomies. They found a 17.2% average difference in callus formation between the nicotine and non-nicotine exposed groups. They also found a significant lag in formation of cortical continuity in the nicotine exposed group. Biomechanical testing also revealed the nicotine exposed bones were 26% weaker in 3-point bending compared with a placebo group.[17] Ishikawa et al conducted a retrospective review of the rate of hindfoot fusions in smokers as compared with nonsmokers. They evaluated a group of 160 patients undergoing a combination of isolated subtalar, talonavicular, and calcaneocuboid fusions as well as double and triple arthrodeses. They found a significantly higher nonunion rate in the smoking group as compared with the nonsmoking group (18.6% versus 7.1%). A trend was also demonstrated that those patients who had quit smoking prior to surgery had a higher nonunion rate of 11.1% compared with nonsmokers, but it was lower than active smokers.[18]

A correlation between smoking and delayed healing of ligaments has also been demonstrated. Gill et al evaluated mice who received injury to the medial collateral ligament. They found a higher Type I collagen gene expression in the nonsmoking exposed group. They also found decreased cellular density at the injured site at day 7 in the mice exposed to smoke.[19] Multiple studies have correlated cigarette smoking to low back pain. Kelsey et al determined that cigarette smoking in the year prior to presenting to a physician increased the risk of having a prolapsed disk. They also discerned a weak dose response for smoking and subsequent risk of disk prolapse.[20] An et al demonstrated a higher relative risk of lumbar disk disease in smokers. They were able to correlate actual disk disease to smoking and not just the subjective complaint of low back pain.[21] Newby et al demonstrated in their study that smoking has a dramatic adverse effect on the endogenous fibrinolytic capacity of the vascular endothelium, which leads to an increase in the risk of atherothrombotic disease or microvascular occlusive disease.[22] Jayson et al have subsequently demonstrated that a decrease in fibrinolytic activity is common in many chronic back pain syndromes.[23]

Wound healing delays due to nicotine and cigarette smoking has been studied as well. This effect of cigarette smoking is very significant to the foot and ankle surgeon. Mosely and Finseth were among the first to demonstrate the detrimental effects of cigarette smoking on wound healing. They suggested that the vasocontriction and levels of carbon monoxide in the blood could retard proper wound healing. They showed that smoking a single cigarette caused severe digital vasoconstriciton.[24] Leow and Maibach showed in their review a decrease in cutaneous blood flow in those subjects exposed to nicotine.[5] Jensen et al showed a decrease in the subcutaneous oxygen tension in the forearm of those patients exposed to cigarette smoking.[25] Forrest et al examined the skin hemodynamics of rats who had skin flaps that received nicotine beforehand. They found a much smaller area of viability in the flaps of those rats

exposed to the nicotine.[26] Abidi et al demonstrated prolonged wound healing times in patients who smoked in the perioperative period, although it was not statistically significant.[27]

There are also many studies that reveal an increased rate of osteoporosis in smokers. Cornuz er al found an increased relative risk of hip fractures in women who smoked.[28] La Vecchia et al showed very similar results in their own study.[29] Although most of the studies show a higher relative risk of fracture and osteoporosis in women, there are studies correlating similar findings in men.[30]

Postoperative complications are an important aspect of podiatric and orthopaedic surgery and must be considered for any patient undergoing any sort of surgical intervention. Moller et al studied 811 consecutive patients who underwent hip or knee arthroplasty. Of the 811 patients 232 were smokers and 579 were nonsmokers. They were able to conclude that smoking alone was the single most important risk factor for the development of complications after elective arthroplasty of the hip or knee. The smokers had higher rates of wound complications as well as cardiopulmonary complications. The group of smokers had extended hospital stays if they experienced wound complications. The smoking group also were more likely to receive more surgical intervention down the road.[31]

In conlusion, the effects of cigarette smoking on the musculokeletal system are numerous and can be quite detrimental. The rates of smoking in the US remain startlingly high, especially in the younger population. These above mentioned studies as well as many others have correlated cigarette smoking with adverse effects on bone mineral density, lumbar disk health, the relative risk of hip and wrist fractures, as well as the dynamics of bone and wound healing.[32] All of these above complications can and do in some ways impact the podiatric surgeon and his or her patient population. It is therefore important for the podiatric surgeon to be conscious of the risks of cigarette smoking and its effects on the musculoskeletal system so as to make educated decisions about who is at risk and who is an appropriate surgical candidate.

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