
Injectable Silicone and the Foot: A 41-Year Clinical and Histologic History

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BACKGROUND. Since 1964, the author has investigated injectable liquid silicone as a soft tissue substitute for the loss of plantar fat. This form of fatty tissue depletion over the sole is closely linked to a common painful weight-bearing foot disorder, metatarsalgia, and to painless diabetic foot ulcers.

OBJECTIVES. To present the history of injectable silicone, corporate interest, individuals who helped pursue approval, its misuses, and events that have delayed its availability.

MATERIALS AND METHODS. Dow Corning Corporation's 360 Medical Fluid of 350 centistoke was injected beneath corns and calluses in 1,585 patients. Diabetic neuropathic foot ulcers were injected after healing in an effort to prevent their recurrence. Sur-

gical and postmortem specimens were gathered for histologic analysis.

RESULTS. There was no evidence of significant adverse response in long-term clinical follow-up. Silicone specimens studied by two departments of pathology found no inflammation, infection, allergy, or granulomas.

CONCLUSIONS. Medical Fluid silicone appears to be safe, effective, and stable biomaterial for treating weight-bearing loss of plantar fat. Trademarked PodiSil (Richard-James Inc., Peabody, MA, USA), a 350-centistoke injectable silicone has been approved for marketing in Europe for the prevention of diabetic foot ulcers.

SOL W. BALKIN, DPM, HAS INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

The Clinical Problem

Human feet traverse 100,000 miles in a 75-year life span, so it is understandable that forefoot plantar pain—metatarsalgia—is the most common pressure-related foot disorder. When including lesser digits, about 5% or 15 million adults in the United States have trouble with corns or calluses.

Feet that lack the warning sign of pain, as with diabetic neuropathy, develop painless corns or plantar calluses that become painless ulcers and are epidemic in scope. Skin insensitivity and high peak pressure points are implicated in 80% of 100,000 diabetic lower extremity amputations yearly in the United States. Early problems go unnoticed because people without pain rarely look at the bottoms of their feet. Calluses and forefoot wounds are further overlooked because many physicians also fail to examine patients' feet. Medical professionals can help reduce the amputation rate by requiring that diabetic patients remove their shoes and stockings. In a 1-minute examination, the digital and plantar surfaces of both feet can be tested for lack of skin sensation and the presence of painless corns, calluses, bunions, or hammer toes. Any of these may be silent signs of impending ulceration—or worse.

A Critical Causation Factor

The cumulative effects of excessive weight-bearing forces in both painful and painless feet are linked to a localized loss of essential adipose tissue. In feet with sensory protection, a lack of plantar fibrofatty padding leaves microneural and pressure-sensitive pacinian corpuscles unprotected from the gouging effects of bone. Fat pad depletion results in weight-bearing pain that ranges from moderate to intolerable. A decrease in plantar fat in the neuropathic foot places the patient at risk of wounds that can remain open for months or years. The key to relieving pressure-bearing pain or preventing or healing a plantar ulcer is pressure reduction. Over-the-counter remedies, professionally made in-shoe supports, and special shoes are mostly ineffective when dealing with forefoot pain or ulceration owing to fat pad atrophy.

Animal Studies

The Dow Corning Corporation stated that it would investigate only 360 Medical Fluid of 350-centistoke viscosity as used in their facial study. In 1967, the Medical Research Committee at Cedars-Sinai Medical Center, Los Angeles, California, USA, approved an animal research proposal of mine. At their vivarium, Charles A. Carton, a clinical professor of neurological surgery at the UCLA Medical Center, Los Angeles, permitted the injection of silicone into the pads of 40 dogs under his study. Dr. Carton was investigating end-to-end blood vessel anastomosis for eventual use in brain aneurysms. Under general anesthesia, the cen-

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tral pads were injected with 2 to 4 mL of Dow's 360 Medical Fluid. Specimens were retrieved for histologic analysis when the animals were euthanized. The longest-duration specimen was 15 months. No inflammation or granulomas were found.¹

Collagen and Autologous Fat

Forefoot pressure reduction by injection of collagen started in 1985 when the Collagen Corporation (Palo Alto, CA, USA) received US Food and Drug Administration (FDA) approval to market Keragen. This product was used widely by podiatrists to subdermally augment corns and calluses. Sales dwindled, and it was removed from the market in 1990 when found ineffective because it dissipated rapidly on weight bearing. Keragen was highly promoted and understudied. In 1993, a procedure to restore plantar fat was introduced: harvesting and injecting autologous fat into the heel or ball. Four to 6 weeks of non-weight bearing by special shoes or crutches was required postinjection. This procedure never became popular because autologous fat was soon reabsorbed.

Historical Callus Care

Centuries of health care providers have offered patients with calluses lifelong trimming, pads, in-shoe supports, and a myriad of topical agents. In the past 100 years, many bone surgical procedures have been advocated. Surgery to relieve painful calluses requires removal of the plantar portion of a lesser metatarsal head, its entire removal, or dorsal elevation. With a severe callus under a first metatarsal head, sesamoid excision is considered an acceptable option. Similarly, plantar ulcers beneath bony prominences present equally challenging conservative or surgical choices that invariably involve pressure reduction.

Origin of Injectable Silicone for the Foot

The idea of using injectable fluid silicone to augment plantar fat came during a hospital staff lecture in 1963. The speaker, Harvey D. Kagan, an osteopathic physician, who was granted an MD degree in 1962, presented before and after slides on injectable silicone for female breast enlargement. Dr. Kagan introduced the procedure into the United States from Rin Sakurai, MD, of Tokyo, Japan, an early originator of injectable silicone use (Figure 1). Dr. Sakurai reputedly injected over 100,000 patients, saw 60 patients a day, and claimed to have started injecting breasts in 1946.² Dr. Kagan stated that he had injected some 100 women during the previous 1½ years. The amounts he injected were massive: from 750 to 2,000 cc for breast and body contouring.³ Injecting women's breasts, although never authorized by any regulatory agency, became a popular procedure worldwide. Among an estimated 50,000

women who received these injections in the United States were 10,000 showgirls and waitresses in Nevada.⁴

Legal Action

Following silicone breast injections, physicians in Nevada encountered numerous women with serious breast problems. Some required partial or total mastectomy for infection and skin necrosis, whereas, nationwide, a few deaths occurred after intravascular injections. In 1975, the State of Nevada banned the sale and use of liquid silicone into the human body and made a violation a felony.⁵ This law was amended in 1987 to allow the use of silicone injections to treat detached retinas.⁶ In 1976, California passed legislation that made silicone breast injections a misdemeanor but allowed its use for medical purposes. Had the California law been as restrictive as that in Nevada, it would have effectively ended my work. Sadly, complications are ongoing because ill-informed or uncaring physicians and charlatans continue to augment breasts,⁷ legs,⁸ and faces⁹ with unknown silicones or other oily substances.

Misuse beyond Breast Injections

Silicone injections were widely misused long before Dow Corning Corporation's official facial studies conducted in the 1960s and 1970s. There were no established techniques or amounts to inject for specific indications.

Authorized facial investigators were likewise unaware of a safe single or total amount that could be injected at one site. Some officially studied facial hemiatrophy patients received several hundred milliliters, with resulting complications, including migration. One woman in the study was known to have suffered a significant loss of facial tissue. The patient developed a severe chronic inflammatory reaction and required an en bloc excision of the area and flap reconstruction. She had Weber-Christian



Figure 1. In 1966, at a geisha house in Tokyo for a discussion of fluid silicone with Rin Sakurai, MD, on the right. Mrs. Balkin is on the left.

disease, which may have been a contraindication in using liquid silicone.¹⁰

Private practice physicians used silicones of unknown origin and purity, assuming that, made sterile, this relatively inert material would be safe regardless of the amount injected. Other than breast injections, legs were recontoured. Buttocks and penises were enlarged, with physicians unaware that the volumes used far exceeded the amount that would remain stable.

Two examples of misuse came to my attention. A young male who received penile injections related the following history to me: A Las Vegas chiropractor came to a West Hollywood, California, home with silicone and weekly injected the penises of homosexual males. The injections were designed to make a visual bulge in tight pants. He was a bisexual and said that his penis hurt during anal intercourse and also turned women off with its appearance (Figure 2). He was referred to Franklin Ashley, MD, head of plastic surgery at the University of California, Los Angeles. The man called months later to say that some silicone was removed, but painful problems during sex persisted.

Another instance of misuse came from a young woman who was dissatisfied with her thin legs and convinced by a physician that he could make her calves shapely with silicone injections. After failure, she was distraught and presented painless but marked edematous ankles and feet where the silicone had migrated (Figure 3). Complications following honest mistakes, stupidity, or greed have so clouded the issue of injectable silicone that the availability of the fluid for useful applications has been blocked.

Silicone Foot Injections

Compared with the huge silicone amounts Dr. Kagan injected, it appeared reasonable that tiny fractional doses into the foot would be safe. Dr. Kagan was informed of my

intended podiatric use and provided a 50 mL bottle of Sakurai fluid. Independent study began on April 4, 1964, when a 76-year-old male patient agreed to receive silicone for a painful plantar callus of 6 years' duration. The callus required palliative trimming every 3 to 4 weeks to maintain pain-free walking. There was guarded optimism that the silicone would provide relief, assuming that the fluid might dissipate on weight bearing. Deeply subdermal, 0.20 mL of silicone was placed under the left fifth metatarsal head during each of four weekly visits. To my amazement and delight, following the fourth injection, he stated that there was no longer any weight-bearing pain. Discomfort returned after 1 year, and two booster amounts were given, which again stopped the pain. Callus trimming was reduced to once yearly for 3 years followed by 3 years with no need of care until his death. This success became routine in following years.

Human Histologic Host Response

In the mid-1970s, Leo Kaplan, MD, head of anatomic pathology at Cedars-Sinai Medical Center, agreed to review the microscopic slides, paraffin blocks, and post-mortem specimens of silicone-injected patients (Figure 4). He found that the fluid was retained in situ owing to an essentially noninflammatory histiocytic silicone engulfment and fibrous tissue response. Dr. Kaplan performed a partial autopsy on one patient and a full autopsy on



Figure 2. Attempted penile enlargement by multiple silicone injections in a bisexual male produced a gross deformity.



Figure 3. Following bilateral silicone calf injections, a woman experienced extensive fluid migration to her ankles and feet. Normally prominent anatomic landmarks, the medial and lateral malleolar bones and Achilles tendon, were obscured.

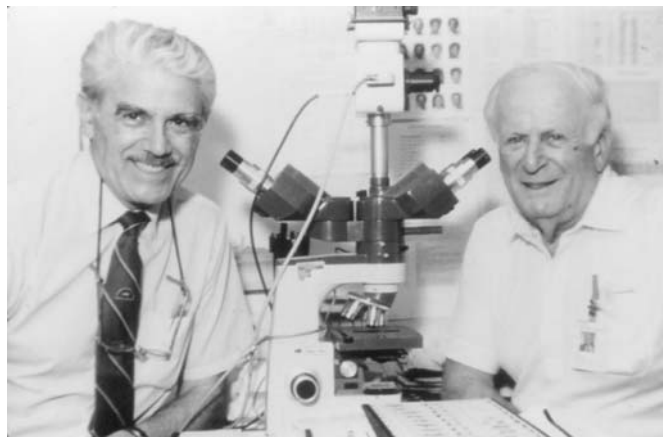


Figure 4. Leo Kaplan, MD, on the right at his teaching microscope at Cedars-Sinai Medical Center in 1975. Dr. Balkin is on the left.

another to determine migration to inguinal, hypogastric, iliac, and periaortic lymph nodes. Tissue from major viscera, such as the liver, kidney, lungs, and spleen, was also sampled. No evidence of silicone migration was found beyond the inguinal nodes.

A 25-year study of silicone's pressure-reducing effects in diabetic feet with histopathologic analysis was published in 1991.¹¹ Scott Nelson, MD, of the Department of Pathology at UCLA Medical Center, reviewed Dr. Kaplan's work plus newly gathered silicone-injected tissue. One hundred forty-eight surgical and postmortem specimens were gathered from 49 patients. The longest period that silicone was in vivo in a specimen was 38 years. Regional lymph nodes were sampled from 12 of the deceased patients. Long-term histopathologic analysis of foot-injected specimens found that the host response to injections consisted of a banal and stable fibrous tissue formation.¹²

Corporate Interest and Authorized Study

In the early 1980s, Robert Rylee II, president of health care at the Dow Corning Corporation, recognized the patient benefits and marketing potential of silicone for the foot. Under the guidance of Eldon Frisch, a Dow Corning body parts specialist, the Institutional Review Board of Los Angeles County–University of Southern California Medical Center approved a protocol to investigate injectable silicone. A 2-year study began in 1986 in the Podiatry Department headed by Howard J. Marshall, DPM. One hundred twelve patients with foot pressure disorders were admitted into the study. Most patients presented with digital or plantar pain, seven had diabetic neuropathy, and three had leprosy (Hansen's disease) with foot insensitivity. Although the results were promising, Dow Corning chose not to pursue further studies. This was partly due to the difficulty in getting a sufficient number of transient patients to return for follow-up and Dow's

concerns on how to control injection misuse. Additionally, there were early medical and media reports about alleged immune diseases caused by the silicone gel-filled breast implants they marketed. The breast implant issue came to a head in January 1992 when David Kessler, head of the FDA, instructed that they be removed from the market. A multibillion dollar class action suit forced Dow Corning out of the medical silicone device industry, which ended their efforts toward gaining fluid silicone approval for the foot. That action set my work back some 15 years.

Nir Kossovsky, MD, a pathologist at UCLA Medical Center, was a key witness for the plaintiffs' attorneys. He was very engaging and convinced juries that silicone implants caused inflammation, which he said could progress to connective tissue disease—a hypothetical sequence stated as fact. There remains no good evidence for it.¹³

England's Department of Health conducted three separate studies in the 1990s and, finding no link between the breast implant and disease, did not remove them from the market. France banned the implants for 1 year but, finding no related health problems, reinstated their use.

Don McGhan of the McGhan Medical Corporation, a California-based maker of silicone breast implants, decided to seek marketing of fluid silicone for the foot. Owing to legal and media demonization of silicone products, the study was conducted outside the United States. In 1996, the company sponsored the first double-blind, placebo-controlled study involving silicone in the insensitive diabetic foot. The trial was conducted in England at the Manchester Royal Infirmary and headed by Andrew J. M. Boulton, MD, professor of medicine. The published findings indicated that silicone thickens subcutaneous tissue, thereby reducing pressure, which is critical for the treatment and prevention of diabetic foot ulcers.¹⁴ Despite impressive results, an attempt to market the fluid was suspended owing to deepening product liability concerns.

In 2000, a third company, Wright Medical Technology (Arlington, TN, USA), pursued injectable silicone for the foot. Wright made elastomeric silicone implants developed by orthopedist Alfred Swanson, MD, for arthritic lesser joints of the hand and foot. Swanson's work revolutionized hand and foot reconstruction by permitting a surgical return to pain-free function. Wright also decided that getting the fluid to market was too risky at the time, and for a third time, liquid silicone for the foot was placed in limbo.

Richard-James Inc. (Peabody, MA, USA) was the fourth company to express interest. In 1997, this company obtained FDA approval to market Silikon 1000 for the treatment of detached retina. Retinal surgeons consider this use the standard of treatment. Richard-James Inc. made significant progress when in July 2004 it received a CE Mark allowing the marketing of PodiSil, a 350-centistoke silicone fluid in Europe. The fluid is indicated for the reduction of abnormal pressures and the prevention of

diabetic foot ulcers. Efforts are under way to seek federally authorized diabetic foot studies in the United States.

Results

Between April 1964 and January 2005, 1,585 of my patients with 4,000 to 5,000 digital or plantar sites received 25,000 recorded silicone injections. Long-term follow-up indicates that 60 to 80% experienced moderate to complete pain relief and elimination of calluses. Fifty percent of plantar injected sites treated for pain required one or multiple booster injections 1 to 20 years following the original silicone implants.

Some local and generally asymptomatic fluid migration occurred in a few overinjected feet, rarely requiring surgical removal. No other complications, such as tumors, infection, inflammation, rejection, or allergic response, have been observed.

A lack of significant adverse responses is attributed to having used only Dow Corning 360 Medical Fluid Silicone after the initial 50 patients received the Sakurai fluid. The singular complication observed in a few was a persistent distinct purplish-brown skin discoloration. In up to 20 years of follow-up in these patients, the skin color lightened but did not return to normal. No skin color changes were seen with the Dow 360 Medical Fluid.

Additional Potentially Valuable Uses

Of equal or greater importance than investigating silicone for diabetic foot ulcers is its use for decubitus ulcers, also termed pressure sores, which have existed since antiquity. Countless devices and topical agents have been tried, as well as plastic and reconstructive surgery. These debilitating wounds occur in the bedridden and neurologically impaired and in hospitalized patients, including children. It has been suggested that by creating a subdermal soft tissue prosthesis, injectable silicone has the unique potential to prevent pressure sores.¹⁵ Subcutaneous injections would be given at the earliest sign of impending skin breakdown, blanching erythema. Commonly involved sites are ischial tuberosities, the sacrum, the greater trochanter, and the back of the calcaneus, where prolonged bony pressure induces ischemia and soft tissue necrosis. Histologic findings in the foot show that microdroplets of liquid silicone encircle and cushion small arteries, capillaries, and nerves. Theoretically, this encirclement could reduce pressure from these bony prominences.

Beyond the enormous monetary aspect of treating several million patients with these wounds annually, the physical and emotional cost to the patient, family, and others is very great. Authorized investigation is warranted.

Decubitus ulcers are also a major problem of veterinarians in both small pets (dogs) and large animals (horses).¹⁶ Debilitated animals and those convalescing from injury of

illness are unable or unwilling to change body position, making them vulnerable to tissue breakdown. Similar to humans, loss of soft tissue between skin and bone is a risk factor that places the weakened animal at risk.

Acknowledgments My thanks to the patients who consented to receive silicone injections, especially those who agreed to post-mortem specimen removal for histologic study. A special thanks is extended to Leo Kaplan. Also, my gratitude to Robert Rylee, Eldon Frisch, Howard Marshall, Charles Carton, Andrew J. M. Boulton, Scott Nelson, Diane and Wayne Richard, and many others who provided guidance and assistance. Their help made it possible for PodiSil to come to market in Europe. Although the work of Drs. Sakurai and Kagan ultimately produced serious problems, they must also be acknowledged because of giving rise to medically useful injectable silicone. This scientific experience has received the close support of my wife of 46 years, Janelle Balkin. She contributed greatly to clinical application, published articles, and book chapters and has made this 41-year adventure one of fulfillment.

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Commentary

This timely and extraordinarily important article documents the efficacy of liquid silicone injections for weight-bearing abnormalities that untreated in diabetics are a contributory factor in 80,000 lower extremity amputations yearly in the United States alone. In addition, Dr. Balkin offers persuasive arguments that suggest that this therapy is clearly superior to any currently available techniques. If employed worldwide, this modality may spare thousands of individuals from mutilative surgery or lifelong disability. Several other issues are particularly noteworthy:

1. The evidence is impressive from the standpoint of study size, duration, and histologic verification. To my knowledge, there has never been an article regarding silicone for soft tissue augmentation with the scientific validity or therapeutic implications presented here.
2. Dr. Balkin's chronologic outline of the highs and lows in his attempt to promote this therapy confer an orderly historical

perspective to the use of silicone while exorcising media-fueled demonology, which has made silicone the target of unfounded bias and millions of dollars worth of litigation. This is a rare article that illuminates the forces (profit, efficacy, and legal liabilities) that impart momentum or inertia to the integration of promising therapies.

3. To give credit where it is due, at the end of this one man's 40-year odyssey there was no pot of gold. There were no speaking engagements or any type of financial considerations in his development of this therapy. All of his work was done because Dr. Balkin believed that it was the right thing to do. Aside from being a milestone in the reevaluation and integration of a particularly humane therapy, this article is a testament to the man who did it to relieve human suffering. I am honored to be asked to review his work.

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