Liquid Injectable Silicone: A Review of Its History, Immunology, Technical Considerations, Complications, and Potential

Rhoda S. Narins, M.D.
Kenneth Beer, M.D.
White Plains, N.Y.; and West Palm Beach, Fla.

Summary: For over five decades, liquid injectable silicone has been used for soft-tissue augmentation. Its use has engendered polarized reactions from the public and from physicians. Adherents of this product tout its inert chemical structure, ease of use, and low cost. Opponents of silicone cite the many reports of complications, including granulomas, pneumonitis, and disfiguring nodules that are usually the result of large-volume injection and/or industrial grade or adulterated material. Unfortunately, as recently as 2006, reports in The New England Journal of Medicine and The New York Times failed to distinguish between the use of medical grade silicone injected by physicians trained in the microdroplet technique and the use of large volumes of industrial grade products injected by unlicensed or unskilled practitioners. This review separates these two markedly different procedures. In addition, it provides an overview of the chemical structure of liquid injectable silicone, the immunology of silicone reactions within the body, treatment for cosmetic improvement including human immunodeficiency virus lipoatrophy, technical considerations for its injection, complications seen following injections, and some considerations of the future for silicone soft-tissue augmentation. (Plast. Reconstr. Surg. 118 (Suppl.): 77S, 2006.)

The search for the ideal filling material has been ongoing for centuries. Various materials, including collagens, autologous fat, hyaluronic acids, poly-L-lactic acid, and calcium hydroxylapatite, are among the products currently used for this indication. In the past, many materials have been injected for soft-tissue augmentation including paraffin (mineral oil) and other, nonbiocompatible products. Among the gamut of substances injected, no filling material has generated more controversy than liquid injectable silicone. Its proponents describe it as a near perfect filling agent with “superiority of routinely obtainable corrections and persistence of results.”1 Opponents of silicone cite its unpredictability and believe it should not be injected into the human body. Unfortunately for both physicians and patients alike, the history of silicone injections has been marred by the suspension of common sense, a lack of standardization of the mat, impurity of product injected, absence of guidelines for volumes used, a lack of follow-up, recommendation for intervals between injections, and a host of other confounding factors. Despite the fact that proper and improper injections of silicone result in outcomes that are totally unrelated, many discussions of liquid silicone equate the horrific effects that occur after large volumes of contaminated or industrial grade silicone are used by unskilled individuals with data garnered from microdroplet injections performed by reputable physicians with decades of experience.

This review discusses, compares, and contrasts the differences between the ethical use of liquid injectable silicone and its misuse. In addition,
the history, structure, and complications following the use of liquid silicone are discussed. A brief overview of immunologic and technical considerations is presented. More detailed discussions of these topics is presented in a number of useful publications, and an inexperienced injector should refer to these references and undergo thorough training with a physician skilled in silicone injections before beginning to inject patients with this material.2–23

STRUCTURE, PHYSICAL CHARACTERISTICS, AND SUITABILITY FOR BIOLOGICAL APPLICATIONS

In the early 1900s, a British chemist coined the term “silicone” to describe a large family of synthetic polymers containing elemental silicon. The viscosity of these compounds is a function of the polymerization and cross-linkage of their molecules. They can exist as solids (elastomers), gels, and liquids. The scientific name for liquid silicone is dimethylpolysiloxane fluid. Siloxanes are compounds in which the element silicon is conjugated with oxygen and methane. The term itself is a mnemonic acronym derived from silicon, oxygen, and methane. The viscosity of silicone fluids is measured in centistokes (cS), with 100 cS being the viscosity of water. Adatosil 5000 and Silicon 1000 have viscosities designated by their trademark appellations. They are the only silicone fluids approved for use in any indication by the U.S. Food and Drug Administration. Dow Corning 360 fluid, which was used widely in the past for soft-tissue augmentation and used today to coat needles, syringes, and intravenous tubing, may or may not share the same applications, risks, and benefits, as the current, more viscous fluids. The results and complications noted following the use of other silicone fluids may or may not be applicable to outcomes obtained using Adatosil 5000 or Silicon 1000.

SUITABILITY FOR BIOLOGICAL APPLICATIONS

In many ways, liquid silicone appears to fulfill most of the criteria for being the ideal implantable substance. It is permanent, noncarcinogenic, minimally antigenic, and does not support bacterial growth. Unaffected by exposure to sunlight and most chemicals, it can easily be heat sterilized. Its viscosity remains constant throughout the range of temperatures experienced by patients. Different types of silicone products interact in distinct ways in biological systems. However, it is important to note that silicone products are “not chemically identical or generically equivalent.”24 Different forms (e.g., elastomers, liquids, gels) of silicone implanted into different anatomical sites may have a differing potential for benefits and complications. For instance, granulomas have never been reported following the injection of liquid silicone into the feet25 but have been reported following facial injections. Accordingly, the risks and benefits associated with different products (i.e., breast implants) and elastomeric silicones cannot be directly compared with liquid injectable silicone.

Notably absent from this list of virtues is silicone’s potential for misuse, adulteration, and substitution. Also absent from the list is the stigma associated with silicone misuse. When miniscule droplets of pharmaceutical grade silicone are implanted at appropriate depths and anatomical locations using the microdroplet technique, they are encapsulated by a delicate network of fibroplasia. This results in a structure that is not palpable, has the texture of adjacent tissue, and will typically not migrate.

HISTORY

With the publication of toxicologic information in 1948 that found silicone to be “physiologically inert,”25 interest within the medical community grew because of the need for biocompatible medical and surgical materials. Use of liquid silicone to improve body contours became popular first in Germany, Switzerland, and Japan during the 1940s, and thousands of patients were treated during that decade. Beginning in the 1960s, liquid silicone use in the United States was characterized by two dramatically divergent approaches associated with two diametrically opposite experiences.

The first approach is best represented by the experience in Las Vegas, Nevada, where enormous (up to 2 liters) volumes of Dow Corning 360 fluid was, in many instances, contaminated by heavy metals and other impurities. Approximately 20,000 to 40,000 individuals were injected under these circumstances, and the injected areas included breasts, faces, legs, and buttocks. Large volumes (750 to 2000 cc) were injected. This era of indiscriminate injection of impure product ended with a consent decree with Dow Corning in 1965.26 Silicone was also intentionally adulterated with various formulas, including the Sakurai formula, to increase inflammation and the fibroplasia that resulted following injection. The Sakurai formula mixed olive oil with silicone in an attempt to induce fibroplasias that would prevent migration and, according to Sakurai, was used in over 100,000 patients.25 This intentional adulteration
followed publications in various journals that suggested that silicone was nontoxic even when adulterated.27–29

The second experience with silicone was pioneered by Norman Orentreich, who developed the microdroplet technique. This technique was developed to obtain a more gradual correction and minimize the complications that had been seen with large-volume injections. Adherents of the microdroplet technique advocate the use of tiny amounts of medical grade silicone to induce a gradual fibroplasia. A review of the literature from this school has significantly fewer complications associated with this technique than are associated with the large-volume injection of impure material. When considering silicone as a soft-tissue augmentation product, it is important to bear this distinction in mind.

**FORMAL STUDIES**

In 1965, a large-scale study was launched by the Dow Corning Corporation to secure approval for liquid silicone by the U.S. Food and Drug Administration. A highly purified 350-cS silicone fluid (MDX 4-4011) was created and used specifically for the study. During the first phase of the study, which followed 1300 patients, one instance of migration was noted in a single patient following the treatment of lower extremity atrophy with large volumes of material. The second phase of the study involved 128 patients with severe lipodystrophy who were also treated using large volumes of material (average, 21 cc). Severe facial necrosis and panniculitis occurred in several patients in association with inflammatory diseases.30,31 Although the study suggested that silicone was safe and effective, the study had design flaws that included a lack of standardization for the frequency of silicone injections and for the volume of silicone injected at each session. Additional design flaws in the study design included a lack of long-term follow-up.5

Silicone usage continues because the alternatives to it are less than optimal and are not permanent. For instance, other absorbable injectable fillers and implants such as poly-L-lactic acid, calcium hydroxyapatite, and hyaluronic acids are helpful in treating human immunodeficiency virus–associated facial lipoatrophy and age-related soft-tissue loss, but they are limited by cost and short duration of correction. In addition, poly-L-lactic acid must be reconstituted. These limitations were and continue to remain some of the reasons that medical grade silicone, injected using the microdroplet technique, has a niche as a safe and effective alternative to these products.32,33

**ONGOING CLINICAL TRIALS**

A 1000-cS fluid, SilSkin, is currently undergoing phase II clinical trials by physicians at three sites. Legal issues with the Richard James Company have prevented phase III clinical trials from starting. Other studies using Silikon 1000 by Drs. Derek Jones, Harold Brody, and Alastair Carruthers have been conducted on human immunodeficiency virus patients.32,33 These studies evaluate silicone for the treatment of nasolabial creases and human immunodeficiency virus–associated lipoatrophy. Unlike the studies performed decades ago, these studies are more rigorously designed and have designated areas that are treated, controlled amounts of material injected per session, and no more than 1 cc per side of the face per month. In addition, there is a limited number of injections permitted and a well-designed follow-up period that will provide data for years after the injections are completed. This improved design should produce data that are more objective and scientifically meaningful. To date, over 1000 patients have been treated at four centers, with no serious adverse events noted after 4 years of study. It is hoped that this study will provide objective information regarding outcomes following the use of standardized small volumes of medical grade silicone.

**TECHNICAL CONSIDERATIONS**

Once implanted, liquid injectable silicone is permanent and, as such, it is much less forgiving and much more technique sensitive than temporary fillers. Specific technical considerations applicable to liquid injectable silicone include the need to inject miniscule amounts of material at a very precise depth in the subdermal plane. Injections that are too superficial will result in visible papules, whereas injections of large amounts of material in a single session will result in globs of silicone that may result in palpable nodules and may migrate. In addition, the techniques required for proper injections of silicone mandate that multiple injection sessions are planned at monthly intervals or greater, in contrast to materials such as hyalurons or collagen, where a single injection will usually provide the degree of filling desired.

One other consideration that must be considered if one is contemplating injecting silicone into one’s patients is that not all malpractice carriers will cover its use. Before injection of liquid injectable silicone, it is important to determine whether your malpractice policy will cover a claim arising...
from a silicone injection. This is usually on a state-by-state basis. No other agent currently used for soft-tissue augmentation is as controversial as silicone. Although liquid silicone is unquestionably an excellent filling agent, its use has significant political, public relations, and medicolegal implications for the clinicians who inject it.

**INJECTION TECHNIQUE CAVEATS**

Among experienced injectors, there is widespread agreement that silicone (1) must be used in small quantities of approximately 0.01 ml; (2) overcorrection must be avoided; (3) improvements must be achieved slowly; and (4) injections cannot be carried out superficially and material must be precisely placed in the deep dermal or preferably in the subdermal plane. Silicone is similar to poly-L-lactic acid, with both materials producing gradual improvement following multiple treatment sessions of material placed in the dermal-subcutaneous junction. Silicone injections elicit a mild fibroplastic response, resulting in a slow increase in tissue volume. Although the volume of silicone used is important for the correction obtained, collagen production is at least equally important to the final outcome. That is why it is important to wait some time in between injection sessions and let the fibroplasia take place. That way, patients are not overcorrected.

**MICRODROPLET METHOD**

This technique uses tiny droplets of silicone (0.01 to 0.03 cc) that are deposited into the subcutis by a series of injections spaced approximately 2 to 10 mm apart. The needle is inserted into the skin, which may be tented up as the microdroplet is deposited. Care must be taken to aim the needle medially, away from the bulk of the cheek, when injecting the nasolabial and marionette lines. Many other areas of the face can be treated with microdroplet silicone injections. These include the cheek hollows, midface, glabella, and tear troughs, and the chin, lips, and cheekbones can be enhanced. Application of a topical anesthetic cream provides sufficient analgesia for most patients. However, a regional anesthetic block is generally used before injection of the lips. Overcorrection must be avoided, and injections that are too superficial may result in beading.

The use of Becton Dickinson 3/10cc insulin U-100 Syringes (Becton Dickinson, Franklin Lakes, N.J.) has been advocated by several experienced silicone injectors, but any 1-cc syringe is adequate provided it has a Luer-Lok attachment to withstand the pressure associated with silicone injections. Injections are typically carried out at 1- to 2-month intervals using a 27- or 30-gauge RJ Max Flo needle. Usually, patients need less than 5 cc for total correction, but total treatment volumes as high as 5 to 10 cc (1 to 2 teaspoons) may sometimes be used, especially for human immunodeficiency virus–associated lipoatrophy. This volume of material requires several months to inject. Large volumes of silicone may increase the risk of serious complications by increasing antigenic burden.

**ABSOLUTE CONTRAINDICATIONS**

Breast augmentation using liquid injectable silicone should not be attempted because the large volumes necessary will lead to migration, thick-walled cystic spaces, or granulomata. Silicone is contraindicated for injections into horizontal creases such as the transverse forehead rhytides, where the skin is thin and rests against bone, or the mental crease, where it frequently results in ridging or beading. The penis, bones, tendons, and cysts should not be injected with silicone. Intravascular injections must be scrupulously avoided.
RELATIVE CONTRAINDICATIONS

Patients with chronic inflammatory diseases, those with multiple allergies, and patients who have infectious processes in close proximity to injections—for example, sinus infections (glabella) or lip injections (dental caries)—may be at greater risk for inflammatory complications following silicone injections. Medicolegal considerations mitigate against injecting silicone into patients who are pregnant. There is no scientific link between collagen vascular diseases and silicone.

The senior author has no problem injecting silicone into these patients. Physicians with limited experience should avoid these injections. In addition, great caution should be exercised when contemplating injections of silicone into a patient who has previously been injected with silicone by another physician or at another location. The reason for caution in this latter category of patient is that in the event of an adverse event, it will be impossible to determine whether the adverse event was associated with the prior injection (which may not have been performed with medical grade product or with the microdroplet technique) or with the current injections. In most instances, the patient will blame the most recent treating physician for any complication, and one may find oneself shouldering the liability for injections of silicone performed by another practitioner. The legal complications and aggravation that may result from this are not worth the benefits in almost all circumstances.

COMPLICATIONS

There is a striking contrast between the occurrence and severity of complications following the improper use of silicone of unknown purity and large volume injected by inexperienced physicians or lay persons and the complications that follow injections of pharmaceutical grade silicone by skilled physicians using microdroplet techniques. Treatment of silicone complications usually involves the use of both oral and injectable intralesional corticosteroids and oral antibiotics. Complications associated with silicone injections, as with any soft-tissue augmentation product, may be divided into those that are serious and those that are minor.

MINOR COMPLICATIONS

Injection of any filling agent may be followed by bruising, erythema, and edema, and silicone is no exception. Fulton et al. report that most patients who received silicone injections to the lips developed bruising. Minor complications specific to liquid silicone include textural changes of the skin, peau d’orange effect, and a bluish tinge to the skin. In addition, small nodules can occur occasionally after injections. These complications are technique dependent and result from injecting too much silicone and/or injecting it too superficially. Because it has a neutral pH, silicone injections are less painful than many other injections. In addition, silicone causes less edema, erythema, and swelling than many other available fillers.

One complication unique to silicone is known as “beading.” This occurs when silicone is placed in the superficial dermis and is subsequently encapsulated by collagen. Nodules develop at rates dependent on the location injected. Fulton et al. reported nodule formation at a rate of 2 percent following silicone injections into the lips (an area prone to repeated and constant movement). This relatively high rate is in marked contrast to the overall rate of nodule formation of one in 10,000 in other studies published. In a discussion of the nodules formed following silicone injections, Fulton et al. noted that the histiocytic granulomas formed are “similar to the tissue reactions seen with polylactic acid.” The nodules noted by these authors were treated with intralesional cortisone injections, excision, or observation.

Granuloma formation is not unique to silicone injections; it also occurs following the injection of other injectable materials. In general, a granulomatous response is a generic immune response mounted against a foreign body, and silicone granulomas may or may not be immunologically different from other granulomas. To date, there has not been a well-designed study of the immunologic differences, including T-helper cell type 1 and type 2 populations, between silicone granulomata and those of other entities. Such a study would help to determine whether silicone elicits a different immunologic response than other materials and, if so, how they differ.

A single report of a granulomatous rosacea-like syndrome/drug interaction was reported by Rapaport. This report documented an eruption that followed treatment with etanercept in a patient who had been injected with silicone 36 years previously. It is difficult to assess the causality of the silicone injections in this instance, and it is possible that the etanercept simply unmasked an underlying predisposition for granulomatous rosacea in this individual. To our knowledge, this remains the only report of this type despite several additional years of patient exposure to etanercept.
Bigata et al. reported a single patient who developed granulomas 8 months after silicone injection for cosmetic indications. The authors were unable to determine the type or purity of the silicone injected in this single case, so it is impossible to categorize this reaction as a reaction to pure silicone or to an adulterated product. In this case, the nodules resolved after 3 years.

Treatments for silicone granulomas have involved the use of antibiotics, topical steroids, systemic steroids, and the topical immunomodulator imiquimod. In the case report using imiquimod, Bauman et al. report that Aldara resulted in resolution of silicone granulomas of the lips. The type of silicone injected in this case was thought to be Silicex, a commercial grade silicone that is contraindicated for injection into animals or humans.

**SERIOUS COMPLICATIONS**

Serious complications such as severe edema of the area injected and localized discoloration of the area injected occur with a frequency of a fraction of 1 percent in most studies, although some recent reports place the rate at 2 percent. Pneumonitis has been reported following large-volume injections of impure silicone by an unlicensed practitioner. In this report, an open lung biopsy revealed lipoid vacuoles.

Other complications, including cellulitis, ulcerations, migration, and nodule formation, have also been reported with silicone injections. Recurrent cellulitis was reported in patients with dental abscesses and chronic allergies. Silicone migration is thought to be the result of large-volume injections, which do not allow encapsulation of the material. Despite the absence of any scientific link between collagen vascular diseases and silicone, the authors recommend avoiding injections into patients with a known history of collagen vascular diseases because of the medicolegal risk that might occur with a flare of the underlying disease in such a patient.

During a U.S. Food and Drug Administration–approved clinical trial (ostensibly a clinically controlled situation), the data regarding complication rates were marred by a lack of standardization for quantity of material injected and for the intervals between injections. One early U.S. Food and Drug Administration–approved study of silicone reported two serious complications. The first complication involved migration of material in a patient treated with large-volume injections of the extremities. The second complication occurred in a patient with Weber-Christian disease, rheumatoid arthritis, and atypical mycobacterial infection. This patient suffered facial necrosis that occurred some 11 years after her last injection of silicone. Similar necrosis was reported two patients (one of whom had Weber-Christian disease and the other who did not) by Achauer.

Notably absent from any discussion of silicone complications is significant mention of problems when the plantar foot is injected. Indeed, Balkin reports 1585 patients treated with silicone over the span of more than 40 years, with the only complication being “some local and generally asymptomatic fluid migration occurred in a few overinjected feet.” It is not known whether the lack of complications seen in silicone injections of the foot is attributable to the absence of a portal for infections (the feet, unlike the face, lack sebaceous glands), a function of some as yet unrecognized unique anatomical feature of the feet, or the standardized procedures among the practitioners injecting. It may be because material injected into the feet was limited to medical grade products free from contaminants. This last possibility is most consistent with the experience of physicians that have safely and effectively used medical grade silicone for facial soft-tissue augmentation. Not only are silicone injections of the feet devoid of significant complications but, according to Balkin, silicone has a near perfect record for relieving the pain associated with loss of the plantar fat pads. It also works very well for relief of painful corns.

This near perfect clinical record of silicone injections into the feet has been correlated histopathologically. In one of the few long-term reports on the histopathology of liquid injected silicone, 148 specimens obtained from 49 patients who had received injections into the plantar fat pad area were evaluated. Histopathologic evaluation revealed encapsulation without granuloma formation in these individuals. Podosil, a silicone product, may be approved soon in Europe for treatment of foot problems.

In contradistinction to its ethical usage, the complications arising from the psychopathic usage are as sensational and outrageous as the methods and materials used. Unfortunately for physicians and patients alike, the distinction between these two methods of injection is lost by the media and legislators alike. The most common headline one reads regarding silicone unquestionably refers to the outcomes of criminal misuse of agents that may not be silicone at all.

Several deaths have been reported as a result of large-volume silicone injections performed by unlicensed personnel using impure products. These deaths were caused in most instances from
industrial grade material injected in high volumes that resulted in respiratory failure. Deaths in Florida, California, and Texas have resulted in criminal prosecutions against the unlicensed personnel that performed them. Less serious complications from unlicensed usage of silicone include infections with mycobacterium and granuloma formation.41,42

In addition, physicians injecting silicone must be able to tell those few patients who become silicone addicts to discontinue injections before becoming “potato heads” and must be capable of refusing treatment to those patients suffering from body dysmorphic syndrome. All practitioners who use silicone will see patients who have been overinjected. In these patients, the physician has an ethical duty to refuse further treatment.

IMMUNOLOGY

The immunologic response to purified liquid injectable silicone injected in minute quantities is, at the present time, unknown. It is know that all foreign bodies can elicit an immunologic reaction and that granulomas may be a generic response to foreign materials of all types.40 Although silicones appear to be nonantigenic, they are not completely biologically inert. Silicones undergo biological oxidation to silica and, like tattoo pigments, are incorporated into the reticular endothelial system.1 It is anticipated that the use of molecular biologic techniques will facilitate an understanding of the roles of contaminants, volume injected, and potential impact of infectious and inflammatory processes on injected liquid silicone once it has been injected. To date, there has been very little information about whether adverse events associated with silicone are a result of an aberrant host response in a susceptible individual, an infection with an unusual response, or a normal host response to a contaminant; in addition, there are many other biologically important questions. The use of polymerase chain reaction, cytokine profiles, and immunohistochemistry will most likely facilitate this understanding and, in turn, help us to understand what happens when there is an adverse reaction to liquid injectable silicone.

The granulomas that occasionally form as a reaction to silicone bear many similarities to cutaneous sarcoid granulomas, and one potential benefit of an immunologic understanding of silicone granulomata is a molecular understanding of sarcoidal granulomas. It is interesting to note that, as with sarcoidosis, silicone complications may occur following “persistent exposure” to a low-potency antigen that initiates an inflammatory cascade.42 Despite the fact that extensive clinical trials suggest that silicone is fundamentally safe, there has not yet been any application of these molecular biological techniques to elucidate how the body reacts to this product.43,44

CONCLUSIONS

Two facts are certain about the future of liquid injectable silicone for cosmetic soft-tissue augmentation. First, it will continue to be injected both properly and improperly. Second, the key to its successful use will lie in an understanding of the microdroplet technique, the use of a regulated U.S. Food and Drug Administration–approved product, and the avoidance and treatment of complications.

Future directions for treatments will include molecules engineered to interact with an energy source (perhaps silicone embedded with a chromophore, which might allow a “permanent” filler to be disassembled in the event of an untoward reaction or change of beauty ideals). Alternatively, better delineation of the immunology of silicone injections may permit the immune cells to scavenge a bioengineered silicone molecule much the same way that cutaneous dendritic cells and macrophages eradicate tattoo ink when stimulated with various energy sources. The single report of Aldara usage to treat silicone granuloma may presage a day when toll-like receptors are manipulated to scavenge these granulomas and those associated with sarcoid as well. Whatever the future holds for silicone injections, it is reasonable to assume that the injections will continue.

Rhoda S. Narins, M.D.
Department of Dermatology
New York University Medical School
2222 Westchester Avenue
White Plains, N.Y. 10604
rsnmd@att.net

ACKNOWLEDGMENT

The authors thank David Duffy, M.D., clinical professor of medicine, University of Southern California, for much-appreciated consultations on the manuscript.

DISCLOSURES

Rhoda S. Narins, M.D., has no disclosures for silicone. Disclosures for other fillers include being an investigator and on the medical board of Q-Med and Medicis (Restylane) and Dermik (Sculptra) and being an investigator and on the medical board and owning stock options for ColBar LifeScience (Evolence), Bioform (Radiesse), and Artes (Artefill). Kenneth Beer, M.D., is
a speaker for Medicis and conducts clinical trials for Medicis and Bioform.

REFERENCES


