Complications of Fillers: Overview

DAVID M. DUFFY, MD

Department of Dermatology, University of Southern California, Los Angeles, California

BACKGROUND. **Avoiding complications requires thorough training and medical, anatomic, and esthetic common sense. Complications can occur as a function of anatomic location, technique deficiencies, the type of defect treated, identifiable host factors, infectious processes, and allergies as a consequence of intrinsic characteristics of any particular filler. They can also occur in the absence of any identifiable host factors and flawless technique. Complications following temporary fillers often occur soon after augmentation, may resolve spontaneously, and are usually easy to treat. Conversely, complications that occur after using permanent or semipermanent fillers can appear months to years after augmentation and prove very difficult to treat.**

OBJECTIVE. **To analyze and describe complications that have occurred following soft tissue augmentation and to present strategies for avoiding, recognizing, and treating them.**

METHODS. **Protocols and observations derived from a 24-year experience using a wide variety of soft tissue augmenting agents are presented in association with pertinent clinical literature. Characteristic complications associated with specific types of soft tissue augmenting agents are presented in tabular form.**

CONCLUSION. **Tissue fillers offer patients an opportunity for instant gratification with minimum downtime and, in general, an extremely favorable risk-to-benefit ratio. The best way to minimize complications in both your patients and yourself is to avoid them.**

DAVID M. DUFFY, MD, HAS INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

Avoiding Complications and Informing the Patient

Tissue augmenting agents (temporary, semipermanent, and permanent) provide an outstanding opportunity for the correction of certain defects that cannot be treated effectively using any other modality. An enormous variety of soft tissue "fillers" are currently being offered, and more are sure to follow. Despite the protests of dyspeptic academicians who belittle the necessity for training and the motives for using fillers, "Anyone can do them, they can be learned easily and require little effort and generate a lot of money." [1] In fact, complications, both minor and serious, can occur following the use of any filler. Late complications may be triggered by drugs, trauma, and infectious processes.[2]

A well-informed patient can be an ally and is less likely to be a litigant. Patients should be told quite frankly about the virtues and drawback of any agent. It is sometimes worthwhile to tell patients that you will begin with a temporary filler to determine how they respond to it. Although permanent implants are intuitively appealing, permanent complications (the dark side of permanent implants) are also easy to understand. I tell my patients that there are only a few ways to correct a depression in the skin. Fillers elevate wrinkles and scars like the wrinkles in a balloon, and, accordingly, they are used to treat defects that are easily stretched. They can also be used to increase the volume of the lips and correct the atrophic changes that follow trauma or the aging process, particularly in the central face and lips. Patients are also told about the disadvantages in attempting to correct superficial wrinkles, particularly those occurring in areas of high mobility or repetitive movement (ie, the repetitive pursing of the orbicularis oris muscle may be partially responsible for the production of beading on the lip border, which can be seen with any number of injectable fillers). The trade-off between resurfacing procedures and fillers is also carefully explained.

Testing and Getting to Know the Patient

As a general rule, cutaneous defects that are easily effaced by general traction can be excellent candidates for tissue augmentation. When in doubt, the injection of a small amount of local anesthetic or normal saline underneath a specific area provides a "preview" to determine how effective a filler will be at elevating a defect that you specifically want elevated (without elevating surrounding tissue). It is often advantageous to initiate soft tissue augmentation using temporary fillers such as CosmoDerm or Restylane (INAMED Aesthetics, Santa Barbara, CA, USA) (which do not require allergy testing). More permanent fillers, such as Radiesse (hydroxyapatite) (BioForm Medical, San Mateo, CA, USA) Sculptra injectable poly-L-lactic acid (Dermik Aesthetics, Berwyn, PA, USA) (Figure 1), and liquid silicone (Silikon, Alcon Labs, Fort Worth, TX, USA; AdatoSil, Bausch & Lomb, Claremont, CA, USA), can also be employed; however, the use of temporary fillers first gives both the patient and the physician an idea of the suitability of the defects treated for augmentation but cannot, unfortunately, predict complications using more permanent fillers.

Address correspondence and reprint requests to: David M. Duffy, MD, 4201 Torrance Blvd., Suite 710, Torrance, CA 90503, or e-mail: info@drdavidmduffy.com.

 • Published by BC Decker Inc
ISSN: 1076–0512 • Dermatol Surg 2005;31:1626–1633.

Common Complications

Since all tissue fillers are delivered via injection, complications that follow any form of skin piercing can be seen with any of them. These include needle marks, swelling, persistent ecchymosis (Figure 2), pain, itching, outbreaks of herpes, and infectious processes. Many complications are technique related. These include palpable implants, uneven distribution, visible implants, overcorrection, undercorrection, allergies, hypersensitivity reactions (Figure 3, A to C) and nodularity (permanent or transient based on the type of implant and its depth) (Figure 4, A and B).[3] Many of these problems could virtually be eliminated with proper patient selection, that is, careful histories to avoid treatment in patients using medications that can promote bruising and careful training in the use, technique, and niceties of any particular agent. To acquire skill in the use of agents that are not yet approved by the US Food and Drug Administration but appear to be on the verge of getting this approval, training in countries where such fillers are legal is worthwhile.

Choosing a Filler and Avoiding Overcorrection

When using permanent and semipermanent implants, overcorrection, delayed foreign body reactions, and/or migration are the primary causes of patient dissatisfaction. My experience suggests that many nonpermanent fillers can be injected more superficially in the dermis when extremely small volumes are employed. However, agents such as hyaluronic acid or Radiesse can impart a bluish or whitish color to the skin when placed very close to the surface. Minor overcorrections can be dispersed by using the wooden end of a cotton-tipped applicator firmly applied. As a general rule, the more permanent a filler is, the more deeply it is injected. Accordingly, agents such as Radiesse and liquid silicone are injected more deeply, whereas agents that are designed for superficial effects (Zyderm I (INAMED Aesthetics) are more easily used for superficial defects. It is worth remembering that judgment errors carried out using permanent fillers may be permanent. It is also worth keeping in mind the fact that certain fillers, such

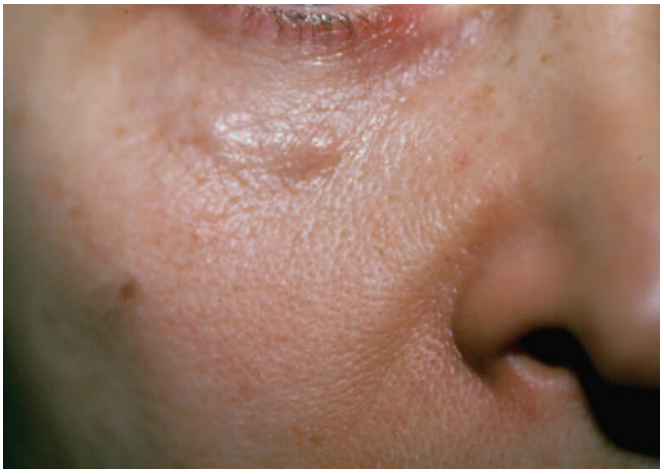

Figure 1. These nodules occurred following the use of poly-L-lactic acid (Sculptra Dermik, Berwyn, PA, USA). These lesions resolved spontaneously over several months.

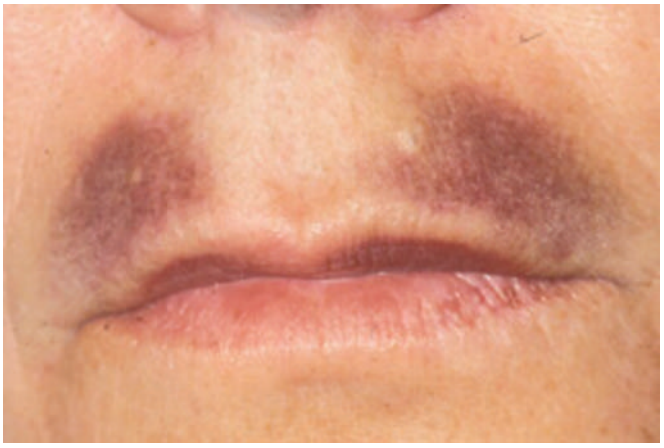

Figure 2. This patient developed severe bruising that lasted several weeks after augmentation with silicone. She had forgotten to discontinue aspirin before treatment.

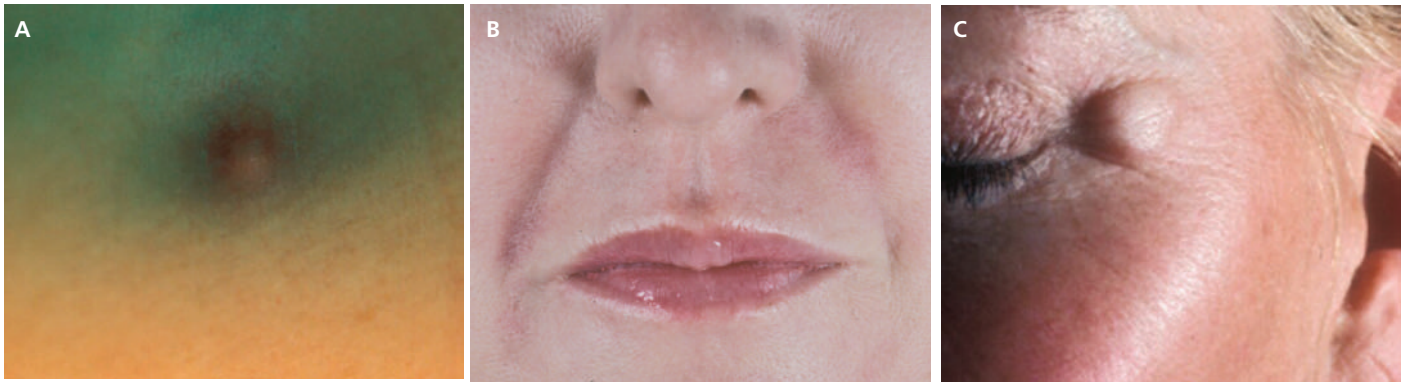

Figure 3. (A) This nodule developed at a previously negative skin test site following treatment with Zyderm. (B) Nodularity involving the nasolabial folds is noted in conjunction with delayed test-site reaction. Nodularity responded spontaneously without treatment in this photograph taken several months later. (C) This periocular nodule appeared several months after an uneventful soft tissue augmentation using Zyderm I. It appeared in association with an upper respiratory infection and responded to intralesional corticosteroids.

as liquid silicone, may induce excessive fibrosis when they are injected too superficially. This fibrotic process can result in nodules, ridging, beading, textural changes, and, in the case of depressed scars, hypertrophic scar-like elevations.

Areas that Must Be Approached Cautiously

Although experts can get away with it, injecting horizontal lines such as the forehead lines is often associated with ridging on either side of the rhytid. The crow's feet, situated as they are in extraordinarily distensible skin, are also an area where ridging or beading will occur because the material more easily displaces the very flexible skin lateral to the treated areas. CosmoDerm, Zyderm I, and Restylane Fine Line will be the most forgiving agents in these areas. Although ulcerations can occur in almost any area (Figure 5), the glabella is particularly problematic. Over 50% of tissue necrosis following Zyplast (INAMED Aesthetics) occurs in this area, and its use is contraindicated there (Figure 6, A and B).[3] Deep injections of almost any filler may occlude the arterial supply to the glabella and be followed by tissue necrosis. The lips are subject to a variety of traumas, bacterial contamination, and viral infections. Patients with recurrent dental or sinus infections or outbreaks of herpes may be at risk of complications when these infections occur in close proximity to the treated areas, particularly when using permanent fillers (Figure 7, A to E). This may be due to the phenomenon of molecular mimicry, in which bacterial and virus infections act synergistically to produce inflammatory and granulomatous complications.[4–10] The use of large volumes of permanent or semipermanent agents in the lips is probably contraindicated.[11] V-shaped, superficial rhytids (purse-string wrinkles) often defeat attempts to elevate them flush to the surface and develop ridging or beading lateral to the wrinkles, where the skin is more flexible. The location and configuration of certain defects are important; that is, varicelliform scars, ice-pick scars and depressed scars, which occur in distensible skin, can respond to injections by "doughnutting" (Figure 8) where the periphery of the defect is elevated. When in doubt, the use of a temporary filler with compression dispersion at the periphery of the lesion is a good idea. There is a general agreement that certain kinds of defects are the best candidates for augmentation. These include the nasolabial and melolabial folds, certain types of scars, and atrophic changes involving the lips and central face, which can be treated better with fillers than any other modality available.

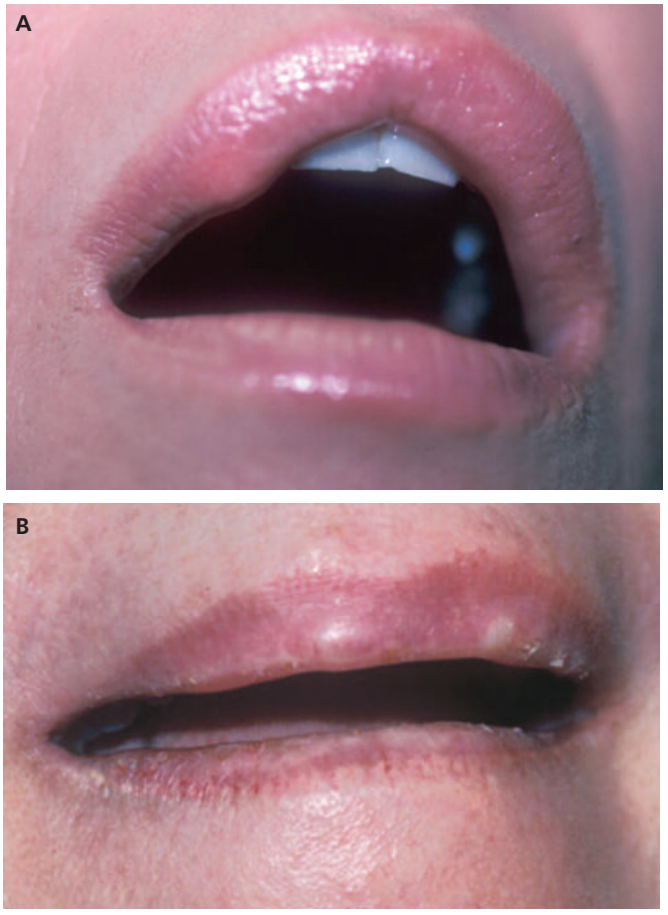

Figure 4. (A) This nodule occurred 3 weeks after treatment with Radiesse. When used in the lips, this agent is often associated with an unacceptably high incidence of nodules in this location. (B) These nodules occurred several months after an estimated 0.2 cc of liquid silicone was employed in the vermilion portion of the lip. Partial resolution occurred following intralesional corticosteroids.

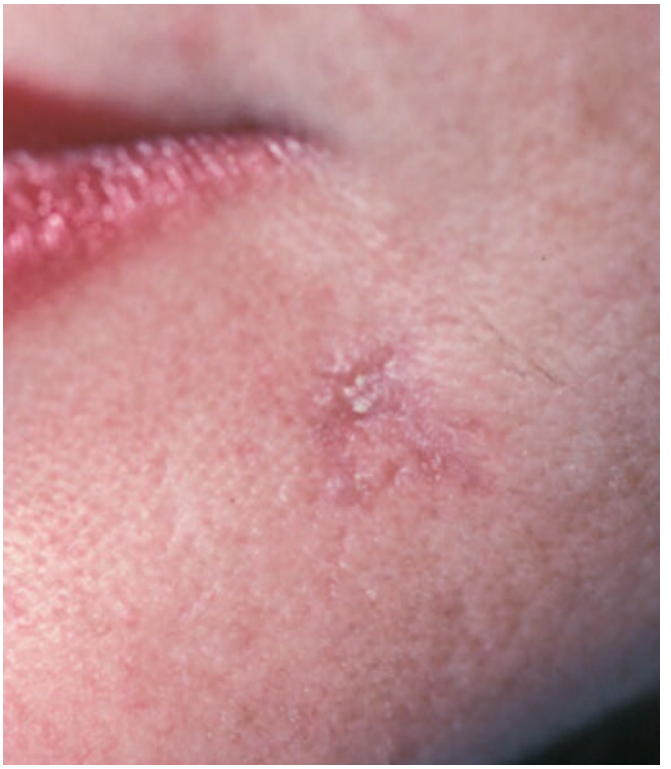

Figure 5. This small scar followed an ulcer that developed after the injection of Zyderm II. It was preceded by prolonged blanching.

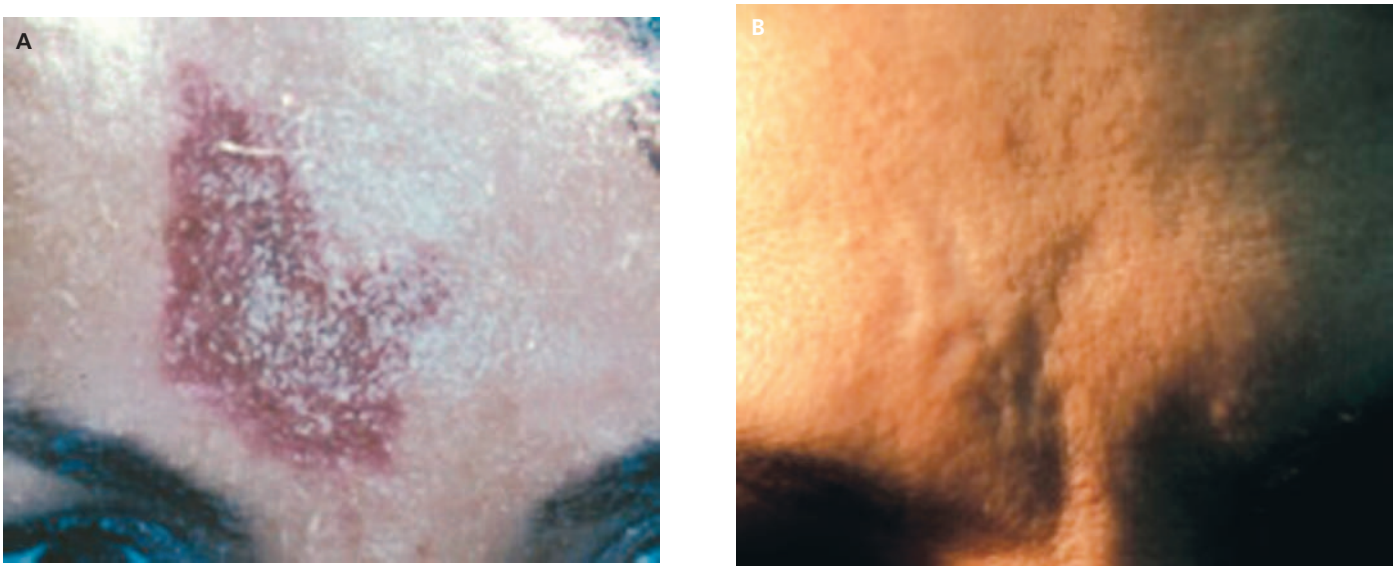

Figure 6. (A) and (B) These photographs demonstrate the process of ulceration and scarring that followed the use of Zyplast for glabellar rhytid.

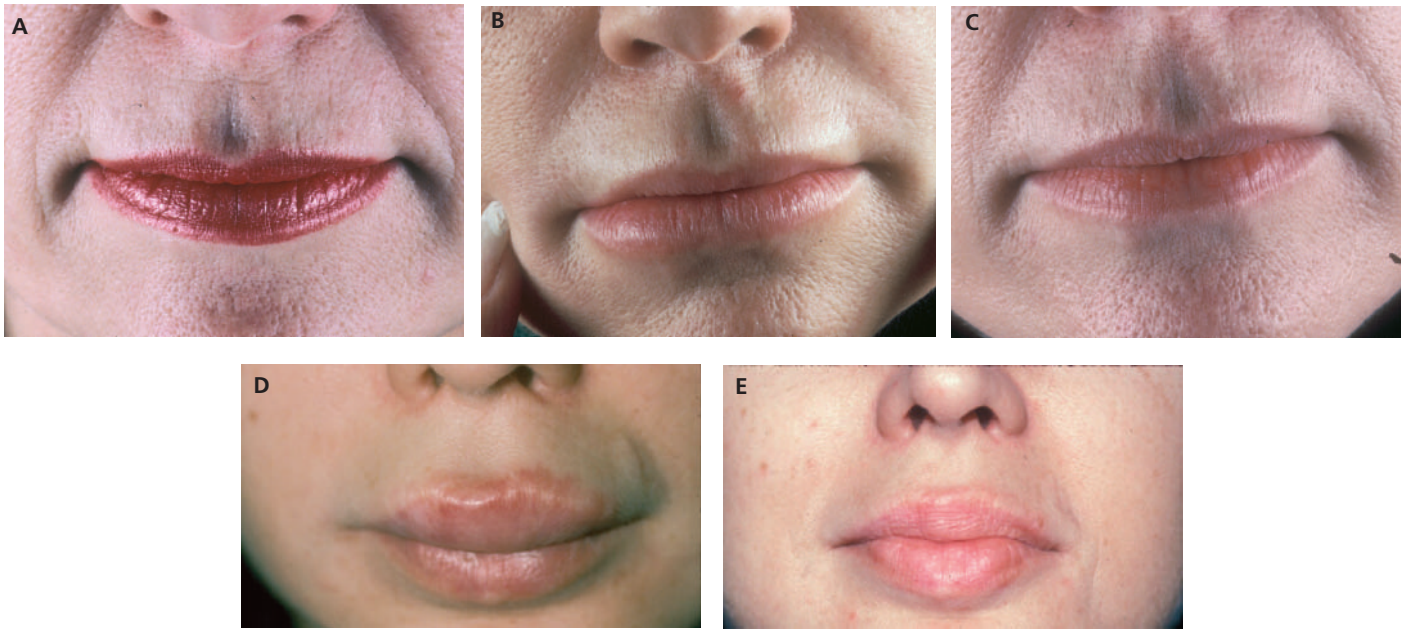

Figure 7. (A) Pretreatment appearance of the upper lip before the injection of an estimated 0.3 cc of pure liquid silicone. (B) Patient was satisfied with post-treatment results until at 6 months she developed severe swelling in association with herpes labialis. (C) Resolution can be noted following antiherpetic medications; no recurrence was reported in 20 years. (D) Severe edema associated with a dental infection occurred in this patient who received unknown volumes of liquid silicone. (E) Spontaneous resolution occurred following removal of carious teeth.

A brief comparison and complications following the use of commonly used injectable fillers are presented in Table 1.

Complications to the Practitioner

There are two general categories of practitioner risks. First, there is the transmission of infectious processes from the patient being treated to the physician who sticks himself with a needle. A second category of complications exists in the possibility of legal actions taken against physicians who use permanent implants, particularly those such as silicone, which have controversy associated with their use. The use of permanent implants may establish a lifelong relationship between the practitioner and the patient. Accordingly, a frank and completely honest discussion of all of the possibilities, good and bad, that can follow the

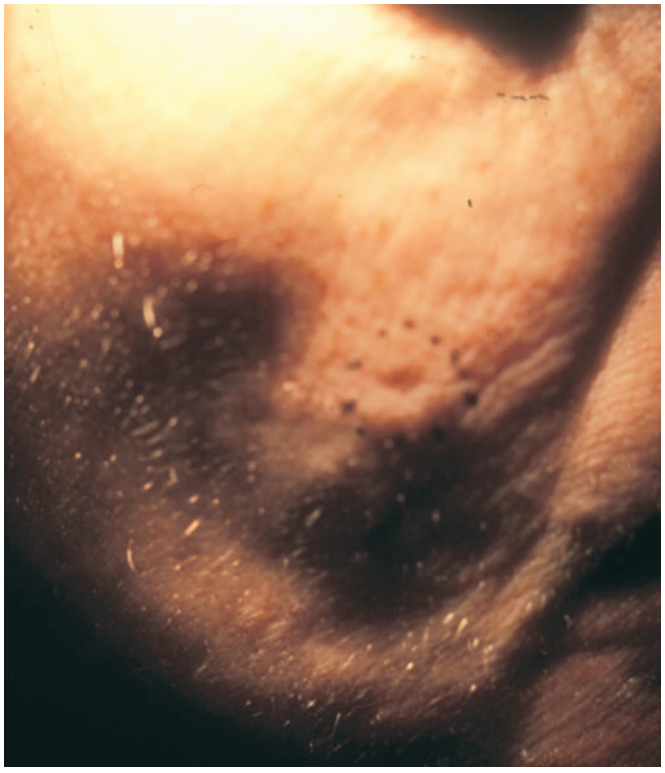

Figure 8. "Doughnutting" occurs when the periphery of a bound-down scar is more easily elevated than the scar itself.

use of permanent implants is a vital part of the proper use of permanent agents. It is best to know your patient very well before employing such agents.

Complications: Do's, Don'ts

Bleeding, bruising, needle marks, and swelling are common. Measures to minimize these problems include discontinuance of aspirin, anticoagulants, anti-inflammatory drugs, vitamin E, and ingestion of alcohol prior to therapy. Firm pressure applied quickly at the first sign of bruise followed by ice-packs can be useful. The use of small needles, such as MaxFlo (Richard James Corp., Peabody, MA, USA), is also valuable. Severe swelling, which occasionally follows the use of hyaluronic acid or Radiesse injections, occasionally necessitates the use of oral corticosteroids and antihistamines—for complete resolution.

Intermittent Swelling

Intermittent swelling may occur weeks to years after treatment following many types of implants and can be precipitated by alcohol consumption, sunlight, vigorous exercise, and vasodilatory episodes.

Allergic Reactions

Allergic reactions are extremely uncommon following the use of widely employed soft tissue augmenting agents, such as bovine collagen. Depending on the severity, location, and type of implant employed, a variety of treatments have been employed, including systemic and intralesional steroids, topical tacrolimus, and tincture of time.

Superficial Beading

Superficial beading consisting of small visible and palpable nodules usually involves the borders of a rigid wrinkle, which is difficult to elevate. Most will resolve spontaneously when using nonpermanent implants. Beading is most common when treating the horizontal creases of the forehead and perioral "pucker" rhytids. When beading occurs following the use of a permanent implant, a number of modalities have been employed with varying degrees of success, including intralesional steroids, dermabrasion, CO_2 resurfacing, and surgical excision. Small nodules that often occur on the lateral aspects of the mucosal surface of the upper lip following Radiesse will often respond gradually to vigorous massage. They can also respond to intralesional steroids, incision, and drainage using an 18-gauge needle or, as a last resort, surgical excision. My experience suggests that the use of Radiesse to increase lip volume is often followed by an unacceptable degree of nodulosis.

Systemic Complaints

These occur in 0.01% of patients treated with Zyderm and include arthralgia, myalgia, headaches, nausea, and urticaria. These patients do not have anti-Zyderm antibodies. Treatment is generally not necessary.[3]

Autoimmune Disease

To date, no widely employed filling agent appears to be related to autoimmune disease, and although autoimmune syndromes, including inflammatory myositis, have been reported involving silicone breast implants and bovine collagen, more recent studies would appear to exonerate implantable devices of all sorts from any association with rheumatologic disorders.[12–14]

Serious Complications

One case of amaurosis, possibly owing to thrombus formation in the retinal artery,[3] has been reported following an injection of Zyderm II into the glabella. The use of Zyplast to treat the glabella is contraindicated, and agents such as Cymetra (LifeCell, Branchburg, NJ, USA) should also not be used for glabellar rhytids. More viscous mate-

Table 1. Fillers at a Glance

Injectable	*Description*	*Adverse Reactions/ Side Effects*	*Outcomes*	*Legal Status*
Collagen (Zyderm, Zyplast) (INAMED Aesthetics, Santa Barbara, CA, USA)	Collagen from bovine skin	Allergic reaction. Skin test required. Sensitization 1–2%. Hypersensitivity, necrosis, infection, cystic reaction, systemic complaints (0.5%). Amaurosis, 1 case, anaphylactoid reactions.	Lasting up to 6 mo*	FDA approved
Cosmoderm/Cosmoplast (INAMED Aesthetics)	Human source	? Sensitization, 1.3%. No skin test required.	Lasting up to 6 mo*	FDA approved
Autologous collagen	Harvested from the patient, treated	Ecchymosis, possible infections. No allergies/hypersensitivity reaction.	Lasting up to 6 mo*	FDA approval not required (extemporaneous preparations)
Cadaveric/derived from human tissue				
Autologen (Collagenesis, Beverly, MA, USA)	Collagen fibers prepared from patient tissue	Ecchymosis, possible infections	Not permanent*	FDA manufacturing standards
Dermalogen (Collagenesis)	Cadaveric, human dermis	Ecchymosis, transmission of prions/viral infections not reported. Foreign body reactions may occur. Hypersensitivity reactions may occur.	Not permanent*	FDA approved
Cymetra (LifeCell, Branchburg, NJ, USA) (micronized Alloderm)	Injectable human collagen derived from cadaver tissue. Screened for contamination	Ecchymosis. Transmission of prions/viral infections not reported.	Semipermanent	Subject to tissue bank regulations
Fascian (Fascia Biosystems, Beverly Hills, CA, USA)	Injectable from human donor fascia (collagenous tissue)	Ecchymosis. Transmission of prions/viral infections not reported.	Up to 6 mo*	Subject to tissue bank regulations
Isolagen (Isolagen, Inc., Exton, PA, USA)	Cultured autologous fibroblasts. Source: from patient.	Ecchymosis, possible infection	Not permanent*	FDA-approved manufacturing standards. Currently seeking device approval.
Hyaluronic acid				
Restylane/Perlane (Medicis Aesthetics Holdings Inc., Scotsdale, AZ, USA)	Nonanimal derived-hyaluronic acid	Rare allergic/hypersensitivity reactions. Acneiform eruptions, granulomas.	Up to 1 yr*	Restylane is FDA approved. Perlane is not FDA approved.
Hylan-B (INAMED Aesthetics)	Rooster combs of domestic fowl	Rare allergic/hypersensitivity reactions. Acneiform eruptions.	Not permanent*	FDA approved.
Semipermanent				
Artecoll (Artes Medical Inc, San Diego, CA ,USA)	75% collagen, 25% PMMA (Plexiglas spheres)	Lumping, granulomas, migration. Allergic reactions. Foreign body granuloma 0.01%	Immediate results,* semipermanent†	In use outside US; FDA approval pending

Table 1. Fillers at a Glance continued

Injectable	*Description*	*Adverse Reactions/ Side Effects*	*Outcomes*	*Legal Status*
Radiesse (formerly Radiance) (BioForm Medical, San Mateo, CA, USA)	Injectable calcium hydroxyapatite microspheres substance found in bone and teeth	Lumps, granulomas, clumping, migration. Little risk of allergic reaction.	Immediate results.* Reported to last 2–5 yr†	FDA approved only for vocal cord paralysis and urinary incontinence. Off-label use permitted.
Expanded polytetrafluoroethylene (Gore-Tex, W.L. Gore & Associates, Inc., Newark, DE, USA))	Prepared from Teflon (SoftForm)	Displacement of implant, extrusion of implant, infections, ecchymosis, herpes simplex exacerbation	Permanent*	FDA approved
Fat	Patient adipose tissue	Bruising, infection, edema	Not permanent*	No FDA requirements
Endoplast 50 (Laboratories Filorga, Europe)	Solubilized elastin peptides with bovine collagen	As with bovine collagen	Not permanent*	Not FDA approved
Sculptra (Dermik, Berwyn, PA, USA)	L-Polylactic acid, non–animal derived	Hypersensitivity? Allergic reaction?	1 –3 yr*	FDA approved for HIV facial wasting
Reviderm Intra (Rofil Medical International, Breda, the Netherlands	Dextran beads in Hyalon gel of non-animal origin	Granulomas? Hypersensitivity reactions? Overcorrection	Permanent*	In use outside US; not FDA approved
Silicone (Silikon [Alcon Labs, Fort Worth, TX, USA;], AdatoSil [AdatoSil Bausch & Lomb, Claremont, CA, USA])	Pure polymers derived from siloxane, 1,000/5,000 centistokes	Granulomas, migration (in excessive volumes), inflammatory reactions	Scars,* rhytids†	FDA approved for retinal tamponade. Off-label use permitted in 1997.

FDA = US Food and Drug Administration; HIV = human immunodeficiency virus; PMMA = polymethylmethacrylate.
*Immediate.
†Gradual.

rials such as these (which usually need to be injected more deeply and require more force for injection) probably create a greater risk of inadvertent intra-arterial injection and tissue necrosis secondary to occlusion of cutaneous arterioles. This process is often associated with prolonged blanching and pain at the injection site, and its occurrence should prompt immediate administration of heat, massage, and nitroglycerin paste. Hydrocolloidal dressings may minimize scarring; surgery should be avoided. To avoid perforation of the eye, make sure the needle is tightly attached to the syringe (Luer-Lock, Becton Dickinson, Franklin Lakes, NJ, USA). Direct all injections away from the eyes.

Exquisitely painful fluctuant cysts can occur following Zyplast injections and may be delayed (sometimes for days or weeks) before erythema and swelling are noted. Treatment consists of incision and drainage; intermittent systemic or intralesional steroids have been used. Systemic antibiotics are not generally helpful. Most allergic treatment-site reactions will resolve without scarring. When scarring occurs, excision, punch replacement grafts, dermabrasion, or laser resurfacing may be useful (unpublished personal data).[3]

Inflammatory and Noninflammatory Complications

Granulomas are a generic possibility following the implantation of any type of foreign material.[15–20] They may be asymptomatic or associated with erythema and swelling (sometimes years after treatment) with permanent fillers such as silicone.[8,10,11] Inflammatory granulomas are usually treated with oral and intralesional steroids in association with antibiotics such as minocycline, which target granulomas directly.[21,22] Noninflammatory fibrotic nodules can be treated using intralesional steroids and 5-fluorouracil.[23] Biologic immune response modifiers may be of future value for patients whose immunohistochemical analyses determine the mechanism and types of inflammatory cells and cytokines. Baumann and Halem reported successful

treatment of "silicone granulomata" with imiquimod,[24] which has also been used successfully to treat a granuloma that followed cosmetic tattooing.[25]

Conclusion

Soft tissue augmenting agents fill a very valuable niche in the treatment of a wide variety of cosmetic applications that cannot be treated effectively in any other way. In general, the less permanent agents are much more forgiving and permit both the doctor and the patient to change their minds should problems develop. The possibility of delayed complications (sometimes occurring years after treatment) has prevented some practitioners from employing long-lasting agents. Conversely, because of the rarity of serious complications when these agents are used properly, there are practitioners who could give equally valid arguments that permanent results are desirable. Indeed, it is fair to ask the question, "Should we use permanent injectable fillers for elective cosmetic treatments?" Arguments pro and con can be applied to any potentially risky procedure that is carried out solely for cosmetic purposes. This would include cosmetic surgical procedures that are carried out on a daily basis without fanfare or hand wringing.

References

1. Wolff K. Quo vadis dermatology: a scenario for the future. J Am Acad Dermatol 2003;48:605–8.
2. Duffy DM. Tissue injectable liquid silicone: new perspectives. In: Klein A, editor. Augmentation in clinical practice: procedures and techniques. New York: Marcel Dekker; 1998. p. 237–63.
3. Hanke CW. Adverse reactions to bovine collagen. In: Klein A, editor. Augmentation in clinical practice: procedures and techniques. New York: Marcel Dekker; 1998. p. 145.
4. Duffy D. Silicone granulomata management. Dermatol Times 2003;May:75–6.
5. Guttman-Yassky E, Weltfiend S, Bergman R. Resolution of orofacial granulomatosis with amalgam removal. J Eur Acad Dermatol Venereol 2003;17:344–7.
6. Hoffmann C, Schuller-Petrovic, Soyer HP, Kerl H. Adverse reactions after cosmetic lip augmentation with permanent biologically inert implant materials. J Am Acad Dermatol 1999;40:100–2.
7. Rudolph CM, Mullegger RR, Schuller-Petrovic S, et al. Unusual herpes simplex virus infection mimicking foreign body reaction after cosmetic lip augmentation with expanded polytetrafluoroethylene threads. Dermatol Surg 2003;29:195–7.
8. Blanchard M. Filler material may cause nodules, lumps in lips. Cosmetic Surg Times 2002;5:20–1.
9. Mang WL, Sawatzki K. Complications after implantation of PMMA (polymethylmethacrylate) for soft tissue augmentation. Z Hautkrankheit 1998;73:42–4.
10. Reisberger E-M, Landthaler M, Wiest L, et al. Foreign body granulomas caused by polymethylmethacrylate microspheres. Arch Dermatol 2003;139:17–20.
11. Duffy DM. In search of the perfect lip. Presentation at AAD 61st Annual Meeting, San Francisco; Forum 545, March 25, 2003.
12. Fisher AA. Reactions at silicone-injected sites on the face associated with silicone breast implant "inflammation" or "rejection." Curr Contact News 1990;45:393–5.
13. Hochberg MC. Cosmetic surgical procedures and connective tissue disease: the Cleopatra syndrome revisited. Ann Intern Med 1993;118:981–2.
14. Committee on the Safety of Silicone Breast Implants. Safety of silicone breast implants. In: Bondurant S, Ernster V, Herdman R, editors. Institute of Medicine, National Academy of Sciences. Washington (DC): National Academy Press; 2000.
15. Barr RJ, King DF, McDonald AM, Bartlow GA. Necrobiotic granulomas associated with bovine collagen test site injections. J Am Acad Dermatol 1982;6:867–9.
16. Barr RJ, Stegman SJ. Delayed skin test reaction to injectable collagen implant (Zyderm). J Am Acad Dermatol 1984;10:652–8.
17. Brooks NA. Foreign body granuloma produced by an injectable collagen implant at a test site. J Dermatol Surg Oncol 1982;8:111–4.
18. Alani R, Busam K. Acupuncture granulomas. J Am Acad Dermatol 2001;45:S225–6.
19. Zirkin H, Avinoach I, Edelwitz P. A tattoo and localized lymphadenopathy: a case report. Cutis 2001;67:471–2.
20. Darsow U, Bruckbauer H, Worret WI, et al. Subcutaneous oleomas induced by self-injection of sesame seed oil for muscle augmentation. J Am Acad Dermatol 2000;42 2:292–4.
21. Webster GF, Toso SM, Hegemann L. Inhibition of a model of in vitro granuloma formation by tetracyclines and ciprofloxacin. Involvement of protein kinase C. Arch Dermatol 1994;130:748–52.
22. Sente P, Bachelez H, Ollivaud L, et al. Minocycline for the treatment of cutaneous silicone granulomas. Br J Dermatol 1999;140:963–91.
23. Blugerman G, Schavelzon D, Dreszman R. Intralesional use of 5-FU in subcutaneous fibrosis. J Drugs Dermatol 2003;2:169–71.
24. Baumann LS, Halem ML. Lip silicone granulomatous foreign body reaction treated with Aldara (imiquimod 5%). Dermatol Surg 2003;29:429–32.
25. Solis R, Diven D, Colome-Grimmer M, et al. Experimental nonsurgical tattoo removal in a guinea pig model with topical imiquimod and tretinoin. Dermatol Surg 2002;28:83–7.