



A SUPPLEMENT TO

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The Advanced Art of Facial Fillers



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TARGET AUDIENCE: This activity has been developed for dermatologists, plastic surgeons, fellows, and residents in plastic surgery and dermatology.

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A companion educational webcast is located at www.advancedfacialfillers.com and www.sdefderm.com

All photos are courtesy of Jason Michaels, MD.

Educational Needs

The natural aging process—when fat and collagen under the skin begins to diminish—affects each individual differently. Many people find that the impact of aging negatively impacts their quality of life; therefore, they seek treatment to improve their appearance.

Physicians have many treatment options, surgical and nonsurgical, when addressing aging of the skin. Soft tissue fillers, which are among the nonsurgical group, are often considered the first line in the treatment of aging skin and are frequently used in combinations or with other techniques for facial rejuvenation. A variety of filler substances exist that address a wide range of cosmetic flaws, each bringing subtle, distinctive benefits. In some patients, more than one filler may be used to achieve the best results.

With several filler options available, physicians need to be aware of the benefits and potential risks of each. Filling substances commonly used by dermatologists and plastic surgeons include collagen, autologous fat, poly-L-lactic acid, calcium hydroxyapatite, and hyaluronic acid. Hyaluronic acid replaces lost volume and restores youthful contours to the skin to smooth away moderate to severe facial wrinkles and folds. Hyaluronic acid is a natural component of human skin and is the framework in which skin cells live. There are several hyaluronic acid products available, each having various characteristics, although all hyaluronic acid products bind water and give the skin volume.

Since each patient needs to be treated individually, physicians need to tailor their choice of dermal filler to the patient as well as learn proper injection techniques to avoid complications. To do so, dermatologists, plastic surgeons, and other health care professionals need to stay up-to-date on the latest innovations in the filler arena, as well as be proficient in injection technique.

Learning Objectives

After reading this supplement, participants should be able to:

- Discuss the causes, processes, and sites of facial biometric volume loss.
- Demonstrate knowledge of the treatment options for correcting facial biometric volume loss, including recently approved and investigational agents, and state the differences between stimulatory and replacement fillers.
- Compare the indications, side effects, and contraindications of the different filler options.
- Describe the various injection techniques, based on a clear understanding of the benefits and potential risks of each.

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Dr Comstock is a speaker for Allergan, Medicis, and Obagi.

Dr Michaels has nothing to disclose.

Educational Reviewer:

Robert Reina, MS, MBA has nothing to disclose.

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CME Planning Committee

Jennifer DiBenedetto of the EOCME has nothing to disclose regarding conflicts of interest.

Special Needs

We encourage participation by all individuals. If you have any special needs, please contact Sandy Bakos at (973) 630-2043 or s.bakos@elsevier.com.



The Advanced Art of Facial Fillers



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Increasing numbers of patients are becoming aware of and are seeking treatment with nonsurgical options for facial correction and rejuvenation of aging skin. Nonsurgical options are overwhelmingly the most commonly used modalities. For example, of the nearly 11.5 million cosmetic procedures performed in the United States in 2006, 82% were nonsurgical.¹

The trend toward nonsurgical cosmetic correction is continuing, driven mainly by the availability and continued development of a variety of effective and safe facial filler agents. In fact, in many cases, fillers are considered to be the first-line nonsurgical option for improving age- and photo-damage-related changes in the face, such as lines, wrinkles, and volume loss. In addition, the development of and improvements in other nonsurgical modalities also have contributed substantially to the range of options that can be offered to patients.

Various types of injectable fillers are available now for correction and rejuvenation of appearance. In some patients, the clinician may opt to use a combination of fillers, depending on an individual's specific needs. Injection of one or more fillers may be part of an overall treatment plan that also includes other modalities—for example, injection of botulinum toxin type A to prevent wrinkle formation, skin resurfacing procedures to smooth existing wrinkles, and/or laser blending of sun-induced lesions such as lentigines.

This supplement focuses on the injectable fillers commonly used by physicians: autologous fat, calcium hydroxyapatite, collagen, hyaluronic acid, and poly-L-lactic acid.

The Aging Face: Intrinsic and Extrinsic Factors

Intrinsic aging results from genetically programmed physiologic and histologic changes in all body tissues. The term “extrinsic aging” describes the changes that occur in tissue as a result of long-term exposure to environmental insults. Extrinsic aging is superimposed on the changes that result from intrinsic aging processes. The main agents of extrinsic aging of the skin include dehydration, exposure to toxins such as cigarette smoke, inadequate nutrition, and—especially—ultraviolet (UV) radiation damage from sun exposure.²

In the skin, intrinsic aging is characterized at the cellular level by changes that include epidermal thinning and, in the dermis, reduced numbers of fibroblasts, mast cells, and blood vessels.^{2,3} Photodamage—that is, changes that result from chronic exposure to UV radiation—adds to the intrinsic changes. In photodam-

aged skin, a flattening of the dermoepidermal junction often is seen, as is an increase in hyperplastic fibroblasts, among other cellular changes.²⁻⁴

The clinical signs of intrinsic aging in the skin include a loss of elasticity and an apparent thinning, as well as an increase in the prominence of blood vessels. Photodamaged skin typically also appears rough, sallow, and lax. In addition, photodamaged skin usually is hyperpigmented and red, demonstrating mottling and solar lentigines.^{2,3} The visible signs of photodamage typically is most severe in lighter-skinned individuals, most commonly on the face, neck, scalp, dorsa of the forearms and hands, and, in individuals with hair loss, on the scalp.⁵

In the face, specifically, both intrinsic and extrinsic aging is evident in the loss of soft tissue (dermal thinning, reduction of collagen and elastin, lipoatrophy, and muscle atrophy) as well as changes in the underlying skeletal structures—bone, cartilage, and teeth. The loss of soft tissue results in wrinkling and sagging of the skin, and facial fat tends to migrate downward and inward, producing jowls (**Figure 1**).

Fat loss in the lateral and central part of the face tends to create the appearance of lateral flattening and facial elongation.^{5,6} Under the eyes, the loss of muscle tone and bony framework can cause the natural fat pad in the tear trough to push out laterally (**Figure 2** on page 4). In addition, the malar fat pad tends to rotate inward and downward, creating a prominent nasolabial fold (**Figure 3** on page 4).

Figure 1. Jowls



Migration of facial fat downward and inward results in the formation of prejowl sulci.

With the loss of hard tissue in the cheek area, the zygomatic arch narrows. In the lower face, the maxillae, mandible, and teeth provide the underlying structure that defines a substantial portion of the face; diminishing bony tissue in the mouth area causes a “caved-in” appearance.^{4,5}

Volumizing Versus Facelift Surgery

Before facial fillers became available, the only remedy for loose, lax skin was surgery to pull the skin taut over the remaining muscle, fat, and bone and to remove the excess tissues. The postsurgical results could be extremely appealing, provided that the patient had a sufficient amount of natural subcutaneous fat prior to surgery. However, individuals with less-than-optimal subcutaneous fat or those who undergo more than one facelift procedure risk an unnaturally “pulled” look and the appearance of having an unusually pointed chin and nose—in sum, the loss of the “heart shape” (fuller cheeks, with softening contours down to the chin) associated with a youthful face.

In contrast, in appropriately selected patients, injectable fillers eliminate shadows, hollows, and concavity on the face and restore the soft contours characteristic of younger underlying tissue. Replacing lost volume allows

the clinician to sculpt facial contours with a more authentic, natural look.

Facial Filling Agents

Several nonbiodegradable and biodegradable fillers currently are marketed in the United States.

Nonbiodegradable Agents

Several silicone products are available that have an indefinite longevity. Like the polymethylmethacrylate (PMMA)/bovine collagen product that is discussed below, the currently available silicone agents represent a new generation of products in their class. Previously available silicone agents were not purified and resulted in a high incidence of latent granulomas.

With both the silicone and PMMA/bovine collagen agents, particular care must be taken to prevent overfill or improper placement. These can be problems with all filling agents, but with the slowly biodegradable and nonbiodegradable fillers, the results are either very long-lasting or permanent; the only recourse to correct overfilling or improper placement of silicone, PMMA/bovine collagen, and similar agents is to surgically remove the product.

Slowly Biodegradable Agents

One product recently introduced in the United States consists of synthetic microspheres of PMMA suspended in purified bovine collagen. This is a new generation of a similar product that was taken off the market because of an association with latent granulomas. This is a relatively expensive product but it may have a longevity of 5 to 10 years. To date, no reports of latent reactions have been reported with the new product.

Calcium hydroxylapatite (CaHA) consists of artificially produced bone mineral microspheres in an aqueous, carboxymethylcellulose gel. The bone mineral content is completely biodegraded and is nonallergenic. The product stimulates natural collagen growth and forms a bony matrix to

support the newly formed collagen. Over a period of 6 to 8 weeks after injection, the gel matrix is absorbed; eventually, the bone mineral microspheres break down into calcium and phosphate ions. The volumizing effect diminishes gradually, and the clinical effects last for 2 to 5 years. This agent is approved for correcting moderate to severe facial folds and wrinkles; it is also approved for the correction of lipoatrophy in individuals with HIV infection. In addition, CaHA has been used for many years as a radiographic marker and to improve vocal chord insufficiency and oromaxillofacial defects.

Poly-L-lactic acid (PLA) was initially approved in the United States for the correction of facial lipoatrophy in patients with human immunodeficiency virus (HIV) infection. Since that time, PLA has been used investigational—and off-label clinically—for the correction of fine lines, wrinkles, folds, and creases, as well as for augmentation, repositioning, and contouring of the cheeks, chin, and lips. The PLA microparticles are absorbed slowly over a period of several weeks after injection, but the newly generated collagen and the clinical effects last for at least 18 to 24 months.

CaHA and poly-L-lactic acid are considered stimulatory fillers—that is, they induce a fibroblastic response that results in the formation of

Figure 2. Tear Troughs



The natural fat pads under the eyes push out laterally when muscle tone and tissue structural support is lost.

Figure 3. Nasolabial Folds



In a younger face, fat pads provide a fullness in the cheekbones. In the aging face, the malar fat pads tend to rotate downward and inward, causing a loss of fullness in the cheeks and the formation of a prominent nasolabial fold.

collagen and other connective tissue. This property allows the clinical effects to last a number of years.

Autologous fat transfer involves the extraction of a patient's fat cells from the abdomen, thigh, or buttocks, processing of the material, and subsequent subdermal injection into the face. This is a semipermanent filler material, although localized resorption can occur. Autologous fat transfer is nonallergenic to the donor-recipient. This is a relatively costly and time-consuming process. Also, because it requires the use of large-gauge needles for reinjection, bruising and swelling are more common than with other fillers. In addition, sequential treatments usually are necessary to achieve the desired volume, so the downtime for the patient is longer than with other products.

Biodegradable Agents

Hyaluronic acid is a naturally occurring, water-soluble protein that was synthesized in the 1960s. In the skin, hyaluronic acid is the fluid portion of the connective tissue matrix that forms the scaffolding for collagen and elastin fibers. Hyaluronic acid used in dermal fillers is derived from various sources, including rooster combs and bacterial cultures. The product is approved for the correction of fine to severe wrinkles and moderate to severe folds such as deep nasolabial and glabellar folds, as well as for most types of scars, facial contours, restoration of the lip border, and lip enhancement.

The hyaluronic acid products in use today are referred to as nonanimal stabilized hyaluronic acid fillers. Hyaluronic acid molecules are consistent across species, so the risk for allergenicity is very low. Claims of longevity of clinical effects vary among specific products, but, in general, hyaluronic acid fillers have duration ranging from 6 to 12 months. (In our experience and that of some other clinicians, the duration seems to be longer than 12 months when hyaluronic acid is used in the upper face.)

Several hyaluronic acid products are available, with each having various characteristics, although all share the main mechanism of action in that they provide volume by binding water.

For individuals who desire facial correction but are uncertain or have reservations about some aspect of such therapy, hyaluronic acid products hold a distinct advantage in that the clinical effects can be reversed by subsequent injection of hyaluronidase. This enzyme is fast-acting, producing degradation of injected hyaluronic acid within minutes.

**"REPLACING LOST VOLUME
[WITH FACIAL FILLERS]
ALLOWS THE CLINICIAN
TO SCULPT FACIAL CONTOURS
WITH A MORE AUTHENTIC,
NATURAL LOOK."**

Avoiding Complications and Side Effects

Regardless of the type of filler chosen, injection of the upper face requires a high level of skill to avoid problems such as tissue necrosis or the formation of small emboli, which can occur if an artery is inadvertently injected. Injectors should have a sound knowledge of facial anatomy to minimize the possibility of ulcerations and inadvertent nerve damage.

Depending on the filler used, injecting at the appropriate depth is critical to achieving natural and cosmetically pleasing results. To avoid palpable nodules, care must be taken not to deposit excess product in bolus injections at any site; instead, a fluid, smooth injection technique is preferred. The glabellar area, in particular, should be approached with caution; to avoid necrosis, material should not be injected too deeply in this region. Conversely, an injection of a hyaluronic acid filler that is too superficial can result in a Tyndall effect—a "bluish" tint to the skin.

It is also important to be aware of facial symmetry. Most faces are asymmetrical to some degree, but erratic injections could grossly add to the effect if not approached with a critical eye.

Major arteries, veins, and nerves are also located below the eyes. One technique to avoid complications in this area is to place the needle at the bone and inject in a retrograde direction, rather than pushing down on the syringe and injecting ahead of the needle tip.

To prevent transmission of bacterial, viral, or fungal infections, instructions in the product labeling regarding product sterility should be strictly followed. Many products intended for single use on an individual patient are individually wrapped and it seems that the trend is growing toward single-use packaging. Any product that remains after a patient is injected should be discarded; this product should never be used to inject a second patient.

Antibacterial skin preparation should be routine prior to injection, and only products that are approved by the US Food and Drug Administration and marketed in the United States should be used. The sterility and quality of products purchased outside of the United States cannot be assured; purchasing filling agents from other sources is both medically and legally risky.

The most common side effect that occurs with facial injections is bruising. The risk for bruising is directly correlated with needle size and the velocity of injection. To minimize bruising, particularly in the upper face, the smallest needle possible should be used (of course, accommodating for the viscosity of the injected agent) and the material should be injected slowly. Patients who are scheduled to undergo injection of hyaluronic acid filler should be advised to avoid ingesting anticoagulant medications or herbal or food products with anticoagulant properties (including alpha omega-3-fatty acids, dong quai, echinacea, feverfew, fish oils, flaxseed oil, garlic, and papaya). We

have found that this helps minimize bruising, which tends to occur slightly more commonly with hyaluronic acid than with other facial fillers.

Finally, adequate pain control is important for patient comfort and to prevent a patient from moving during an injection and risking unnecessary bruising and/or improper or inaccurate placement of filler. For injections on most areas of the face, we use topical anesthesia—lidocaine 6%/tetracaine 6% or betacaine 20%/lidocaine 8%/tetracaine 4%. For injecting more sensitive areas, we use a small amount of injected anesthetics, usually no more than 0.05 to 0.1 cc of a particular product. For treating areas around the lips, we frequently use nerve blocks.

Some Applications of Hyaluronic Acid

In our practice, we use the full range of filling agents available. For this brief discussion of practical application of fillers, however, we will limit the illustrations to the use of hyaluronic acid, which can be used virtually anywhere on the face. Hyaluronic acid is also easy to use, nonallergenic, and associated with minimal to no side effects.

Injection Patterns

The standard injection patterns for placing injectable filler materials are

linear threading, serial punctures, fanning, and cross-hatching. In terms of injection depth, depending on the product, hyaluronic acid may be placed in the mid-dermal plane—that is, between the papillary and the reticular dermis—or, in some cases, in the reticular dermis or upper subcutaneous tissue. Often the subdermal plane is a critical plane for contouring the skin.

“INJECTORS SHOULD HAVE A SOUND KNOWLEDGE OF FACIAL ANATOMY TO MINIMIZE THE POSSIBILITY OF ULCERATIONS AND INADVERTENT NERVE DAMAGE.”

Injecting the Proper Amount of Filler

Occasionally, patients request correction of multiple sites during one visit, using only one syringe of product. In such cases, patients should be advised that this strategy typically results in a less-than-satisfactory cosmetic outcome because the amounts

injected at various sites may not be sufficient to achieve correction.

However, overcorrection also can be a problem. In our practices, we have seen a number of patients who have been injected with so much filler in certain areas that the appearance is not natural. Overcorrection is most noticeable in the tear troughs, upper cutaneous lip region, and body of the lips. For patients who require filling of deep wrinkles, folds, or scars, better results are likely if the clinician is conservative in the amount of filler injected. If necessary, additional filler can be injected at a follow-up visit in 2 weeks to 2 months.

The amount of filler injected also should be based on age-appropriate contours. To illustrate the injection of a proper amount of filler in the upper face, consider the cheek profiles of the mother and daughter in **Figure 4**. Note that the contour of the mother's face is flatter than that of the child's face. A rounder contour on the adult would look unnatural.

Injecting Lips

Defining and accentuating the vermilion border is very important to enhancing the appearance of the lips, which are the central focal point of the lower third of the face (**Figure 5**). However, injection of too much filling

Figure 4. Age-Appropriate Enhancement of the Cheek



Natural-looking and satisfying cosmetic results with facial fillers depends on the creation of age-appropriate contours.

Figure 5. Enhancement of the Lips



Injection of the proper amount of filling agent in the vermilion border of the lips results in excellent definition and accentuation.

agent can result in a protuberant lip (“trout pout”), as illustrated in **Figure 6**. To inject the vermilion border, begin at the center and work out laterally using a serial threading retrograde injection technique. To augment the size of the lips, careful and controlled depot injections can be deposited at the wet-to-dry margin in the “pillows” of the lips.

When a patient who is seeking lip enhancement is older than about 40 years of age, it is important to inject not only the lips but to treat the perioral area as a unit, also addressing any vertical wrinkles or marionette lines. Otherwise, the patient will have fuller lips, but likely will not be satisfied with the result because she will still appear to have an “unhappy,” downturned mouth.

Other Hyaluronic Acid Applications

Figures 7 and 8 illustrate the excellent cosmetic results that can be obtained with hyaluronic acid products for treating nasolabial folds and glabellar lines. In treating glabellar lines, it is important to avoid injecting too deeply and risking necrosis. However, injections that are too superficial will produce a bluish hue in the area when light reflects off the injected hyaluronic acid product close to the surface of the skin.

Figure 6. Overcorrection of Lips



An unnatural and unattractive result of overfilling of the lips is commonly referred to as “trout pout.”

Conclusion

Today’s patient who seeks cosmetic improvement for an aging face typically is educated, sophisticated, and usually aware of the range of possibilities available for achieving the desired correction. Often, one modality alone will not suffice, and clinicians who provide cosmetic procedures must be prepared to address each patient’s needs, desires, and expectations from this standpoint.

Facial fillers have been well accepted by both clinicians and patients and,

overall, are well tolerated. Participation in hands-on training and other educational programs will enable clinicians to choose injectable filler products appropriately and administer them safely and successfully.

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Figure 7 Correction of Nasolabial Folds



Hyaluronic acid was used to soften the nasolabial folds in this patient.

Figure 8. Correction of Glabellar Lines



Proper depth of injection of filler material is crucial to achieve satisfactory cosmetic results and, simultaneously, prevent complications such as tissue necrosis.

CME Post-Test Answer Sheet and Evaluation Form

Release Date of Activity: July 2008 • Expiration Date of Activity for AMA PRA Credit: July 31, 2009

Estimated Time to Complete this Activity: 1 hour

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CME Questions

Instructions: For each question or incomplete statement, choose the answer or completion that is correct. Circle the most appropriate.

- 1. When malar fat pads rotate inward and downward, the result is:
a. Marionette lines
b. Nasolabial folds
c. Prejowl sulci
d. Tear troughs
2. A flattening of the dermoepidermal junction often is seen as a result of:
a. Improper injection technique in placing facial fillers
b. Intrinsic aging
c. Loss of Langerhans' cells
d. Ultraviolet light damage
3. Three of the following facial fillers are categorized as slowly biodegradable. The exception is:
a. Autologous fat
b. Calcium hydroxylapatite
c. Poly-L-lactic acid
d. Silicone
4. Hyaluronic acid is:
a. The fluid portion of the connective tissue matrix in skin
b. Indicated for use in all facial areas except the lips
c. Only slightly allergenic in humans
d. Unsuitable for correcting deep folds
5. The most common side effect with facial injections is:
a. Bruising
b. Erythema
c. Pain
d. Swelling

Please Print (All information is confidential.)

Name: _____ Specialty: _____

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PRETEST ASSESSMENT: Please rate your current knowledge of facial fillers on a scale of 1 to 5, with 1 being the lowest and 5 the highest. 1 2 3 4 5

POST-TEST ASSESSMENT: Please rate your current knowledge of facial fillers on a scale of 1 to 5, with 1 being the lowest and 5 the highest. 1 2 3 4 5

COURSE EVALUATION: Please evaluate the effectiveness of this activity by circling your choice on a scale of 1 to 5, with 1 being the lowest and 5 the highest.

Objective #1. Discuss the causes, processes, and sites of facial biometric volume loss. 1 2 3 4 5

Objective #2. Demonstrate knowledge of the treatment options for correcting facial biometric volume loss, including recently approved and investigational agents, and state the differences between stimulatory and replacement fillers 1 2 3 4 5

Objective #3. Compare the indications, side effects, and contraindications of the different filler options. 1 2 3 4 5

Objective #4. Describe the various injection techniques, based on a clear understanding of the benefits and potential risks of each. 1 2 3 4 5

1. How do you rate the overall quality of the activity? 1 2 3 4 5

2. How do you rate the educational content of the activity? 1 2 3 4 5

3. After participation in this activity, have you decided to change one or more aspects in the treatment of your patients? ___ Yes ___ No

If yes, what change(s) will you make? _____

If no, why not? _____

4. Was the presented information fair, objective, balanced, and free of bias in the discussion of any commercial product or service? ___ Yes ___ No

If no, please comment: _____

5. Suggested topics for future activities: _____

6. Suggested authors for future activities: _____

7. Would you be willing to participate in postactivity follow-up surveys? ___ Yes ___ No

8. Would you be willing to participate in a phone, e-mail, or in-person discussion exploring ways to improve our CME activities? ___ Yes ___ No