

*The sheer number of available agents represents a benefit and a challenge. Dermatologists must understand what each agent does and when to use it.*

**T**here's no denying that interest in the use of dermal fillers for facial rejuvenation continues to grow among both patients and dermatologists. In addition to rhytides, volume loss is a hallmark of the aging face, and available filler agents offer a way to quickly and efficiently correct both complaints with minimal pain and recovery time. The relatively recent emergence of several filler agents and the anticipated approval of others presents dermatologists with increased opportunities to provide patients with natural-looking, lasting results.

Given the pace of development of filler agents "we have a lot of options to choose from and over the next year to two years, as more products come out, I think it will be an exciting time for us," observed cosmetic dermatologist Mark G. Rubin, MD at the 24th Annual Fall Clinical Dermatology Conference in Las Vegas in October. Effective patient management depends on selection of the filler agent or agents best-suited to the particular patient's needs. Additionally, dermatologists and patients should consider the adjunctive use of complimentary cosmetic services or procedures, as necessary, to augment cosmesis.

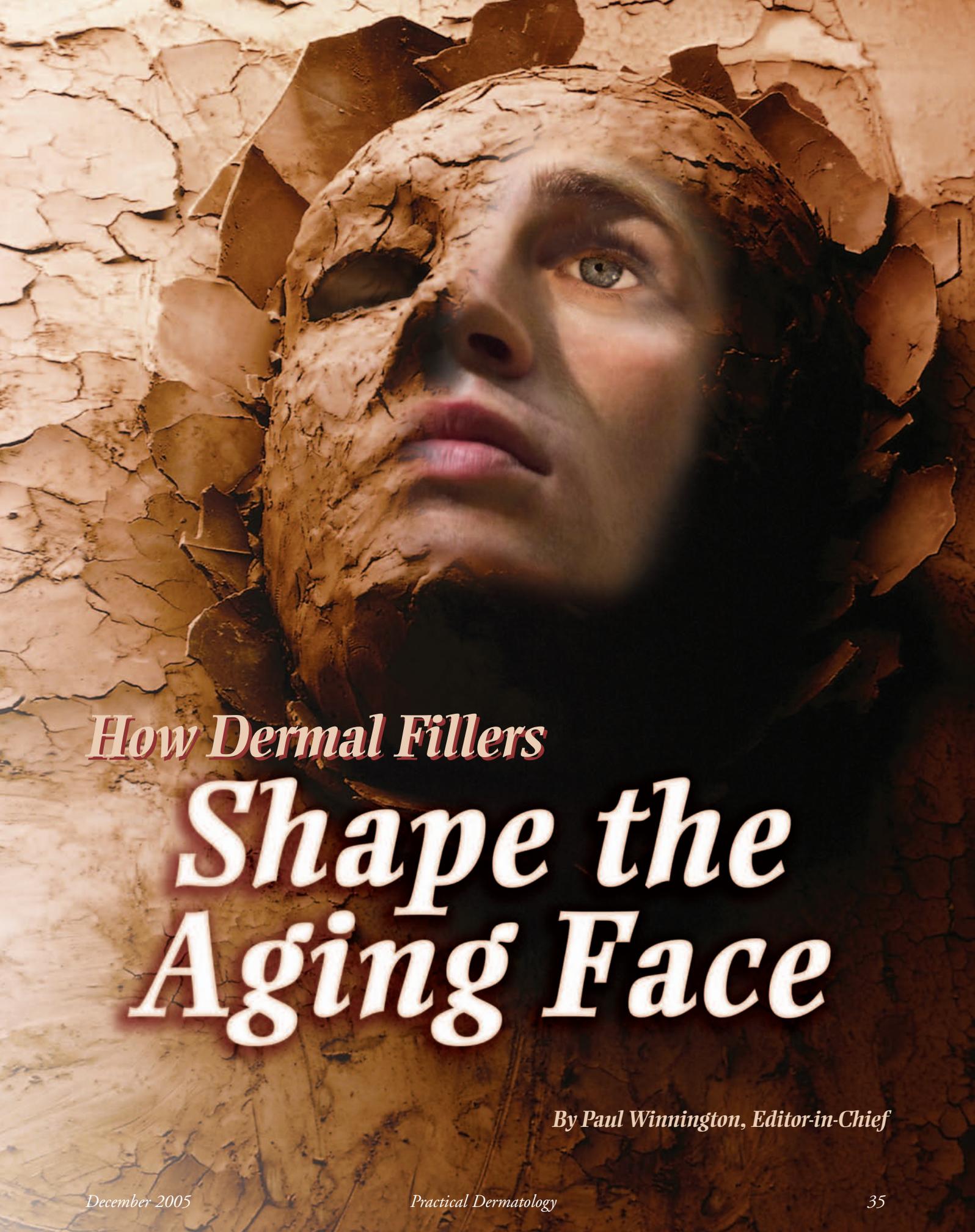
To make the best treatment decisions, dermatologists must know the strengths and weaknesses of available and forthcoming dermal fillers. The following is a review of key points relat-

ed to each filler, based on Dr. Rubin's presentation at the conference.

### ***Collagen Products***

The first of the marketed dermal fillers, Zyderm and Zyplast (Inamed, Inc.) still represent the gold standard, Dr. Rubin observed. The bovine collagen products derived from a protected herd (to avoid any concerns regarding BSE or "Mad Cow") produce notable and long-lasting correction of lines and wrinkles. However, there are drawbacks associated with the bovine collagen agents, including the need for refrigeration and, of course, the risk of allergic reactions. Patients must undergo skin testing prior to receiving treatment with Zyderm and Zyplast. Many specialists advocate a re-challenge prior to treatment for patients who have an initial negative test.

Cosmoderm and Cosmoplast (Inamed), which came out in 2003, are essentially identical to their counterparts Zyderm and Zyplast except that the collagen component is a bioengineered human collagen rather than bovine. While in theory there should be no allergic reactions to Cosmoderm or Cosmoplast, Dr. Rubin noted that reactions to the products have been reported. A total of six reactions were reported as of June 2003; additional unreported reactions are suspected.



*How Dermal Fillers*

# *Shape the Aging Face*

*By Paul Winnington, Editor-in-Chief*

## *Fillers at a Glance*

	<i>Longevity</i>	<i>Reactions/Allergy</i>	<i>Injection tips</i>
<i>Silicone</i>	<i>Permanent</i>	<i>Possible. May be delayed</i>	<i>Not approved. Not widely recommended</i>
<i>Zyderm/Zyplast Bovine collagen</i>	<i>Short-term (Several months)</i>	<i>2-3% allergic reaction rate; skin test required</i>	<i>Contains lidocaine; requires refrigeration; small gauge needle</i>
<i>Cosmoderm/Cosmoplast Bioengineered human collagen</i>	<i>Short-term (Several months)</i>	<i>Possible, probably not allergy to collagen; no skin test</i>	<i>Contains lidocaine; small gauge needle</i>
<i>Artecoll/Artefill PMMM in purified bovine collagen</i>	<i>Long-term (One year or more)</i>	<i>Allergy, redness, granulomas – largely technique dependent</i>	<i>Contains lidocaine; Use 26-gauge needle; inject deep dermis</i>
<i>Radiesse Calcium hydroxylapatite</i>	<i>Long-term (One year or more)</i>	<i>Nodules, specifically in lips</i>	<i>Use caution treating lips, especially for novice</i>
<i>Restylane, Hylaform, Hylaform Plus, Captique Hyaluronic acid</i>	<i>Short-term (Several months to one year)</i>	<i>Post-injection swelling, prominent needle marks</i>	<i>Injection more painful than collagen, no lidocaine</i>
<i>Sculptra Poly-L-lactic acid</i>	<i>Long-term (One year or more)</i>		<i>Volumizer targets areas not individual wrinkles. Results evident gradually over time; repeat (3-6) treatments every 4-6 weeks; uses 25 or 26-gauge needle</i>

Based on the presentation "Dermal Fillers" by Mark G. Rubin, MD. 24th Annual Fall Clinical Dermatology Conference, Las Vegas, NV; October 22, 2005.

However, these reactions may not be due to the collagen component of the fillers, Dr. Rubin stated. Five of the six reported patients submitted blood samples, and these showed no collagen anti-bodies. Additionally, whereas reactions to collagen tend to be long-lasting (up to about a year in some patients), the reported reactions to Cosmoderm and Cosmoplast were self-limited, lasting just a few weeks. These facts suggest that the reactions were to something other than collagen, perhaps latex or another allergen introduced as part of the treatment procedure.

Both Zyderm/Zyplast and Cosmoderm/Cosmoplast are administered with a small-gauge needle for enhanced

comfort and contain lidocaine to diminish pain associated with injections.

### *Polymethyl Methacrylate*

Artecoll (Artes Medical) is a promising filler agent used in Europe and Canada and likely to reach the US market as Artefill in 2006. Based on findings thus far, Artefill is likely to be indicated for long-term (but not permanent) correction, Dr. Rubin said. European data document the persistent effect of Artecoll for up to 15 years in some patients. Artecoll/Artefill consists of polymethyl methacrylate (PMMM) microspheres suspended in bovine collagen. The purified bovine component

poses less risk for allergenicity than other bovine collagen products, but skin testing is recommended.

From the initiation of clinical trials for Arteplast (PMMM microspheres suspended in gelatin) in the mid 1990's to the development of Artefill, PMMM-based fillers have a history of use and refinements, Dr. Rubin noted. Clinical experience showed that the gelatin-base of Arteplast absorbed rapidly, allowing the PMMM microspheres to gather into visible "lumps," which were unsatisfactory. Some of these "lumps" were simply the result of product migration or poor injection technique, some represented granuloma formation.

Artecoll contains smoother microspheres of PMMM in 3.5% bovine collagen with 0.3% lidocaine. The PMMM microspheres instigate fibroplasia that leads to enhanced collagen formation at the injection site. However, the inert material does endure at the injection sites. Long-term histopathologic studies of patients treated with Artecoll reveal 25 percent PMMM and 75 percent of the patient's own collagen at treated sites, Dr. Rubin reported. Artes reports a 0.01% occurrence rate for granulomas with Artecoll. Recent Canadian data report granulomas in about one in 6,000 Artecoll-treated patients.

Artefill contains a further refined "ultrasmooth" microsphere that is smoother than that used in Artecoll, possibly further diminishing the risks of granuloma formation.

Dr. Rubin stressed that most granulomas resolve long-term with use of intralesional steroids. At least half of patients will trace onset of granulomas to a trauma or virus. Many granulomas may be technique related. To enhance cosmesis and minimize risk of granulomas, the PMMM product must be deposited to the deep dermal, Dr. Rubin stressed. Superficial injection can produce itching, redness, and hypertrophic scarring, while subcutaneous injection will not produce sufficient clinically-notable correction.

Dr. Rubin also noted the need to accurately describe PMMM technology to interested patients, as some individuals may be reluctant to receive injections with what is essentially a plexiglass material.

### ***Calcium hydroxylapatite***

Radiesse (BioForm Medical) contains calcium hydroxylapatite (CaHa) crystals, a synthetic analog of the inorganic constituent of bone and teeth, suspended in a sodium methylcellulose base. When injected into soft tissue, CaHa does not calcify; it remains flexible and somewhat soft. Data regarding placement of CaHa in human skin are limited, although collagenesis is noted at treatment sites. Additionally, ingrowth of fibrous stroma has been documented, which holds the inorganic material in place.

Duration of CaHa in human skin has not been demonstrated. Dog bladder studies showed that the material began

to degrade after about one and one-half years. CaHa is non-toxic and non-antigenic. However, there is a risk of nodule formation, particularly when CaHa is injected in the lips. Two studies show that about 10 percent of patients treated with lip injections developed nodules, Dr. Rubin said. Therefore, use in the lips is not recommended for novices.

### ***Hyaluronic acid***

Hyaluronic acid (HA) is a polysaccharide that attracts and binds water to produce what Dr. Rubin described as “a nice, subtle, soft contour that improves over time.” Available options include Restylane (non-animal stabilized HA or NASHA, Medicis), Hylaform and Hylaform Plus (avian-derived HA, Inamed), and Captique (NASHA, Inamed). There are at this point no published studies comparing these various options head-to-head, though data for the agents individually suggest that there may be some differences in duration of effect.

HA products appear to be more long-lasting than collagen products and are especially suited for treatment of nasolabial folds as well as more subtle lines, Dr. Rubin said. While there are rare reactions to HA, there is no need for skin testing prior to treatment.

Compared to collagen products, injection of HA products may be more painful and produce more significant swelling up to 48-hours post-injection. As a result of decreased platelet aggregation, needle marks may be more prominent, Dr. Rubin added. But, he said, HA offers more flexibility for clinicians. Clinicians can massage and manipulate the material immediately following placement under the skin in order to achieve ideal placement and cosmetic effect.

Another HA-based product called Juvaderm (Inamed) is under FDA review and likely to be forthcoming.

### ***Poly-L-Lactic Acid***

Sculptra (Dermik) is not a true “filler” and is not intended for treatment of specific wrinkles. Rather, the agent is a volumizer that targets larger treatment areas. Treatment may result in

subtle wrinkle improvement due to lifting and tightening effects, Dr. Rubin noted. Consisting of poly-L-lactic Acid reconstituted with water, Sculptra is approved in the US for treatment of HIV-associated facial lipoatrophy but has been used in the clinic for age-associated volume loss.

Both patients and physicians must understand and anticipate Sculptra’s onset of action, Dr. Rubin warned. Immediately following injection, clinically evident swelling will result from the placement of the materials and fibroblast response. However, swelling will diminish overnight. Whereas the dermal fillers discussed above may demonstrate most significant improvement over weeks to months, they

will produce some level of immediate clinically-evident effect. By contrast, patients treated with Sculptra may have no clinical improvement the day after injection. Over several weeks, collagen synthesis occurs, leading to more durable volumizing of the treatment area. Ultrasound evaluation demonstrates skin thickening associated with treatment.

Due to its action, poly-L-lactic acid is described as a bioactivator. Best results require multiple injections (three to six) provided at four to six week intervals.

### ***One Size Fits None***

The degree of wrinkling and volume loss, the nature of the patient’s concern with them, and the desired longevity of improvement varies from case-to-case. Therefore, there is no

one approach to use of dermal fillers that applies to every patient. As Dr. Rubin put it, “There is a multitude of products out there. There is no one product that is the right one for every patient.”

For best results, dermatologists must approach each case with a fresh look at the patient’s needs and desires. Recognize that some cases may require use of more than one dermal filler and that optimal results may require adjunctive use of additional cosmetic procedures and services. Finally, recall that injection technique is critical to achieving optimal results; injection technique is as important as agent selection. 

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