

# Modern Approaches to Skin Care

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## Abstract

Recent years have seen an increased interest in minimally invasive and noninvasive cosmetic surgery and facial aesthetics. There has been a concomitant surge in the focus on skin care, which, by nature, is minimally invasive, and an exponential growth in the popularity and availability of minimally invasive dermatologic procedures and products. This review seeks to provide an overview of the most commonly employed skin care modalities, such as their mechanisms, indications for use, advantages and disadvantages, and side effects. The authors aim to provide the audience with a fundamental understanding of the options currently available to cosmetic surgeons and practitioners. Topics include retinoids, chemical peels, skin-lightening agents, lasers, microneedling, topical antioxidants, and injectables.

## Keywords

- ▶ skin care
- ▶ modern
- ▶ topical
- ▶ laser
- ▶ injectables

It is essential for every facial aesthetic surgeon to master noninvasive facial rejuvenation techniques. Facial rejuvenation can take many forms, ranging from topical skin care products, such as retinoids, topical acids, hydroquinone, and other bleaching agents, to lasers, injectable neuromodulators, and fillers. As innovation in the cosmetic field continues to focus on noninvasiveness, skin care has in turn received significant attention. Skin care offers endless possibilities for development, since the majority of procedures can be performed in the office setting. In this article, the authors provide an overview of the current tools available to the cosmetic surgeons. Because the depth and breadth of skin care is so extensive, discussing each technique in detail may prove overwhelming. For this reason, we will discuss only clinically relevant information regarding the most commonly used methods and products. While an overlap exists among the categories of skin care treatments discussed, topics have been organized into retinoids, chemical peels, skin-lightening agents, lasers, microneedling, topical antioxidants, and injectables.

## Retinoids

Retinoids, or retinoic acid products, are commonly used both directly and indirectly for their pigment-lightening abilities. Tretinoin and tazarotene are the two prescription retinoids currently available.<sup>1,2</sup> Dyspigmentation associated with photoaging is caused, on a basic level, by irregular grouping and activation of melanocytes. Retinoids function by normalizing this process.<sup>3</sup> While the benefit is more apparent with prescription retinoids, the popularity of over-the-counter retinols in cosmeceuticals is ever increasing. Retinol, which is converted to retinoic acid within the skin through an oxidative process, differs from retinoic acid in that it produces less skin irritation.<sup>4</sup> Despite the lower potency and higher concentration required, retinol can produce a significant effect on the appearance of photodamage and photoaging.<sup>5</sup>

Retinol is inferior to its prescription counterparts in achieving pigment lightening despite its relative success in treating signs of photoaging. Retinoids can be used to lighten dyspigmentation in an indirect manner, as they are often used as a penetration enhancer to more traditional skin lighteners.<sup>6</sup>

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Retinoids function in this way by causing cutaneous damage, thereby allowing for increased penetration of pigment-lightening agents such as hydroquinone and mequinol. These lightening agents will be discussed in more detail later in this review. Based on this principle, it is not surprising that retinoids can cause erythema, dryness, and scaling of treated areas of skin. To prevent excessive irritation and dermatitis, some preparations of tretinoin-containing skin-lightening agents integrate a topical corticosteroid. Corticosteroids may also decrease postinflammatory hyperpigmentation (PIH).<sup>6,7</sup>

### Topical Acids

Chemical peeling is one of the most common and oldest methods of skin resurfacing for facial rejuvenation used by cosmetic surgeons. Chemical peels function by disrupting specific portions of the epidermis and/or dermis through the reactions induced by the carboxyl or hydroxyl functional groups they contain, which are similar to standard wound healing.<sup>8</sup> The specific depth of damage obtained depends on many factors, including but not limited to the particular agent used and its concentration and pH. Other important factors are patient dependent and include patient skin type and skin condition. Chemical skin peels are known to be effective in the treatment of a wide range of skin conditions and commonly used in treating rhytids, dyspigmentation, scarring, acne, and actinic keratosis.<sup>9,10</sup>

Peels are categorized, in general, according to their depth of penetration and destruction. Superficial peels exert their effects on the epidermis while leaving the basal layer intact. They function to decrease keratinocyte cohesiveness and thereby promote desquamation. They have an additional ability to upregulate epidermal enzymes, causing epidermolysis and exfoliation.<sup>9</sup> Medium peels penetrate as deep as the papillary dermis, while deep peels extend to the midreticular dermis. Unsurprisingly, posttreatment healing time, frequency and severity of side effects, and results show a strong positive association with peel depth.<sup>10</sup> The practitioner must have a strong histopathologic understanding of the skin lesion, as the depth of peel chosen should reflect the cutaneous depth of the lesion. Consultation with the patient should include a thorough inspection of his/her skin type, thickness, and oiliness.

General indications for superficial chemical peels include photoaging, pigmentary disorders, such as melasma and post-inflammatory pigment changes, and acne.<sup>10,11</sup> Superficial peeling agents can be further classified into  $\alpha$ -hydroxy acids (AHAs),  $\beta$ -hydroxy acids (BHAs),  $\beta$ -lipohydroxy acids (LHAs), and tretinoin. Glycolic acid, the most commonly used superficial peeling agent, is an AHA. Jessner's solution (resorcinol, lactic acid, and salicylic acid in ethanol), trichloroacetic acid (TCA), and tretinoin are also used as superficial peels.<sup>10</sup> Medium-depth skin peels are more efficient at treating rhytids than superficial peels; they also treat pigmentary disorders and superficial atrophic scars. In contrast to superficial peels, they are contraindicated for use in melasma, as they may cause PIH.<sup>9</sup> Medium-depth peels induce coagulative necrosis of the epidermis and dermis, which results in keratinocyte regeneration and collagen synthesis.<sup>9,12</sup> Common medium-depth peels include Monet's combination (Jessner's solution with 35% TCA), Brody's combi-

nation (solid carbon dioxide plus 35% TCA), and Coleman's combination (70% glycolic acid and 35% TCA).<sup>10</sup> Some practitioners may actually regard a 35% TCA peel as a deep peel. Deep chemical peels treat severe photoaging, pigmentary disorders, and scarring. They are effective in inducing collagen formation through their penetration to the midreticular dermis, as discussed above. Phenols and croton oil are the main components of deep peels. Deep peeling with phenols is painful and usually requires either sedation or general anesthesia. Its clinical use is limited by the risk of cardiac compromise and therefore requires cardiac monitoring during treatment.<sup>9,12</sup>

While skin resurfacing using chemical peels is relatively safe, it does carry the risk of undesirable side effects. Such sequelae include postoperative edema and erythema as well as desquamation and can occur with peels of all depths.<sup>13</sup> Superficial peels rarely cause complications and are usually short-lived and mild. Side effects of all peels may also include infection, milia formation, dyspigmentation, delayed healing, and scarring. As discussed previously, the risk of these adverse effects also increases as the depth of peel increases. Dyspigmentation ranges from hyperpigmentation to complete achromia, which can be quite devastating.<sup>9</sup> Deeper peels are associated with a higher rate of posttreatment herpes simplex infection. As such, physicians should consider appropriate prophylaxis. In all cases of chemical peeling, the use of sunscreen for photoprotection is highly recommended and may help reduce the occurrence of the above-mentioned side effects.<sup>12</sup>

### Skin-Lightening Agents

Skin-lightening products are commonly used in dermatology and cosmetic surgery practices and have utility in all Fitzpatrick skin types. People with lighter skin types often require local skin lightening agents for treating melasma and PIH, often caused by acne and trauma. Those with darker skin types often have a need for lightening the areas of skin affected by pigmentary changes, such as around the eyes and intertriginous areas. In the past, hydroquinone was the gold standard for skin lightening. However, concerns over its safety have caused regulatory agencies in many countries, including the United States, to question its use. Hydroquinone is used in many different formulations of skin creams, ranging from over-the-counter strengths to prescription doses. It is the abundance of hydroquinone-containing products for sale that has raised health concerns among regulators. Hydroquinone is a phenolic compound that works by damaging melanocytes through a complex enzymatic process. It is an extremely strong oxidant, making it difficult to formulate a stable preparation. Hydroquinone is known to cause onychomycosis and increased concern was drawn when oral hydroquinone induced cancer in rodents. While the risks may be unrelated to its topical use, use of hydroquinone remains controversial due to its toxicity to melanocytes.<sup>14,15</sup> Hydroquinone products pose a challenge to the FDA, as the existence of many formulations predated the actual formation of FDA. The FDA has asked the pharmaceutical industry to perform studies demonstrating the safety of hydroquinone. Thus, the future of hydroquinone in cosmetic clinical practice is unknown and it remains to be seen how the outcomes of safety studies will change its use.<sup>2</sup>

The fears associated with hydroquinone have led to increased research in alternative skin-lightening agents, such as mequinol, azelaic acid, kojic acid, aleosin, licorice extract, ascorbic acid, soy proteins, and retinoids. Since these agents represent only a few in the exhaustive list of products under study, we encourage the readers to turn to the literature for a more meticulous review. Mequinol is the most commonly used alternative to hydroquinone and is approved for use in the United States and Europe. The mechanism of action of mequinol has not been entirely elucidated, though it appears to inhibit the formation of melanin precursors. Mequinol is commonly formulated with tretinoin as an enhancer and has demonstrated success in treating pigmentary disorders such as melasma and solar lentigines.<sup>2,16</sup> Mequinol has been shown to cause long-lasting depigmentation in Caucasian patients though repigmentation typically occurs with time. PIH has also been seen with the combination of mequinol and tretinoin, particularly in African American patients though this usually lightens with time after product discontinuation.<sup>2</sup>

Azelaic acid is another skin-lightening ingredient, currently available as a prescription gel for the treatment of rosacea. Its skin-lightening effects are mild and are generally regarded as inferior to hydroquinone in treating hyperpigmentation. However, it can be combined with retinoids to improve its efficacy. This product is generally safe, but it can cause temporary stinging with topical application. Though the market for treating dyspigmentation is enormous, hydroquinone, mequinol, and azelaic acid are the only three prescription-active ingredients available today. Other ingredients, such as kojic acid, aleosin, licorice extract, ascorbic acid, and soy proteins are members of the over-the-counter realm.<sup>2</sup> Retinoids, which are available as both prescription and over-the-counter, were discussed previously.

### Lasers

Lasers have been part of a cosmetic surgeon's armamentarium for several decades with the carbon dioxide laser demonstrating the first clinical applicability in the treatment of wrinkles and acne scars.<sup>17</sup> Lasers can be adjusted to target specific tissue types based upon absorption and scattering profiles of the tissue. Lasers produce their intended effect when the tissue absorbs the energy produced by the process of light amplification. Water, melanin, and hemoglobin serve as the primary endogenous chromophores in the target tissue, and each has its own absorption profile, which determines the degree of light absorption. Different types of lasers have different specificity and efficacy for targeting certain chromophores. The depth of laser penetration increases with increasing wavelength, which is inversely proportional to the amount of light scattering. This concept is valid until the midinfrared region of the electromagnetic spectrum. At this region, the water in tissue absorbs an increased amount of light, causing more superficial absorption.<sup>18</sup>

There are several basic principles that practitioners should adhere to in selecting the appropriate laser for each clinical circumstance. To target the correct tissue and minimize unwanted damage to surrounding tissues, the wavelength of the laser should match the absorption profile of the

target tissue. The duration of exposure to the laser, otherwise known as pulse width, should be shorter than the thermal relaxation time of the target. The energy of the laser must be adequate to destroy the intended tissue within the appropriate time interval. Additionally, the practitioner must carefully choose the spot size, pulse duration, and pulse delay parameters.<sup>12</sup>

Resurfacing lasers can, in general, be classified as either ablative or nonablative and fractionated or nonfractionated. Ablative lasers are more aggressive than nonablative lasers, as the latter leaves the tissue intact while the former vaporizes it.<sup>19</sup> Fractionated lasers create specific treatment zones while leaving surrounding tissue intact. Nonfractionated lasers, however, exert their effects on the entire treatment area.<sup>12</sup> Ablative, nonfractionated skin resurfacing is performed with lasers that emit photons specifically targeting water molecules in the skin. This results in the destruction of the epidermis, papillary dermis, and occasionally the reticular dermis. This process stimulates collagen synthesis, tissue remodeling, and finally, re-epithelialization.<sup>20</sup> Dermal and epidermal retraction follow, exerting a tightening effect on the skin.<sup>19</sup> The two classic ablative lasers are the carbon dioxide (CO<sub>2</sub>) laser and the erbium: yttrium-aluminum garnet (Er:YAG) laser. CO<sub>2</sub> lasers traditionally emit photons with a wavelength of 10,600 nm. They are most effective in the treatment of facial rhytids, acne scars, and atrophic scars.<sup>19</sup> It is thought to be effective in treating finer wrinkles rather than deeper rhytids and creases, such as those around the eyes and mouth.<sup>21</sup> Er:YAG lasers emit light with a wavelength of 2,940 nm, which falls in the infrared range. This wavelength is more readily absorbed by water molecules, and therefore, penetrates more superficially and causes less unintended damage to the surrounding tissue.<sup>20</sup>

While the CO<sub>2</sub> laser has traditionally been considered superior, a recent comparison of resurfacing and fractional lasers in the treatment of acne scars by You et al demonstrated that Er:YAG and CO<sub>2</sub> lasers were equally effective in treating acne scars; however, the Er:YAG laser was associated with a significantly shorter healing time and decreased discomfort, erythema, and edema compared with the CO<sub>2</sub> laser.<sup>21,22</sup> However, bleeding did increase with continued use of the Er:YAG laser, as it lacks the ability to photocoagulate blood vessels in the same capacity as the CO<sub>2</sub> laser. Ablative lasers produce a dramatic effect though they are associated with prolonged recovery times due to their superficial destruction of the skin. The most common side effect of nonfractionated CO<sub>2</sub> lasers is skin hypopigmentation. The degree of hypopigmentation correlates with the amount of tissue injury though hyperpigmentation may also occur.<sup>19</sup> Through the practice of the senior author (Y.D.) and aesthetician, patients prepped 6 weeks prior to a CO<sub>2</sub> laser procedure with 4% hydroquinone and 1% tretinoin had a decreased risk of hyperpigmentation and hypopigmentation through the suppression of melanocyte activity. Furthermore, if the patient is planning on pursuing chemical peel following laser treatment, the tretinoin may add to an increased penetration of the peel.

Though traditional CO<sub>2</sub> and Er:YAG lasers are nonfractionated, both have fractionated counterparts. Ablative, fractionated lasers preserve the resurfacing power of nonfractionated

lasers, but are associated with reduced trauma to the surrounding tissues. Although safer, they still carry significant risk of scarring, discoloration, and infection. The primary indication for fractionated, ablative lasers is mild skin tightening though they can also effectively treat photodamage, scars, and rhytids. When compared with ablative, nonfractionated lasers, there is a moderate posttreatment downtime and risk of infection.<sup>19</sup> Cohen et al reviewed clinical outcomes and complications of 730 patients who had undergone treatment with fractionated lasers and concluded that fractionated lasers are associated with reduced complication rates and higher degrees of patient satisfaction.<sup>20</sup> Complications, all of which resolved, included herpes simplex virus breakouts, acne eruptions, erythema, and hyperpigmentation, at an overall rate of 4.2%.

Nonablative lasers, including the 1319-nm pulsed energy laser, 1320-nm neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, and the 1450-nm diode laser, cause dermal collagen remodeling by targeting water as their primary chromophores. They are, however, less specific for water than ablative lasers and can cause varying degrees of absorption of hemoglobin and other pigmented molecules. This property results in selection for the dermis without affecting the epidermis.<sup>20</sup> Nonablative lasers are generally used for milder skin lesions and can be used for improving acne and acne scarring, skin texture, mild-to-moderate rhytids, and dyspigmentation. These lasers can be used in patients with darker skin complexions, as they do not cause the pigmentation changes associated with ablative lasers.<sup>19</sup> Nonablative lasers have the advantages of a shorter recovery time and fewer side effects over ablative lasers, but results are subtler and frequently require multiple treatment sessions.<sup>23</sup> Use of pulsed dye lasers (PDLs) is another nonablative approach and rely on organic dyes (e.g., rhodamine 6G) as their medium. PDLs have become the mainstay of treating vascular lesions, such as port-wine stains, facial telangiectasias, hemangiomas, pyogenic granulomas, and Kaposi's sarcoma. Other skin conditions, such as keloids, hypertrophic scars, striae distensae, lymphangiomas, and angiofibromas, may also respond positively to PDLs. Side effects associated with PDLs most commonly include posttreatment purpura and transient depigmentation though scarring may also occur. Superior clinical outcomes are associated with longer wavelengths and extended pulse duration, which allow for deeper tissue penetration.<sup>18</sup>

Intense pulsed light (IPL) is another modality used to treat acne, rosacea, and vascular lesions. Though not technically a laser, it is treated as one in practice and often replaces the PDL. The surgeon has the ability to adjust the wavelength for each use, depending on the targeted treatment. It is unique in its ability to target the red color often missed by other lasers, making it particularly useful for vascular lesions and rosacea. Recovery time is minimal though multiple treatments are often required for long-lasting success.<sup>24</sup>

### Microneedling with Plasma

Cosmetic surgeons today have many more tools in their treatment arsenal for skin resurfacing and rejuvenation than the classic lasers and peels. Microneedling therapy, also known as collagen induction therapy, is one such option.

This treatment was traditionally performed with a handheld skin-needling roller, which is coated in fine needles and rolled over the skin in various orientations. Newer techniques now include an automated needling device that uses a stamp-like motion causing less trauma than when the former technique is used. The depth of the needles is controlled by adjusting the needle depth to 0.25 to 2.5. This in turn creates micropunctures in the skin, which is crucial when working with thicker skin such as in the region of the perioral skin. The trauma induced stimulates fibroblast activity, which promotes the production of new collagen bundles and strengthening of the dermis. Microneedling is used for treating photo damage, striae distensae, and post-acne scarring.<sup>25,26</sup> El-Domyati et al demonstrated subjective improvement in rhytids and skin texture after 6 microneedling sessions performed over 3 months, as well as subjective improvements in post-acne atrophic scarring using microneedling in a separate study.<sup>25,27</sup> Alam et al demonstrated the advantage of microneedling therapy in the appearance of acne scars over time compared with the control group after three treatments, as well as minimal pain in a large, randomized clinical trial.<sup>28</sup> Side effects of microneedling include temporary pain, erythema, and edema. Because the epidermis is largely left intact, many of the risks and side effects associated with other treatment modalities are avoided. Multiple treatment sessions are typically needed to achieve desired results. A more recent development in microneedling therapy is the invention of automated microneedling. This is performed using a pen-like instrument with a handle composed of disposable needles and guides, which can be used to adjust the needle length. The device is placed on the skin and the needles enter in a perpendicular fashion.<sup>29</sup>

In recent years, microneedling with autologous platelet-rich plasma (PRP) has become increasingly popular, particularly in the treatment of atrophic acne scars. PRP is an autologous solution of highly concentrated plasma prepared from patient's blood. The platelets present in PRP contain a plethora of growth factors that are beneficial in the treatment of numerous dermatological conditions. Asif et al demonstrated in a split-face study that sites treated with PRP and microneedling showed statistically significant clinical improvement versus sites treated with distilled water and microneedling.<sup>30</sup>

### Kybella (Kythera Biopharmaceuticals, Inc.)

Submental adipose deposits are of great cosmetic concern for men and women of all ages and can occur independently of body mass.<sup>31</sup> Until recently, submental fat has been addressed primarily with surgical procedures ranging from liposuction to more advanced neck reconstruction. Kybella (deoxycholic acid) is an exciting addition to a cosmetic surgeon's toolbox, as it offers a nonsurgical, noninvasive alternative to the standards of care. At this point, Kybella is the only FDA-approved nonsurgical treatment for submental adipose deposition.<sup>31</sup> Kybella or deoxycholic acid is an endogenous secondary bile acid that is responsible for solubilizing dietary fat and aiding its breakdown and absorption within the gastrointestinal system. It works by causing localized adipolysis or destruction of adipose cells, which prevents them from reaccumulating. It also has a

tissue tightening effect via fibroblast recruitment and promotion of collagen synthesis.<sup>32</sup>

Disadvantages of Kybella include the frequent necessity of multiple treatments, as well as the risk of postprocedure sequelae, which can be significant. Swelling is worse after the first treatment and may take more than a week to resolve. The tissue tightening effects of Kybella may take months to reach its final state, which can be disincentive for patients seeking a more immediate fix.<sup>33</sup> Other postinjection findings include pain and bruising, which are typically mild or moderate and temporary. Pretreatment with oral ibuprofen and/or acetaminophen an hour before treatment and preinjection with lidocaine containing epinephrine 15 minutes before treatment have been shown to aid in the management of pain and bruising. Application of cold packs to the area before and immediately after may also reduce pain and swelling.<sup>34</sup>

While it remains to be seen if Kybella will become the new gold standard in the treatment of submental fat, it is certainly an exciting development in cosmetic surgery. Though the literature describing its clinical success is somewhat sparse given its relatively new presence as a cosmetic injectable, it has been shown both subjectively by patient and physician grading scales, as well as objectively by magnetic resonance imaging (MRI) and caliper measurements, to reduce submental fat.<sup>35</sup> One of the cornerstone studies thus far, the REFINE-1 trial (NCT01542034), included 506 patients with moderate to severe submental fat, who were randomized to Kybella (ATX-101) or placebo for up to six treatment sessions. Both patients and physicians in the Kybella limb treated reported a statistically significant change in submental appearance based on the rating scale used in the study. Additionally, among the 224 patients who were monitored using MRI, those treated with Kybella demonstrated a statistically significant decrease in submental fat.<sup>31</sup> Though more work is needed, these results are extremely promising, and the use of Kybella to improve the appearance of the submental region is likely to increase.

### Injectables and Fillers

Injectables and fillers have become the mainstay in noninvasive facial rejuvenation. Botulinum toxin A is the most widely utilized of these minimally invasive procedures with recent statistics suggesting a 759% increase in use over the last 15 years.<sup>36</sup> Botulinum toxin A (BONT-A) is a substance produced by the gram-positive rod *Clostridium botulinum* and functions to inhibit the presynaptic release of acetylcholine at the neuromuscular junction. This, in turn, diminishes the strength of muscle unit contraction in the treated area. Botulinum toxin A and B are the two most commonly used and potent forms available. BONT-A comes in three Food and Drug Administration (FDA)-approved cosmetic forms, including onabotulinumtoxinA (Botox Cosmetic; Allergan, Inc.), abobotulinumtoxinA (Dysport; Galderma Laboratories), and incobotulinumtoxinA (Xeomin; Merz Pharma). RimabotulinumtoxinB (Myobloc; Solstice Neurosciences, LLC) is the only BONT-B approved by the FDA for use in treating cervical dystonia.

Botox was initially approved by FDA in 2002 for the temporary treatment of glabellar rhytids in patients under the age of 65 years, which was followed by the approval of

Dysport in 2009 and Xeomin in 2011. Botox was approved for the treatment of lateral canthal lines (crow's feet) in 2013. Recently, the recommended dosage of BONT-A has decreased, which may be a result of the trend toward a more natural appearance as well as a boost in physician experience.<sup>37</sup> Interestingly, the literature suggests that the overall dosage required for a particular patient over time does not significantly change.<sup>38</sup> While each patient is unique, the results of Botox and Dysport last for approximately 3 to 4 months.<sup>39</sup> Side effects of BONT use, though uncommon, include erythema, infection, inflammation, pain, ecchymosis, and weakness. Common cosmetic side effects include the "Mephisto" brow, which occurs when the lateral aspect of the eyebrow is positioned superior to the medial aspect, and lip weakness. Evidence shows that such effects occur in approximately 11.1% of patients and are most frequent in the first 2 years of treatment.<sup>38</sup> These side effects can potentially be avoided with meticulous attention to facial anatomy and enlisting proper injection techniques. The "danger zone" for brow ptosis is a region within 2 cm above the eyebrow from the mid-pupillary line to the lateral reach of the brow. Fillers are preferred in the area for this reason.<sup>38</sup> The readers are directed to a multitude of available resources regarding injection technique, as it is too detailed for the purpose of this article.

In addition to the substantial increase in the use of botulinum toxin, the use of soft tissue fillers has seen a 274% increase in use over the last 15 years.<sup>36</sup> Neuromodulators and fillers should not be regarded as competing techniques but as complementary systems that can be used in concert to create a more balanced, desirable outcome. There are numerous options for injectable soft tissue fillers, including hyaluronic acid, Radiesse, and Sculptra. Hyaluronic acid, a naturally occurring substance within human connective tissue, is currently the most commonly used of these fillers. It is operator friendly and has an impressive safety profile and strong ability to improve facial volume and contour. Its effect can last up to 9 months, making it an attractive option for many patients.<sup>39</sup> There are many hyaluronic acid products available today, Restylane (Galderma Laboratories) and Juvederm (Allergan, Inc.) being two of the more common ones. Both are available in formulations containing lidocaine for reducing treatment-related pain. The ideal formulation to use is based on the particular anatomical location, the patient's skin type, and physician's and patient's preference.

Radiesse (Merz Aesthetis, Inc.) is another popular injectable filler, generally used for deeper folds and wrinkles. It is composed of calcium hydroxyapatite, which acts as a scaffold for endogenous collagen growth. Because of its high viscosity and predilection for nodule formation, deep injection is recommended. Nodule formation is most commonly seen on the lips and other dynamic areas of the face. While effects can last up to 2 to 5 years, the typical duration ranges from 9 to 18 months. The literature on Radiesse suggests that it is well tolerated and associated with a high rate of patient satisfaction. Temporary side effects, such as erythema, edema, pain, and itching may occur, but are almost always self-resolving. Even if nodules occur, they typically resolve without intervention.<sup>40</sup>

Sculptra (Galderma Laboratories) is an injectable form of poly-L-lactic acid and works by stimulating fibroblasts and

type I collagen growth. This process has an augmenting effect on soft tissues. A disadvantage is that it often necessitates multiple deep injections to obtain the desired effect. However, the outcomes can be quite long lasting with persistent results seen up to 2 to 3 years.<sup>41</sup> As is the case with Radiesse, Sculptra is prone to nodule formation. This can be avoided with deeper injections, overnight reconstitution times, and postinjection massage. While poly-L-lactic acid was initially approved for the treatment of facial lipodystrophy syndrome associated with human immunodeficiency virus infection, it is also used in healthy patients for purely cosmetic reasons. It is important to manage patient expectations in the preprocedure period because as stated previously, results may take up to 4 to 6 months to achieve and injections are typically performed over an approximately 3-month period. Additionally, due to the water content in the suspension, the immediate improvement seen after injection will dissipate over a few days and not return for several weeks when collagen growth becomes apparent.<sup>4</sup> More studies are needed to better elucidate the role of Sculptra in cosmetic facial rejuvenation.<sup>39,42</sup>

## Vitamins and Antioxidants

Over the last several decades, there has been an increase in the number of skin care products that incorporate vitamins and antioxidants. It is a well-recognized fact that the consumption of vitamins and antioxidants is vital to the health of humans, providing the tools necessary to combat the damaging free radicals that attack tissues at the molecular level. The skin, the largest organ of the body, serves as the primary protection against free radicals generated by external assaults, such as environmental pollutants and ultraviolet (UV) light. Thus, topical use of vitamins and antioxidants in cosmetic and skin care products, in addition to those consumed through diet, may help protect against and potentially correct damage by neutralizing the free radicals.<sup>43</sup> As there is currently an extremely extensive range of vitamins and antioxidants present in skin care products, we have chosen to limit our discussion to vitamin A, C, E, coenzyme Q, and flavonoids.

Vitamin A and its derivatives, including  $\beta$ -carotene, have been common cosmeceutical ingredients for many years. Vitamin A and its precursor  $\beta$ -carotene are potent antioxidants and have been shown to have topical photoprotective effects.<sup>44</sup> In addition to their antioxidant effects, vitamin A products are also beneficial in their ability to normalize keratinization. As retinoids, vitamin A and its derivatives have the ability to regulate epithelial cell development and differentiation. The use of these products can lead to improved skin texture, decreased roughness, and improvement in rhytids. Retinol is the most commonly used vitamin A ingredient in cosmeceuticals today and was discussed earlier.

Vitamin C, ascorbate, is an important skin care ingredient not only for its antioxidant actions, but also because of its function as a cofactor in the hydroxylation reactions required for collagen synthesis. Since humans are unable to naturally synthesize ascorbate, dietary intake is crucial. Vitamin C is an attractive cosmetic ingredient because of its ability to directly counteract UV-induced free radicals, as well as its function in regenerating

another potent antioxidant, vitamin E.<sup>45</sup> The three most common forms of vitamin C used in cosmetics are ascorbyl palmitate, magnesium ascorbyl phosphate, and L-ascorbic acid. Ascorbyl palmitate has been shown to have both antioxidant and anti-inflammatory properties. L-ascorbic acid is the most biologically active form of vitamin C and basic science research has demonstrated its ability to increase the synthesis of procollagen polypeptides, as well as stimulate collagen synthesis.<sup>46</sup>

Vitamin E, a lipid-soluble vitamin, is thought to have many health benefits in various organ systems because of its ability to reduce lipid peroxidation. Vitamin E has strong antioxidant properties and the potential to consume lipid peroxy radicals. Many studies have demonstrated the ability of vitamin E and its derivatives to reduce the erythema and edema associated with UV-radiation exposure. Studies have also shown clinical improvement in signs of skin aging, including skin wrinkling and skin tumor formation.<sup>43,47</sup> Other studies have shown that while vitamin E can reduce UV-induced erythema and edema when applied prior to UV exposure, it seems to have no benefit when applied after.<sup>48</sup> Though promising for its potential photoprotective abilities, more human studies must be performed to truly elucidate the function of vitamin E in skin care.

Vitamins are not the only antioxidants currently used in skin care products. Coenzyme Q and flavonoids are two such examples of popular non-vitamin antioxidants used as cosmeceutical ingredients. Coenzyme Q or ubiquinone is an endogenous, lipid-soluble substance that is highly concentrated in the epidermis. Evidence has shown that coenzyme Q may protect the vitamin E present in skin, strengthening its ability to fight free radicals. Because of this, coenzyme Q has become a popular ingredient in skin care products.<sup>43,49</sup> Flavonoids, which constitute a variety of compounds, are also reported to have dermatologic benefits due to their antioxidant properties. Polyphenols, for example, are best recognized for their skin care benefits.<sup>50</sup> They are found in various plants, and several studies have demonstrated their ability to repair UV-induced DNA damage, making flavonoids an extremely attractive option for skin care.<sup>51</sup>

## Conclusion

Skin care has always been a tremendously important aspect of any facial aesthetic surgeon's practice. Today, more than ever, the focus is shifting toward non- and minimally-invasive procedures, particularly with skin care. Skin care is a multifaceted topic of discussion, since it encompasses physician- and patient-directed care. Patient-directed skin care, which includes topical medications and treatments used by patients at home, is equally important as physician-directed skin care, which includes treatments, such as chemical peels, lasers, and microneedling, for the astute aesthetic surgeon to understand. The popularity and prevalence of over-the-counter skin care products, particularly those with antiaging properties, are increasing at a rapid speed. The multitude of new products and techniques that are being developed can make it challenging for a busy practitioner to stay up-to-date. The authors hope to have provided a concise and informative overview of some of the most relevant concepts in modern skin care.

## Conflict of Interest

None.

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