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Moisturizers: What They Are and a Practical Approach to Product Selection

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ABSTRACT

Moisturizers are widely used products that are important in many dermatologic and cosmetic skin therapies. They contain varying combinations of emollients, occlusives, and humectants to achieve their beneficial effects, and there is an overwhelming number of formulations available. To develop a rational approach for prescribing moisturizers, commercially available products can be categorized on the basis of application site.

Key Words: dry skin, emollients, humectants, moisturizers, occlusives

There is a vast array of moisturizers available on the market today and consumer demand for these products is growing. These products range from value brands that provide basic moisturization to luxury therapeutics with claims of anti-aging benefits. A recent US study found that moisturizers are the third most commonly recommended OTC topical skin product (13.4%) behind hydrocortisone (27.6%) and anti-infectives (23.4%).¹

What Are Moisturizers?

The term moisturizer is a marketing term with little or no scientific meaning. Consumers see moisturizers as actively increasing the water content of the skin. Dermatologists see moisturizers as bland oleaginous substances that are applied to the skin by rubbing.² The term “moisturizer” does not necessarily imply that moisture or water is being added to the skin. Moisturizers are a key component of basic skin care especially when there is alteration of the epidermal barrier and reduced water content in the epidermis.³ They are used to restore the barrier function of the epidermis, to cover tiny fissures in the skin, provide a soothing protective film, and increase the water-content of the epidermis. They may, thus, slow evaporation of the skin's moisture, thereby maintaining hydration and improving the appearance and tactile properties of dry and aging skin. Newer products claim to have other properties such as anti-aging, skin-firming, anticellulite, and sun-protectant effects.

How Do Moisturizers Work?

For many years, epidermal water content has been known to be crucial for skin plasticity and the prevention of “dry skin”.⁴ Traditionally, moisturization was believed to inhibit transepidermal water loss (TEWL) by occlusion. Water originates in the deeper epidermal layers and moves upward to hydrate cells in the stratum corneum (SC), eventually being lost to evaporation.

The SC architecture is the most important factor in water flux and retention in the skin, and in overall level of moisturization.⁵ The four key processes for the formation and functioning of the SC are the corneocyte process, SC lipid process, natural moisturizing factor (NMF) process, and desquamation process.⁶ Corneocytes are the physical barrier of the SC and, when hydrated, contribute to elasticity. The lipid bilayers of the SC function as a moisture barrier and although they prevent the entry of many chemicals, they are the means of entry for most topically applied substances. The NMF is found within corneocytes and is a mix of hygroscopic molecules that, by helping maintain hydration in the corneocyte, keep the SC hydrated. Half of the NMF is amino acids derived from the protein filaggrin in keratinocytes, and the other half is salts, including lactates, urea, and electrolytes. Production of NMF is directly related to external humidity. In desquamation, corneodesmosomes are degraded by water-dependent hydrolytic agents. When there is low moisture in the SC, these enzymes do not work efficiently. Corneocytes accumulate on the skin surface producing the signs of dry skin, e.g., when the moisture content is less than 10%, and when there is loss of continuity of the SC.²

The moisturizing treatment involves repairing the skin barrier, retaining/increasing water content, reducing TEWL, restoring the lipid barriers' ability to attract, hold and redistribute water, and maintaining skin integrity and appearance. Moisturizers perform these functions by acting as humectants, emollients, and occlusives.⁷ Moisturizers containing collagen and other proteins, i.e., keratin and elastin, claim to rejuvenate the skin by replenishing its essential proteins but whether or not they have any effect on skin hydration is questionable.² Moisturizers also act to reduce skin friction and increase skin hydration by providing water directly to the skin from their water phase and by increasing occlusion, as measured as a decrease in TEWL.⁸ Loden suggests that skin care products not only form an inert, epicutaneous layer, but that they also penetrate and influence the structure and function of the skin.⁹

Moisturizers have little effect on the mechanical properties (i.e., distensibility, hysteresis, and elasticity) of the skin but do increase skin hydration significantly, as shown by an increased skin capacitance.¹⁰ When moisturizers are used to improve skin plasticity it is suggested that lipid-rich formulations be used.¹¹

Emollients

Emollients, which are mainly lipids and oils (see Table 1), hydrate and improve the appearance of the skin by contributing to skin softness, enhanced flexibility, and smoothness. The “skin slip” or lubricity of some moisturizers, contributes to consumer satisfaction and product preference.⁵ Consumers desire smooth skin following moisturizer application.³ Emollients serve to fill the cracks between clusters of desquamating corneocytes and are not usually occlusive unless applied heavily.

Long chain saturated fatty acids and fatty alcohols are commonly used in topical pharmaceuticals and cosmetic formulations. They exert their benefits through effects on the skin barrier, partially through improved repair, and on permeability.¹² Examples include stearic, linoleic, linolenic, oleic, and lauric, which can be found in palm oil, coconut oil, and wool fat. A sterol-enriched fraction from canola oil reduced clinical signs of sodium lauryl sulphate (SLS)-induced irritation.¹³ Other lipids (e.g., fish oil, petrolatum, shea butter, and sunflower seed oil) had no effect on the degree of irritation. Loden and Andersson suggested that canola oil assisted the skin in supplying the damaged barrier with adequate lipids. Essential fatty acids (i.e., linoleic and alpha-linoleic acids) influence skin physiology and pathology via their effects on skin barrier functions, eicosanoid production, membrane fluidity, and cell signaling.²

Occlusives

Occlusives reduce TEWL by creating a hydrophobic barrier over the skin and contributing to the matrix between corneocytes, and have the most pronounced effect when applied to slightly dampened skin. There

Astringent Emollients	Cyclomethicone, dimethicone, isopropyl myristate, octyl octanoate
Dry Emollients	Decyl oleate, isopropyl palmitate, isostearyl alcohol
Fatting Emollients	Castor oil, glyceryl stearate, jojoba oil, octyl stearate, propylene glycol
Protective Emollients	Diisopropyl dilinoleate, isopropyl isostearate
Protein Rejuvenators	Collagen, elastin, keratin

Table 1: Common substances with emollient properties

Fatty Acids	Lanolin acid, stearic acid
Fatty Alcohols	Cetyl alcohol, lanolin alcohol, stearyl alcohol
Hydrocarbon Oils/ Waxes	Caprylic/capric triglyceride, mineral oil, paraffin, petrolatum, silicone derivatives (cyclomethicone, dimethicone), squalene
Phospholipids	Lecithin
Polyhydric Alcohols	Propylene glycol
Sterols	Cholesterol
Vegetable Waxes	Candelilla, carnauba
Wax Esters	Beeswax, lanolin, stearyl stearate

Table 2: Common substances with occlusive properties

is a wide range of agents with occlusive properties (see Table 2). Their main limitations include odor, potential allergenicity, and the greasy feel associated with most occlusives.

Petroleum jelly, in a minimum concentration of 5%, reduces TEWL by more than 98% and is the most effective occlusive, followed by lanolin, mineral oil, and silicones (e.g., dimethicone), which only reduce TEWL by 20%-30%.^{2,14} Occlusives are thought to diffuse into the intercellular lipid domains, thus contributing to their efficacy. Petrolatum is widely used as a classic moisturizer. Lanolin, a complex structure of esters, diesters, and hydroxyesters of high molecular weight, lanolin alcohols, and lanolin acids, is also widely used and quite effective.^{14,15}

Humectants

Humectants (see Table 3) are able to attract water from two sources: they enhance water absorption from the dermis into the epidermis, and in humid conditions they also help the SC to absorb water from the external environment. Many humectants also have emollient properties.³

The most effective humectant is the trihydroxylated molecule, glycerol.¹⁶ Immature corneocytes are fragile but mature into more resilient and protective cells as they migrate through the SC.^{7,17} Glycerol hastens the maturity of corneocytes through the activation of residual transglutaminase activity in the SC.¹⁸ Also, by facilitating the digestion of desmosomes and subsequently enhancing desquamation, glycerol reduces the scaling associated with xerosis.¹⁹

Found in the NMF, pyrrolidine carboxylic acid hydrates the skin, and has been shown to improve xerosis.²⁰

Urea is another important humectant. In double-blind studies moisturizers with urea have been shown to

reduce TEWL in atopic and ichthyotic patients,^{21,22} and reduce SLS-induced skin irritation.⁸

Alpha hydroxy acids (e.g., lactate) are effective agents for the treatment of dry skin; following treatment with lotions containing D-, L-lactic acid, the SC prevents xerosis more effectively.²³ Lactic acid, particularly the L-isomer, stimulates ceramide biosynthesis leading to higher SC ceramide levels that result in a superior lipid barrier and more effective resistance against xerosis.

One major drawback of humectants is that some of them can increase TEWL³ by enhancing water absorption from the dermis into the epidermis where it can then be lost into the environment. For this reason, they are almost always combined with an occlusive agent. Occlusive and humectant ingredients work together to enhance epidermal hydration and barrier function.

Where Are They Used?

Moisturizers are often used in a variety of conditions including xerosis that is due to a genetic tendency (e.g., ichthyosis) or is secondary to an underlying

<ul style="list-style-type: none"> • Gelatin • Glycerin • Honey • Hyaluronic acid • Panthenol • Propylene glycol • Sodium and ammonium lactate • Sodium pyrrolidine carboxylic acid • Sorbital • Urea

Table 3: Common substances with humectant properties

disease (e.g., diabetes, hypothyroidism, or atopic dermatitis) (see Table 4). They are also used following epidermal barrier damage from harsh cleansers, topical medications or astringents.

What is the Ideal Moisturizer?

Patients who are confused by media hype often ask this question. The ideal moisturizer should be:²

- Effective—hydrating the SC reduces and prevents TEWL
- An emollient—makes skin smooth and supple and reduces TEWL
- An aid in restoring the lipid barrier, i.e., duplicating and enhancing the skin’s natural moisture retention mechanisms
- Cosmetically elegant and acceptable
- Moisturizing to sensitive skin—i.e., hypoallergenic, nonsensitizing, fragrance free, noncomedogenic
- Affordable
- Long-lasting
- Absorbed rapidly providing immediate hydration.

Formulation Characteristics

Nearly all contain a combination of emollients, occlusives, and humectants. Combining occlusives

and humectants enhances the water-holding capacity of the skin. Also, the esthetic properties of the moisturizer and the stability of the active ingredients can be influenced by the addition of certain emollients.³⁶ When glycerol, a humectant, is combined with occlusive agents, there is a synergistic alleviation of dry skin.³⁷

The predominant form of delivery is the cosmetic emulsion. The process of emulsification combines the phases containing the ingredients. The majority are lotions (oil-in-water emulsions) or creams (water-in-oil emulsions). More complicated emulsions (e.g., oil-in-water-in-oil, oleaginous mixtures, serums, gels, sprays, and milks) are used to deliver and stabilize some active ingredients. The esthetics vary in accordance with consumer preferences and the desired attributes. Compliance will likely be poor if the patients are not satisfied with their prescribed moisturizer.²² Low pH and sensory reactions, e.g., from lactic acid and urea, can cause burning on application and may reduce patient acceptance.

The precise nature of these formulations is not disclosed and the ingredients are not always listed on the product.³⁸

Lotions tend to be thinner and are commonly preferred for daytime facial use. The typical components include propylene glycol, mineral oil, and water. Creams are generally made with heavier lipids, are often applied at night, and are typically composed of petrolatum, lanolin, mineral oil, and water.

Disorders of Cornification	<ul style="list-style-type: none"> • Xerosis²⁴ • Ichthyoses^{25,26} <ul style="list-style-type: none"> - Ichthyosis vulgaris - Bullous congenital ichthyosiform erythroderma - Lamella ichthyosis
Secondary to an Underlying Disease ³	<ul style="list-style-type: none"> • Diabetes • Hypothyroidism • Atopic dermatitis
Irritant Contact Dermatitis at Home and at the Workplace ²⁷⁻²⁹	
Other Dermatologic Disorders ^{30,31}	<ul style="list-style-type: none"> • Acne vulgaris • Rosacea • Retinoid-induced irritant dermatitis • Psoriasis • Epidermolytic hyperkeratosis
Maintenance of Skin Integrity in Special Populations	<ul style="list-style-type: none"> • Elderly patients³² • Diabetic foot³³ • Neonates^{17,34}
Important Component of Skin Cleansers ³⁵	

Table 4: Where are moisturizers used?

Industry adjustment of the oil-water ratio, occlusives, and emollients provides the basis of formulations for different skin types (oily, normal, dry complexions) and sites of application. Ideally, dermatologists should recommend therapeutic moisturizers that are noncomedogenic, devoid of irritant ingredients, and compatible with many therapeutic regimens.³¹

Moisturizers are generally marketed in two categories: face care, and hand and body care.⁵ Within each category are specialized products geared for certain areas such as the lips, eyes, and feet. Common moisturizers available over-the-counter can be classified according to application site (see Table 5).

The face is particularly prone to effects of the environment (e.g., drying in cold, arid conditions, and aging from sun exposure). Moisturizers designed for the face are typically non-greasy, noncomedogenic emollients, with an emphasis on skin feel and aesthetics with maximal skin benefits. Silicone derivatives in particular are targeted for consumers with oily skin. Other ingredients are added to reduce the appearance of excess shine such as oil-absorbent compounds (e.g., kaolin, talc).

Antiaging technology is the fastest growing segment of facial moisturizer market.⁵ Moisturizers play a role in treating and augmenting therapy for the aging face.³⁹ Certain agents are especially useful for photoaged skin and include sun protectants, alpha hydroxy acids (e.g., glycolic acid), and retinol and its derivatives.^{36,40}

Hand and body care is mainly aimed at the prevention and treatment of dry skin. Some specialized products' aims include the reduction of cellulite, firming, bronzing, and minimizing the signs of aging. There are a wide variety of products ranging from those for everyday use and good value to more expensive products for cosmetic and therapeutic use.

Conclusion

As noted in Table 5, the skin care marketplace offers a wide array of moisturizers targeted for face, body, hands, or feet, providing the consumer with good, effective moisturization. Even more clinically effective and cosmetically appealing formulations will occur with improved emulsion technologies, better delivery of active ingredients, and further combinations.

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Directory of Moisturizers

Location	Product	Active Ingredient(s)
Face	Alyria Hydrating Complex (Canderm)	Glycolic acid, glyceryl stearate
	Cetaphil® Daily Facial Moisturizer (Galderma)	Cyclomethicone, glycerin
	Complex 15 Face Cream (Schering Plough)	Dimethicone, lecithin
	Dormer® 211 Face Cream (Dormer)	Hyaluronic acid complex, lecithin
	Dove Sensitive Essentials (Unilever)	Petrolatum, mineral oil, dimethicone
	Enydrial (Roc Laboratories)	Hypoallergenic base
	Eucerin® 5% Facial Cream (Beiersdorf)	5% Urea
	Hydra + Destressant (Roc Laboratories)	Hypoallergenic base
	Hydraphase UV – SPF30 (La Roche Posay)	Glycerin, thermal spring water
	Impruv™ (Stiefel)	Glycerin, shea butter, squalene
	Neostrata® AHA Cream (Canderm)	4% glycolic acid
	Neutrogena Moisture Cream (Johnson and Johnson)	Glycerin, dimethicone, petrolatum
	Nutrilogie 1 Intensive Care for Dry Skin (Vichy Laboratories)	Sphingo-lipid, urea, glycerin
	Nutrilogie 2 Intensive Care for Very Dry Skin (Vichy Laboratories)	Sphingo-lipid, urea, beeswax, shea butter
	Oil of Olay Moisture Cream & Oil of Olay Complete All Day Cream (Proctor and Gamble)	Hypoallergenic base
	Reversa® Skin Smoothing Face and Neck Cream (Dermtek)	8% Glycolic acid
	Spectroderm® (Glaxo Smith Kline Consumer)	Dimethicone, glycerin
	Toleriane Riche Smooth Protective Cream (La Roche Posay)	Shea butter, squalene, glycerin
	Toleriane Soothing Protective Care (La Roche Posay)	Glycerin, squalene
	Vichy Thermal Fix 1 and 2 (Vichy Laboratories)	Filladyn, sunflower oil, glycerin
	Vichy Novadiol Intensive Re-Densifying Care Face and Neck (Vichy Laboratories)	Phytocomplex, beeswax, glycerin
	Akerat Body Care Cream (Avene)	Mineral oil, urea
	Aveeno® Daily Moisturizing Lotion (Johnson and Johnson)	Glycerin, petrolatum, natural colloidal oatmeal
	Cetaphil® Lotion (Galderma)	Glycerin, dimethicone
	Cliniderm Base (Canderm Pharma)	Non-medicated, hypoallergenic base
	Complex 15 Lotion (Schering Plough)	Dimethicone, lecithin
	Curel Alpha Hydroxy Dry Skin Lotion (Jergens)	5% Lactic acid, glycerin, petrolatum
	Curel Therapeutic Moisturizing Lotion (Jergens)	Glycerin, petrolatum
	Dormer® 211 Lotion (Dormer)	Hyaluronic acid complex, lecithin
	Dove® Sensitive Skin (Unilever)	Sunflower seed oil, glycerin, petrolatum, lanolin alcohol
	Episec Lotion (Odan)	Petrolatum, propylene glycol, trimethanolamine
	Eucerin® 10% Urea Lotion (Beiersdorf)	10% Urea
Eucerin® Moisturizing Lotion (Beiersdorf)	Mineral oil, lanolin	
Eucerin® Cream (Beiersdorf)	Petrolatum, mineral oil, lanolin	
Glaxol Base (WellSpring Pharma)	Non-medicated, hypoallergenic base	
Keri® Original (Bristol Myers Squibb)	Lanolin, mineral oil	
Keri® Advanced Moisture Therapy (Bristol Myers Squibb)	Dimethicone, petrolatum	
Body		

	Keri® Age Defy & Protect Moisture Therapy with AHA (Bristol Myers Squibb)	5% Lactic acid, dimethicone, petrolatum
	Lac-hydrin® Lotion (Bristol Myers Squibb)	12% Lactic acid
	Lipidose 1 Re-hydrating Body Milk (Vichy Laboratories)	3% Urea, ammonia lactate, glycerin
	Lipidose 2 Re-lipidising Body Cream (Vichy Laboratories)	Shea butter, glycerin
	Lipikar & Lipikar Baum (La Roche Posay)	Shea butter, glycerin, mineral oil
	Lubiderm® Advanced Moisture Therapy (Pfizer)	Glycerin, mineral oil
	Lubiderm® Lotion Scented/Unscented (Pfizer)	Lanolin, mineral oil, petrolatum
	Moisturel® Cream & Moisturel® Lotion (Bristol Myers Squibb)	Dimethicone, petrolatum
	Neostrata® Lotion (Canderm)	8% Glycolic acid
	Nivea Body Moisturizing Lotion (Beiersdorf)	Glycerin, dimethicone
	Nutraderm® Cream & Nutriderm Lotion (Galderma)	Mineral oil
	Oil of Olay Moisturizing Lotion (Proctor and Gamble)	Glycerin, petrolatum
	Reversa® Skin Smoothing Body Lotion (Dermtek)	10% Glycolic acid
	Trixera Cream (Avene)	Ceramides, linoleic, linolenic acid
	Uremol 10% Lotion (Stiefel)	10% Urea
	Urisec Lotion (Odan)	12% Urea
	Vaseline Intensive Care (Unilever)	Glycerin, petrolatum
Hands	Aveeno® Moisturizing Cream (Johnson and Johnson)	Shea butter, colloidal oatmeal
	Barriere Cream (National Care Products)	Dimethicone
	Cetaphil® Barriere Cream (Galderma)	Shea butter, glycerin, dimethicone
	Cetaphil® Cream (Galderma)	Petrolatum, dimethicone
	Cliniderm® Cream (Canderm)	Hypoallergenic base
	Complex 15 Hand Cream (Schering Plough)	Dimethicone, lecithin
	Dormer® 211 Cream (Dormer)	Hyaluronic acid complex, lecithin
	Lipidose Hands Concentrated Care for Chapped Hands (Vichy Laboratories)	Pro-fibril, glycerin
	Neostrata® Hand and Nail Cream (Canderm)	10% Glyconolactone
	Neutrogena Norwegian Formula Hand Cream (Johnson and Johnson)	Glycerin, dimethicone
	Olay Quench Hand Lotion (Proctor and Gamble)	Hypoallergenic moisturizing base
	Penaten® Cream (Johnson and Johnson)	18% Zinc oxide
	Prevex® Cream (Stiefel)	Petrolatum
	Eucerin® 10% Cream (Beiersdorf)	10% Urea
	Neutrogena Norwegian Formula Foot Cream (Johnson and Johnson)	Glycerin
	Neostrata® Deep Repair Cream (Canderm)	10% Urea, 10% gluconolactone, tea tree oil
	Ultramide 25 (Paladin)	25% Urea
	Uremol® 10% Cream (Stiefel)	10% Urea
	Uremol® 20% Cream (Stiefel)	20% Urea
	Urisec™ Cream (Odan)	22% Urea
Zinc Cream (R. W. Packaging Ltd.)	15% Zinc oxide	
Feet		

Table 5: A summary of some Canadian-marketed moisturizing products/active ingredients by sites of use (many of these products are available in the US as well). This list does not profess to be all-inclusive but includes many of the popular brands used by dermatologists in their practices.

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Poly-L-Lactic Acid as a Facial Filler

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ABSTRACT

Poly-L-lactic acid is a filler recently approved by the US FDA for the correction of facial lipoatrophy in patients infected with the human immunodeficiency virus (HIV). Currently, poly-L-lactic acid, sold under the brand name Sculptra™ (Dermik), is the only product approved by the FDA specifically for this indication. The market for poly-L-lactic acid will likely be larger than the HIV-infected population, as physicians use poly-L-lactic acid off-label to correct lipoatrophy associated with the normal aging process in non-HIV-infected patients. The benefits of poly-L-lactic acid are limited by the fact that multiple treatments are necessary to achieve the desired correction; its results are temporary and its cost is high.

Key Words: facial lipoatrophy, human immunodeficiency virus, HIV, poly-L-lactic acid

Poly-L-lactic acid (PLA) has been used safely in a variety of orthopedic and maxillofacial applications since the mid 1990s.^{1,2} In 1999, PLA was approved in Europe for the correction of scars and wrinkles. Recently the US FDA approved PLA for correction of HIV-associated facial lipoatrophy. Patients with this condition are injected every 2-6 weeks with PLA until the desired correction is achieved. Improvement is not permanent, but studies show continued skin thickening 2-3 years after injection. Adverse events have been minimal.

HIV Facial Lipoatrophy

Facial lipoatrophy can be a severe cosmetic problem for some HIV-infected patients and may be a sign of HIV lipodystrophy syndrome, which commonly occurs in HIV-infected patients who are treated with a combination of antiretroviral medications, especially protease inhibitors and nucleoside reverse transcriptase inhibitors. In these patients, fat redistributes away from the face and limbs, towards the central trunk, breasts, and dorsocervical fat pad. Dyslipidemia, insulin resistance, and osteoporosis may also be associated with the syndrome.

Facial lipoatrophy is characterized by sunken cheeks, bitemporal wasting, and deep nasolabial folds. Patients develop a hollow appearing face. This facial appearance is easily recognizable and can serve as a social stigma for HIV patients causing psychological stress. Many patients with HIV-associated facial lipoatrophy are eager to correct their appearance.

Composition of Sculptra™

Sculptra™ contains particles of PLA, which is a synthetic polymer of the alpha-hydroxy-acid family. Particles are 40-63µm in size and have a molecular weight of 140,000 Daltons. PLA is suspended in sodium carboxymethylcellulose and mannitol. PLA presumably creates a tissue response over the course of weeks to months characterized by a foreign body reaction and production of new collagen.³ The PLA is eventually metabolized to lactic acid monomers that are then metabolized to carbon dioxide or incorporated into glucose.

Sculptra™ is supplied as a freeze-dried product that must be reconstituted with sterile water 24 hours before injection.

Injection Technique

The patient's cheeks are prepped with alcohol and marked with a sterile marking pen. The area to be treated is then anesthetized using multiple sticks of 1% lidocaine with 1:100,000 epinephrine preferably with a 30-gauge needle. One method entails injecting up to 10cc of local anesthesia after marking areas of lipoatrophy; this approach presupposes that Sculptra™ is useful for diffusely adding volume to broad areas of atrophy rather than precisely treating individual rhytides. Alternatively, some practitioners believe anesthesia should be used sparingly to avoid anatomic distortion; topical anesthesia or a regional block may, in this method, be used to augment small quantities of injected local anesthesia. In the Chelsea and Westminster study,⁴ the reconstitution of Sculptra™ was with 2ml sterile water for injection and 1ml 2% lidocaine.

Usually, one vial of Sculptra™ is necessary for each cheek. The package insert⁵ recommends reconstituting each vial with 3-5ml sterile water; however, it is the authors' experience that a 5ml dilution decreases the risk of palpable nodule formation. Likewise, the package insert recommends reconstituting at least 2 hours before injection; however, 24 hours may lead to more complete dispersal of particles.

Injection is usually with a 1/2 inch 26-gauge needle, but some injectors prefer using other, longer needles, such as the 1 1/4 inch 25-gauge needle or the 1 1/2 inch 26-gauge needle. Longer needles may permit treatment with fewer punctures. Needles have a tendency to clog, so multiple needles must be available. Approximately 6 puncture sites are needed for each cheek. Through each puncture site, the suspension is injected in an even fan-like pattern (also referred to as a criss-cross or cross-hatch pattern), with multiple tunnels created at 0.5–1.0 cm intervals in the subcutaneous plane just below the dermis. Semantics can be confusing in this realm, as Dermik recommends serial punctures in the cheeks using threading or tunneling technique at 0.5–1.0 cm intervals.

After finishing the injection, the patient's cheeks are then massaged for 5 minutes to ensure even dispersal of the product. No dressing is needed and the patient is instructed to apply ice packs to the treated areas for 15 minutes out of every hour while awake over the next 24 hours to avoid bruising.

Immediately after injection, the patient's cheeks appear fuller, which is a result of the mechanical effect of the large volume of anesthesia and fluid injected into the skin. Over the next 48 hours the correction disappears and the patient's appearance returns to baseline. The manufacturer's studies show that the skin will gradually thicken. Patients frequently need multiple treatments to achieve the desired correction. Treatments can be spaced at 2-6 week intervals.

The same injection technique can be used to treat facial lipoatrophy associated with the normal aging process in patients not infected with HIV.

Clinical Data

The clinical efficacy of PLA as a facial filler has been described in two large published clinical studies.^{4,5} Similar data, not yet published, were presented to the US FDA when Sculptra™ received approval in August 2004.

Moyle, et al.,⁴ in an open-label, randomized, and blinded 24-week study involving 30 HIV patients who were injected with PLA, demonstrated visible improvement and increased skin thickness. Patients who received injections at weeks -0, -2, and -4 maintained a mean increase in dermal thickness of 4-5mm at weeks 12 and 24 as measured by ultrasound. Reported adverse events were limited to bruising and superficial cellulitis not requiring antibiotics.

Valantin, et al.,⁶ in an open-label, single-arm study of 50 patients with HIV associated facial lipoatrophy reported a mean improvement in skin thickness of 6.8mm at 96 weeks as measured by ultrasound. Patients in this study received PLA at week-0, -2, -4, -6 and possibly another injection at week-8 depending on response. Adverse events were limited to bruising and, in 22 patients, palpable subcutaneous micronodules.

Woerle, et al.,⁷ reviewed their 5-year experience using PLA in 300 patients. Adverse events included bruising, erythema, and palpable subcutaneous nodules. The occurrence of subcutaneous nodules declined to less than 1% when they diluted PLA with a total of 3ml of sterile water and 2ml of 1% lidocaine (for a total dilution of 5ml of fluid). They also began to inject the material into the uppermost portion of the subcutaneous fat rather than the lower dermis.

Cost

Two vials of Sculptra™, typically necessary at each visit to treat both cheeks, cost approximately \$980US, which does not include the physician's fee. Patients typically need multiple treatments and, therefore, multiple vials are needed to achieve the desired correction. The results are not permanent and patients will need future treatments to maintain correction.

Alternatives

The two main alternatives to PLA for the treatment of HIV-associated lipoatrophy are silicone oil and autologous fat transfer.

Silicone oil is manufactured by Alcon Laboratories under the brand name Silikon™ 1000. It is a permanent filler that is US FDA approved for intraocular injection to treat retinal detachment. It has been used off-label to correct rhytides and soft tissue defects. A recent report by Jones, et al.⁸ demonstrated the efficacy and safety of Silikon™ 1000 in the HIV population.

Autologous fat transfer is another alternative to PLA for the treatment of HIV-associated lipoatrophy.

This procedure involves harvesting fat from the abdomen or thighs for reinjection into the cheeks. A major disadvantage of autologous fat transfer is unpredictable fat graft survival. Additionally, in some cases, patients with lipoatrophy in the HIV setting may not have much fat to transfer or may have morphologically and histologically abnormal fat that may be less successfully transplanted.

Conclusion

PLA is a costly but promising treatment option for the correction of HIV-associated lipoatrophy. It has medium-term persistence, and may last up to several years at cosmetically effective levels. Clinicians will likely use PLA off-label to correct age-associated lipoatrophy in the non-HIV-infected patient population. Further clinical experience will be necessary to determine the long-term effectiveness of this product.

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Update on Drugs

Class	Name/Company	Approval Dates and Comments
<i>Immunomodulators</i>	Pimecrolimus and Tacrolimus <i>Elidel[®] Cream and Protopic[®] Ointment</i> Elidel [®] : Novartis Protopic [®] : Astellas (formerly Fujisawa)	TPP Canada issued a Health Advisory in April 2005 informing healthcare providers and patients about safety information indicating a potential cancer risk for these calcineurin inhibitors which are approved for the treatment of eczema in adults and children >2 years of age. They further asked healthcare providers and patients to consider the following: <ul style="list-style-type: none"> • Use these drugs only when other treatments have been shown to be ineffective or unsuitable. • Use a thin layer to control symptoms and only for short periods of time, as long-term safety is unknown. • Avoid use in children under 2 years, as the effect on the developing immune system is unknown. • Avoid use in children and adults with weakened immune systems. • Patients should consult their physician if they have any concerns. TPP Canada will require labeling changes for these products including updates to safety information about the potential cancer risk.
<i>Leishmaniasis</i>	Miltefosine <i>Impavido[®]</i> AEterna Zantaris	The Columbian Food and Drug Agency approved this oral alkylphospholipid in March 2005 for the treatment of the cutaneous form of leishmaniasis as well as the visceral form of this condition.

Drug News

<i>Rubella</i>	According to a Reuters report published on page A13 of the <i>New York Times</i> on 22 March 2005, rubella, a virus that once caused tens of thousands of birth defects and deaths in a single outbreak, has been eliminated from the US. However, US health officials from the Center for Disease Control and Prevention maintain that children must still be vaccinated and pregnant women must still ensure they are immune because the disease exists elsewhere. In 2004, nine rubella cases were reported in the US, all originating in other countries. Rubella, also known as German measles, is a usually mild viral infection that causes fever and rash, but early in pregnancy it can cause birth defects.
<i>A New Immunotherapy Treatment</i>	A team of researchers led by Steven A. Rosenberg, MD at the US National Cancer Institute* have found that patients with advanced melanoma who had not responded to previous therapies experienced a significant reduction in the size of their cancers as a result of receiving a new immunotherapy which consisted of a combination of chemotherapy and reintroduction of their own (autologous) lymphocytes that were activated to attack the tumor. With this treatment, 18/35 patients (51%) experienced an improvement in the amount of tumor present at diverse sites in the body including the skin. Fifteen of the 18 patients had a partial response lasting from 2 months to more than 2 years. The 3 remaining patients had complete clearance of the tumor. * <i>J Clin Oncol</i> 23(10):2346-57 (2005 Apr 1).

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