Dermal Fillers
The Next Generation
Tracey Hotta, BScN, RN, CPSN

In today's busy and demanding world, we no longer have the luxury of taking weeks to recover from a surgical procedure and are more frequently seeking quicker alternatives. The use of dermal fillers meets this need but in no way replaces a surgical intervention. Previously, bovine collagen was the only approved dermal filler. However, today there are several options available including a human collagen, a variety of hyaluronic acids, and a permanent injectable product. Each of the products has different uses, indications, and adverse reactions. The experienced injector now has a wider selection of products from which to choose to ensure that the patient receives what is best suited for his or her particular situation. These new products are becoming increasingly popular, due to acceptability and affordability, but are not without potential complications and adverse reactions. This article discusses the use of Cosmoderm/Cosmoplast, Hylaform, Restylane/Perlane, and Artecoll dermal fillers.

SKIN COMPOSITION

It is important to understand the structure of the skin because the depth, composition, and indications for use differ by product. The skin consists of three layers: the epidermis, the dermis, and the subcutaneous layer (see Figure 1).

The epidermis is the outermost layer and it serves as our protective barrier. The epidermis consists of a tightly packed layer of cells that are in a constant state of cell renewal. This renewal process slows with aging as skin tends to feel heavier and fine lines appear. The use of exfoliants (e.g., glycolic acid, vitamin A) are helpful to accelerate the renewal process, soften the hardened stratum corneum, and minimize the appearance of fine lines.

The second layer, the dermis, is the most important layer when injecting dermal fillers. The dermis is comprised of two important substances: a loose network of collagen fibers, within an interstitial substance composed largely of hyaluronic acid. Collagen provides tensile strength to the dermis by forming a framework in which new cells can grow. The aging process causes the collagen framework to weaken and the skin to lose its elasticity. This results in the formation of lines and furrows on the face that may be successfully treated with a dermal filler.

Hyaluronic acid is a polysaccharide, which has the ability to attract water. Water is necessary to keep the skin plump and moisturized. With advancing age, the skin cells lose their ability to produce hyaluronic acid. In addition, the molecular weight of the hyaluronic acid decreases, thus decreasing the skin's ability to hold water and leading to fine lines and folds. Both collagen and hyaluronic acid are commonly found in dermal fillers.

Third is the subcutaneous layer, which is a layer of fatty tissue that gives contour to the skin. Aging also reduces the amount of subcutaneous tissue, which is not replaced with these dermal fillers.

PRODUCTS

Several types of dermal fillers exist and can be broadly grouped into collagen and hyaluronic acid fillers.
The skin has 3 layers: The epidermis, the dermis, and the subcutaneous layer. (Used with permission from Canderm Pharma, Saint-Laurent, Quebec, Canada.)

The ideal product would be biocompatible, nonantigenic, nonpyrogenic, noninflammatory, nontoxic, easy to use, nonmigratory, long lasting yet absorbable, natural looking, and affordable (see Table 1).

### HUMAN COLLAGEN DERMAL FILLERS

#### Cosmoderm/Cosmoplast

Collagen is a naturally occurring protein that supports various body tissue including skin and joints. Human-derived dermal fillers were approved in Canada in December 2002. The Food and Drug Administration (FDA) approved them in the U.S. in March 2003. These are the only commercially available dermal fillers in the world that contain natural human collagen. The natural human collagen has been purified from living dermal tissue grown under sterile and controlled laboratory conditions. Because this product is human engineered, it is considered to be less immunogenic and it is speculated that it will degrade more slowly and last longer (Helwick, 2003).

Cosmoderm is composed of highly purified human-based collagen that is dispersed in phosphate-buffered physiological saline containing 0.3% lidocaine. Lidocaine minimizes injection discomfort, which is a great benefit especially when used in enhancing lip borders. Cosmoplast contains the same properties, but is cross-linked with glutaraldehyde to increase its strength and possible longevity in the dermis. Because the collagen is of human origin, it does not require a skin test prior to treatment. Therefore, the client may have a same-day treatment because the 28-day waiting period after a bovine collagen skin test is not needed.

### Injection Tips

The collagen implant is injected either into the upper dermis (Cosmoderm) or the mid to deep dermis (Cosmoplast) to fill the deficit so the wrinkle or fold is more flush with the skin. The preferred injection technique for Cosmoderm and Cosmoplast is using serial puncture with the accurate depth-gauge (ADG) assist device. In the serial-puncture technique, multiple injections are made along the wrinkle in a smooth and continuous line. It is important to massage the treated area to ensure even distribution of the product.

Cosmoderm is used in the treatment of superficial lines and the glabella. It is placed in the papillary dermis with the needle's angle between 10° and 25°. An overcorrection of 200% is recommended except for perioral and periorbital lines. Overcorrection in these areas may be slow to resolve due to minimal tissue stresses at these sites.

Cosmoplast is injected into the mid to deep reticular dermis and is ideal for treating deeper lines, enhancing lips, and smoothing facial scars that pass the "stretch" test. A stretch test is performed by stretching the defect or wrinkle between the index finger and the thumb. If the defect smooths out, it is anticipated that there will be a satisfactory result from the dermal filler. When injecting Cosmoplast, the needle should be placed at a 45° angle. The treated area should be corrected to 100%. Careful layering of Cosmoderm and Cosmoplast can be performed to eliminate a wrinkle or scar but is best done 2 to 3 days after the initial treatment.

Cosmoderm over Cosmoplast must be kept refrigerated. Removal from the refrigerator 30 minutes prior to injecting will help facilitate the injection procedure. Inspection of the syringe prior to use is required to ensure that the product has not become separated. If separation occurs, the product should not be used but returned back to the manufacturer.

Collagen treatments are not recommended for all patients. The treatment is contraindicated in individuals with an allergy to lidocaine, or a history of anaphylactic reactions or allergic response to any collagen product. It must be used cautiously in patients with autoimmune diseases such as rheumatoid arthritis, scleroderma, and lupus erythematosus. These patients may have increased susceptibility to hypersensitivity responses or accelerated clearance of their implants.

### HYALURONIC ACID DERMAL FILLERS

The search for the perfect injectable material has resulted in the development of hyaluronic-based dermal fillers, which have been flooding the injectable market. The advantage of these products is that they do not require a skin test. Hyaluronic acid is biocompatible because it is naturally occurring, in the same identical form, in the intercellular space of the dermis. The two products that will be
discussed will be Hylaform and Restylane/Perlane. Restylane and Perlane were approved in Canada in 1996, and Hylaform was approved in Canada in 1998. In December 2003, Restylane received FDA approval in the United States. At the time of this publication, Hylaform is still undergoing clinical trials, awaiting FDA approval.

There are several limitations of natural hyaluron: it rapidly dissolves in water, it cannot hold its shape, and it is rapidly absorbed by the body. In the 1980s natural hyaluron was chemically modified, called cross-linking, to produce a chemically stable product that does not dissolve rapidly in water and becomes more viscous. This new product is complementary for soft tissue enhancement because of its insolubility and resistance to degradation and migration.

Besides the cross-linking it is important to assess the particle size and the number of particles/ml of each product. The physical properties of the gel are modified in each product to make it close to the ideal for its intended application. When assessing the cross section of the skin, the epidermal layer has tightly packed cells with very little intracellular space. Assessing further into the dermis, the cell structure becomes less organized with a loose network of collagen and elastic fibers. Because of this characteristic, the particle size of the implant must be matched to the tissues. Small implant particles, if injected into the deep dermis, will be quickly lost because they can easily pass through the coarse network of the tissue matrix. Conversely, if a large particle implant is injected into the superficial dermis, the tissue matrix is much finer and it may stretch or tear the matrix causing an uneven treatment result (see Figure 2).

**ROOSTER COMB-DERIVED HYALURON**

**Hylaform**

Hylaform, introduced to the Canadian market in 1998, is a highly purified source of hyaluronic acid that is chemically cross-linked and is extracted from rooster combs. The purification process used to eliminate the inflammatory fraction in rooster comb hyaluronic acid was developed by Dr. Balazs, the inventor of Hylaform over 25 years ago. Since that time the process has become well known and is widely used.

Each 0.75 mg syringe of Hylaform contains 5.5 mg of Hylan B gel, sodium chloride, and water; however, the particle size is different for each range of product. The larger molecular network with larger gel particles provides better tissue filling. Hylaform Fineline has very small particles, 300 μm, and is used to treat fine rhytids, periorbital lines, or to overlay atop of Hylaform Plus. Hylaform Regular is 500 μm and is ideal for treating perioral lines, facial rhytids, and shallow facial scars. Hylaform Plus, the strongest of the three, has a particle size of 700 μm, requiring less product to produce the desired result. It is indicated for treatment of deep nasolabial folds, oral commissures, and lip enhancement. Because the source is extracted from rooster combs, persons who are sensitive to avian products should be treated cautiously with Hylaform. Other precautions include a history of herpes virus or active lesions in the treated area.

**RESTYLANE AND PERLANE**

**Restylane and Perlane**

Restylane was first introduced into Canada in 1996, 2 years before Hylaform. It is a non-animal-stabilized hyaluronic acid that is biosynthetically produced by bacterial fermentation. This product also uses cross-linking to stabilize it, so that the hyaluronic acid remains in the tissues for a longer period of time.

The resulting visco-elastic transparent gel has a concentration of 20 mg/ml and is no longer water-soluble; however, it retains its affinity for water and its ability to swell and form hydrated copolymers. The product is available in three strengths, all of which are 20 mg/ml of hyaluronic acid. The difference between the products is the fact that they are tissue tailored.

Restylane Fine Line is injected into the superficial dermis to treat superficial facial lines. It has 200,000 particles/ml with a particle size of 150 μm.

Restylane is injected into the mid dermis and is indicated for the treatment of perioral lines, shallow facial folds, and scars. It contains 100,000 particles/ml with a particle size of 250 μm.

Perlane is injected into the deep dermis and is ideal for the treatment of nasolabial folds, oral com-
Artecoll is a sterile microimplant that consists of high-purity purified polymethyl methacrylate (PMMA) particles suspended in a bovine collagen solution along with lidocaine. These microspheres have a defined size of 30-40 μm with a smooth, residue-free surface. The microspheres are large enough to escape phagocytosis but small enough that they may be injected superficially through a 27-gauge hypodermic needle. Care must be taken to stop injecting before the needle is completely removed. When treating fine wrinkles and superficial scars, the Hyalform Fineline/Restylane Fine Line is best placed in the papillary dermis using a 30-gauge hypodermic needle. Enough material should be injected so the defect is fully corrected but with no degree of overcorrection.

Injection Tips

The hyaluronic acid products are best injected by using a linear threading technique. In the linear threading technique, the needle's full length is inserted under the wrinkle and the product is injected while slowly pulling the needle backwards. Care must be taken to stop injecting before the needle is completely removed. When treating fine wrinkles and superficial scars, the Hyalform Fineline/Restylane Fine Line is best placed in the papillary dermis using a 30-gauge hypodermic needle. Enough material should be injected so the defect is fully corrected but with no degree of overcorrection.

For deeper furrow lines or scars, deep placement of Hyalform Plus or Perlane in the mid to deep dermis (reticular layer) is typically needed to obtain correction and is best done by using a 27-gauge needle. This may be layered on top using the Fineline material. The site should be treated only to eliminate the wrinkle or scar with no overcorrection. It is important to note that hyaluronic acid stings upon injection; therefore, patients should be given the option of a topical anesthetic or a dental block (numbering of the perioral area by injecting a local anesthetic into the nerve supply to the lips).

PERMANENT INJECTABLE DERMAL FILLER

Artecoll

Artecoll contains 0.3% lidocaine so there is a small amount of anesthetic effect as the product is being injected. The PMMA particles must be delivered in bovine collagen; thus, the manufacturer recommends a collagen skin test. The risk of being allergic to the collagen in Artecoll is <1% (Canderm Pharma Incorporated, 2001). There is a lower concentration of collagen in Artecoll when compared to other bovine collagen products. Artecoll is contraindicated in those who have a positive skin test, allergy to lidocaine, known immune diseases, a history of keloid formation, or flaccid skin. Current treatment with steroids may inhibit growth of connective tissue.

Because the product is injected in the deep dermis and the needle is kept in constant motion so it is distributed in a scaffolding pattern, there is an increased risk of bruising. If too much product is placed in one area, the implanted material may be palpable and may lead to nodule formation. An implant nodule consists of microparticles and its normal tissue reaction. The nodule may become deformed, displaced, and palpable in the soft tissue of the lips and is sometimes visible. A rare but potential side effect is the formation of a granuloma. It becomes obvious 6 to 12 months after the injection of any kind of dermal filler substance. A granuloma is a growing lump and it occurs at all implant sites simultaneously. Without treatment granulomas can grow to the size of a bean but resolve spontaneously after several years. Both nodules and granulomas react well to intralesionally injected Kenalog, a steroid that helps to soften scar tissue. The Kenalog must be injected carefully into the nodule because if it is injected into the surrounding tissue it may cause skin atrophy. Surgical excision may be needed for nodules/granulomas that do not respond to the steroid injection.

Injection Tips

When Artecoll is injected, the product is placed subdermally. This may be measured by piercing through the skin at a 90° angle and placing the needle at a depth of 2 bevel lengths or a 2 mm depth. Immediately turn the needle so it is parallel with the skin's surface. The product is packaged with a 26-gauge hypodermic needle, but a 27-gauge may be used in the more sensitive areas. The product should
<table>
<thead>
<tr>
<th>Product</th>
<th>Hyaluronic Acid</th>
<th>Human Collagen</th>
<th>Artecoll (Rofil Medical International, The Netherlands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composition</td>
<td>5.5 mg hyaluron 8.5 mg sodium chloride Water</td>
<td>20 mg hyaluron Water</td>
<td>PMMA beads dispersed in 3.5% collagen solution and 0.3% lidocaine</td>
</tr>
<tr>
<td>Source</td>
<td>Rooster combs  Bacteria</td>
<td>Genetically engineered live human tissue</td>
<td>Artecoll uses the body's natural ability to encapsulate foreign bodies by the formation of connective tissue surrounding the PMMA microspheres.</td>
</tr>
<tr>
<td>Placement</td>
<td>Mid-dermis      Linear threading technique Do not overinject; overcorrection may cause pressure on adjacent tissue and migration of product.</td>
<td>Papillary dermis Mid- to deep reticular dermis Serial puncture technique with assist device Overcorrect by 150–200%</td>
<td>Bovine collagen from a closed herd in the United States.</td>
</tr>
<tr>
<td>Date of FDA approval</td>
<td>Still awaiting FDA approval December 2003</td>
<td>2003 2003</td>
<td>Still awaiting FDA approval</td>
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<tr>
<td>Considersations</td>
<td>No skin test required Last 4–6 months Store at room temperature Discomfort on injection Is sensitive to molding Immediate results but may have 1–2 days of erythema and swelling May produce a gray streak if too superficial</td>
<td>Contains lidocaine to ease injection Requires refrigeration Immediate results with minimal swelling Lasts 4–6 months May stimulate own collagen formation over time; therefore, less product is needed for ongoing treatments</td>
<td>Requires a skin test &lt;0.1% risk of allergic reaction Requires refrigeration but should be removed 4 hours before injecting Results are complete in 3 months when the implant becomes interwoven by fibroblasts and collagen fibers May require a series of treatments Requires precise deep dermal injection technique to prevent risk of palpable lump Long-lasting results</td>
</tr>
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<td></td>
<td>A glycosaminoglycan biopolymer composed of monosaccharides, giving it the ability to bind water and form hydrated polymers of high viscosity.</td>
<td>The suspended collagen forms a soft cohesive network of fibers, which is responsible for restoring contour.</td>
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<tr>
<td></td>
<td>35 mg/ml saline .3% lidocaine</td>
<td>35 mg/ml saline .3 % lidocaine cross-linked with glutaraldehyde</td>
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<tr>
<td></td>
<td>Particle Size</td>
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<tr>
<td></td>
<td>Fineline 200 μg Fine line 150 μg</td>
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<td></td>
<td>Regular 300 μg Restylane 250 μg</td>
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<tr>
<td></td>
<td>Plus 700 μg Perlane 1000 μg</td>
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<td></td>
<td>A glycosaminoglycan biopolymer composed of monosaccharides, giving it the ability to bind water and form hydrated polymers of high viscosity.</td>
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</table>

Note: PMMA = polymethyl-methacrylate; FDA = Food and Drug Administration. Data from information obtained in the physician package inserts from Inamed Corporation, Q-Med AB, and Rofil Medical.
be injected using the tunneling technique with the needle in constant motion. This injection technique allows the Artecoll to be placed in a scaffold pattern with not too much product in one area. Remember to stop injecting when the needle is being removed. Gently massage the implant between your thumb and finger to ensure even distribution of the product.

It is not uncommon for the tip of the needle to become clogged with Artecoll or a bit of dermis. If this occurs, change the needle and start again. Forcing the plunger will result in injecting an undesired amount of Artecoll in one place.

The Artecoll must be stored in the refrigerator and should be removed 4 hours prior to an injection treatment. A syringe may be stored at room temperature, away from sunlight and heat, to maintain readiness for the potential "emergency" Artecoll treatment. Examine the syringe for separation of product prior to injecting. Heat and light can lead to product separation; if this occurs the material should be discarded.

NURSING CONSIDERATIONS

The concept of a dermal filler injection being a lunch-hour treatment is a great marketing tool, but the client must be warned of the postinjection reactions that may occur with all of the injections. Even though cosmetics may be applied 30 minutes after the injection, residual evidence of the treatment may yet remain.

- Anticipated side effects after any injection may include one or more of the following:
  - Erythema, which may last 1 to 2 hours and may be camouflaged with cosmetics.
  - Swelling, which may last 2 to 12 hours depending on the product used. There tends to be increased swelling with hyaluronic products because of their water-binding properties.
  - Localized tenderness.
  - Palpable lumpiness, which usually resolves within 1 to 2 weeks.
  - The risk of bruising. To minimize this risk, clients who take antiinflammatories, vitamin E, or aspirin are advised to discontinue use approximately 2 to 3 days prior to the injection.
  - Recurrence of a cold sore. Lip-enhancement clients with a history of the herpes virus are at an increased risk of developing a posttreatment cold sore. This is due to the fact that the herpes virus lives within the vermilion border of the lip, which is also the area injected. Clients with a chronic history of cold sores or who have had an outbreak in the past 6 months should be prescribed an antiviral medication (e.g., Acyclovir) as a prophylactic measure.

CONCLUSION

The management of wrinkles, furrows, and aging skin is a relentless quest to match facial appearance with perceived age, and can be achieved to a certain extent with dermal fillers such as collagen and hyaluronic acid products. While nonsurgical dermal filler products are no substitute for the more dramatic and permanent results of surgery, they have become safer, less expensive, and are more user friendly. Still, the search for the perfect injectable dermal filler continues.

REFERENCES


BIBLIOGRAPHY


