Complications of Injectables in the Perioral Region

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Abstract

The continual advent of novel injectables has broadened the potential applications and use for facial aesthetics immensely. There are inherent risks and limitations in predictability associated with any product that is injected freely into human tissues that may possess bioreactivity. This article seeks to elucidate the most commonly feared complications as well as minor complications often overlooked by practitioners. The author also discusses the corresponding appropriate treatments.

Keywords

- filler
- complication
- treatment
- dissolve
- dermal fillers

Coinciding with the ongoing advent of injectable options for facial and perioral rejuvenation, we have also witnessed an increasing number of complications and adverse outcomes. The conscientious practitioner must be vigilant of the immediate and possible long-term risks of any injectable. Dermal fillers, fat, enzymes, and other injectables have demonstrated a great deal of promise for the treatment of the perioral region. Unfortunately, the risks they impose, although uncommon, may be permanent and sometimes irreversible. This article attempts to provide a basic understanding of the risks associated with various injectables as well as potential treatment modalities for the most commonly encountered issues.

Dermal Fillers

Dermal fillers can be categorized as autologous, allograft, biological, and synthetic. Autologous fillers such as the patient's own fat are commonly used in the perioral region in whole and micronized forms. Allograft injections such as Renuva allograft adipose matrix (MTF Biologics) have more recently been introduced to help treat minor aesthetic irregularities in the skin. Biological fillers such as bovine collagen gained United States Food and Drug Administration (FDA) approval and were used commonly between 1981 and 2003 until hyaluronic acid (HLA) fillers entered the market and gained immense popularity.

Currently, in the United States, there are a large variety of synthetic dermal fillers available that we can classify as short-term or temporary, semi-permanent, and permanent. Given their behavior and associated complications, semi-permanent and permanent fillers should be placed in the same category—long-term fillers. These have been recognized for their bioactivity and labeled "stimulateurs."[1] It is important to note that temporary fillers, which are expected to last 6 to 24 months, may often have negative effects lasting up to 10 years, according to the author's experience.

The FDA has approved the following materials for facial injection: collagen, HLA, calcium hydroxylapatite, poly-L-lactic acid (PLLA), and polymethylmethacrylate (PMMA). Permanent fillers are only indicated for use in the nasolabial folds and for acne in patients over 21 years of age. Silicone is no longer listed as approved substance on the FDA website and the only remaining product approved as a permanent filler is PMMA. Any use of PMMA other than as described or the use of silicone would be considered off-label use. Artefill is an FDA-approved PMMA product.

FDA-approved HLA fillers for the face include the following: Restylane, Restylane-L, Restylane Silk, Restylane Lyft, Restylane Defyne, Restylane Defyne, Juvederm Ultra XC, Juvederm Ultra Plus XC, Juvederm Vollure XC, Juvederm Volbella XC, Juvederm Voluma XC, Belotero Balance, Prevelle Silk, Elevess, Captique, and Hylaform. Radiesse, a form of hydroxylapatite, is approved for use in the face and hands. Sculptra is a form of PLLA that can be used in the face as well.

►**Table 1** shows the most commonly used hyaluronic fillers (►**Table 1**):

Major Complications

Major complications associated with dermal injectables are most often seen immediately by the patient or the practitioner and can be potentially devastating. Patient complaints should be examined immediately and taken seriously.

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Table 1 Common hyaluronic acid fillers

Filler	Chain/Conc.	Characteristics	Concentration
Restylane	NASHA	Beaded/medium	20 mg/cc
Restylane Lyft	NASHA	Beaded/thick	20 mg/cc
Restylane Silk	NASHA	Beaded/thin	20 mg/cc
Restylane Refyne	xPresHAn	Linear/thin	20 mg/cc
Restylane Defyne	xPresHAn	Linear/thick	20 mg/cc
Juvederm Ultra	Hylacross	Beaded/ Medium	24 mg/cc
Juvederm Ultra Plus	Hylacross	Beaded/Medium+	24 mg/cc
Juvederm Voluma	Vycross	Linear/thick	20 mg/cc
Juvederm Volbella	Vycross	Linear/thin	15 mg/cc
Juvederm Vollure	Vycross	Linear/medium	17.5 mg/cc
Belotero Balance	CPM	Beaded/thin +	22.5 mg/cc

Vascular Occlusion/Vascular Compression

Vascular occlusion and compression are similar in etiology and treatment. These can be caused by local compression of vessels, intravascular injection of dermal fillers, as well as local or distant emboli. The presentation in the perioral region is variable depending on region, caliber of vessels affected, and zones of prior surgery with atypical vascular patterns. Prior injections with agents causing collagen formation or fibrosis such as Sculptra or Radiesse or the repeat use of polydioxanone (PDO) threads can also decrease the compliance of soft tissues, thus making vascular compression more likely. The presentation may be immediate blanching, fluctuations and worsening of blanching, hyperemia and mottling/livedo reticularis, or simply a dusky appearance in the skin. Capillary refill is typically poor in response to massage, although some may be present due to partial persistent perfusion or perfusion shedding from surrounding areas. Treatment should follow protocol for any vascular event or immediate major complication as elucidated below in the treatment section. With or without treatment, a reperfusion reaction or ischemic skin reaction may occur. This typically results in diffuse hyperemia, vesicular eruption, exudative oozing, swelling, and pain. The practitioner should understand that these are expected sequelae.

Vascular Compromise Protocol

Most protocols detailed in the literature are meant to treat HLA-related complications. Treatment options are limited and this protocol can be used for other types of injectables as well. Although hyaluronidase may not be effective on other types of fillers, there may be some benefit of decreasing mass effect in the area and increasing vessel permeability.[2] Immediate and aggressive treatment of severe complications is always advised. Milder issues such as post-injection asymmetries and edema are typically better managed conservatively until 2 to 3 weeks when the use of hyaluronidase could be minimized.

Initiation of treatment should always begin with removal of filler in the vicinity of the vascular compromise. The goal is to clear intravascular occlusion, remove any compression surrounding the vessels, decrease pressure against the dermis, and to increase vascular permeability. Although you may begin with needle aspiration, it is more effective to proceed with hyaluronidase injection. Hyaluronidase is commercially available in the United States in several forms. The most commonly used are Vitrase (ovine testicular hyaluronidase) (Bausch & Lomb Incorporated) and Hylenex (recombinant human hyaluronidase) (Halozyme Therapeutics). Although allergies have been reported with the use of these medications, this should not delay or preclude use. More problematic allergies have been described as occurring around the eyes[3] There are also a large number of reports that have confused expected ischemic and reperfusion reactions with allergy, erroneously labeling the reaction as an allergy[4]

(a) *Hyaluronidase injection*—The author typically uses a 1:1 mixture of Vitrase with 1% plain lidocaine. The lidocaine helps diminish the burning sensation and discomfort associated with injection. It is important to avoid the use of epinephrine in the mixture to avoiding confounding signs of ischemia. Typically, 50 to 200 units are used in total, injecting diffusely into the surrounding area. If intra-arterial blockage is likely, intra-arterial injection or diffuse injection along the course of the artery may be performed. A multiplane microneedling technique may be used using a 30-gauge needle if the filler bolus is not readily identifiable. Aggressive massage of the areas should be performed to improve permeability of the medication and encourage blood flow. Cannulation via palpation, aspiration, ultrasound, or image guidance may be performed as well if indicated.

(b) *Leeches*—Medical leeches (*Hirudo medicinalis)* may provide a very impressive response in many vascular compromise scenarios. One to two leeches are typically used at the site if possible. If the leech chooses to attach, they will provide immediate decongestion and release various substance including hirudin, which is the most prominent constituent of leech saliva. These substances provide an anticoagulative and antithrombotic response with potential anti-inflammatory, analgesic, and anesthetic properties.

Fig. 1 Medical leech on the nasal tip following ischemic event.

The leeches may have an adverse taste to the area injected. Placing them nearby may still provide systemic and regional benefits as mentioned (►**Fig. 1**).

(c) *Nitroglycerine paste*—Nitro-Bid (2% nitroglycerine ointment or paste) is placed twice daily on the region to improve vasodilation and limit the amount of venous congestion. The patient must be warned about potential drops in blood pressure and headaches. If leeches are used, they should latch and finish treatment prior to placement of any topical solution that would cause an adverse taste.

(d) *Hyperbaric oxygen*—Hyperbaric oxygen treatments may provide more rapid revascularization of tissues and potentially salvage compromised skin. Treatments are initiated immediately and continued daily for 5 days typically. If the patient is claustrophobic, larger chambers are now available and sedative oral medications may be given. Ozone therapy is an alternative but is unlikely to provide any advantage in these situations. Infrared or LED treatments are also unlikely to provide any major advantage but may be used without risk of worsening.

(e) *Aspirin*—Although evidence is lacking, risk is low and we advise the administration of 325 mg of Aspirin.

(f) *Steroids*—Topical and oral steroids may be employed to ameliorate the potential sequelae of edema, pustular eruptions, and post-inflammatory pigmentation that are often seen following ischemic events in the skin. There may also be a potential benefit for minimizing neuropathy following injections near facial foramina.

(g) *Antivirals*—Vesicular eruptions, pain, and hyperemia following ischemic events should be anticipated. They are typically not herpetic in nature; however, antiviral prophylaxis is very low risk and is at the discretion of the practitioner. A vesicular eruption caused by an ischemic event can theoretically incite a herpetic outbreak.

Vascular Compromise Per Area

Nasolabial Folds

Vascular compromise in the nasolabial folds may happen one of several ways. Intravascular injection may cause segmental hypoperfusion in the distribution of the facial artery, including the lateral segment of the labial artery and any branches along the nasolabial fold including the inferior alar artery. In unoperated patients, accidental injection into the more centrally located vasculature such as the inferior alar artery may never be realized given the recurrent blood supply. Major occlusion occurs either because injection was performed in an overly deep plane or if the injections were carried too far medially extending under the nasal ala. Injections in this region should be immediately intradermal when treating creases in the skin, or immediately subdermal for the treatments of deeper folds and shadows. Major complications may arise from deeper injection deep to the superficial musculoaponeurotic system (SMAS) layer[5,6] or into the muscular plane where the major vessels travel.

More superficial, focal blanching may occur from vascular compression or intradermal injection that cuts off the superficial blood supply. For isolated, superficial branching, often needle aspiration and massage may suffice. More significant compromise requires initiation of vascular complication protocols. The sequelae of vascular occlusion may not be realized immediately in various instances where the appearance of issues may be camouflaged. For this reason, patient complaints should be taken very seriously and examined immediately in person or at the very least by photo or video.

Chin and Prejowl

There are several areas inferior to the level of the lips that may be surprisingly sensitive to vascular compromise. Notably, the injecting practitioner should be intimately familiar with vascular patterns in the sulcus mentalis, mental foramen, and prejowl fold.

Intravascular injection along the jawline near the facial artery may render negative sequelae superiorly from the prejowl sulcus to the corner of the mouth and inferiorly into the neck as well. As it courses from the neck to the face, the facial artery travels through or over the submandibular gland and continues over the angle of the mandible in a subplatysmal/sub-SMAS plane. It is important to remember that although the blood supply of the perioral region extends cephalically from the facial artery and external carotid branches, there are recurrent, caudally traveling arteries from these branches as well as from the mental branches. These branches may be compromised in a supraperiosteal plane, in the mental foramen, or in the sub-SMAS plane as well. There have been reports of such compromise in the chin even with supraperiosteal injection and aspiration prophylaxis[7]

The sulcus mentalis is particularly susceptible to superficial intradermal injections. This area has a dense tissue character with poor compliance. It is also a watershed area with small and sensitive terminal branches supplying it. If blanching is noted, needle aspiration with vigorous massage should be performed. If vesicular eruption ensues in the

following days, vascular compromise protocol should be initiated as soon as possible and the patient should be given antiviral medications such as valacyclovir. For major vascular occlusion of a main arterial branch, these regions may be receptive to intravascular cannulation proximal to the injection site and subsequent enzymatic dissolution.

To avoid problems, the primary author injects the chin directly over the periosteum in the region between the canines. Symmetry issues may be modulated with subdermal injections. Lateral to this point along the jawline toward the prejowl sulcus, the primary author advises injection in the immediate subdermal plane. This is a safer plane that also has a higher yield effect when using small volumes to push the prejowl sulcus outwards and downwards in an attempt to camouflage the jowls and smooth the jawline. The marionette lines or prejowl fold are also injected in a directly subdermal plane.

Lips

In the author's practice, the upper lip appears to be the areas most overlooked following a vascular event. Vascular occlusion in this area may be mistaken for a bruise or hematoma. The copious surrounding vascularity allows the lip to heal very well in most instances following vascular insults. Patients may present soon after injection asking the practitioner if something is wrong. Any presentation deviating from standard bruising should be analyzed immediately. The patient may present with bruising in the presence of hyperemia, exaggerated edema, pain, and overall discoloration. This may progress to a blotchy appearance accompanied by a vesicular eruption or even weeping of the skin. ►**Figs. 2–6** demonstrate the changes noted daily from day 1 to 4 after another practitioner performed an intravascular injection in the right upper lip. The patient had returned complaining of a strange appearance and sensation, but was dismissed as normal bruising.

Vascular insults in this region would most likely occur from a lateral lip injection with a needle in the plane of the orbicularis muscle. The main branch of the labial artery travels deep to the dry vermillion in the muscularis layer. Injections in the lip should always be performed in a subdermal or submucosal plane. The cautious practitioner should have a low threshold to treat potential complications. You should always listen to the experienced patient claiming "something just doesn't seem right." In these situations, vascular compromise protocol should be initiated.

Vertical injections performed in the midline to plump midline creases of the lower lip vermillion are also susceptible to localized ischemia. Philtral column injections are generally low risk given the lack of any important vasculature. However, intradermal injection in this region may cause a localized compressive ischemia. This may be relieved by massage, needle aspiration and massage, or rarely hyaluronidase as needed.

Base of Nose

The nasal base includes the alar creases, alar sill, and columellar base. There is a largely redundant blood supply in this region, except for in cases of revision rhinoplasty. One should never inject an area in the nasal base that is noncompliant or lacks dead space to fill.

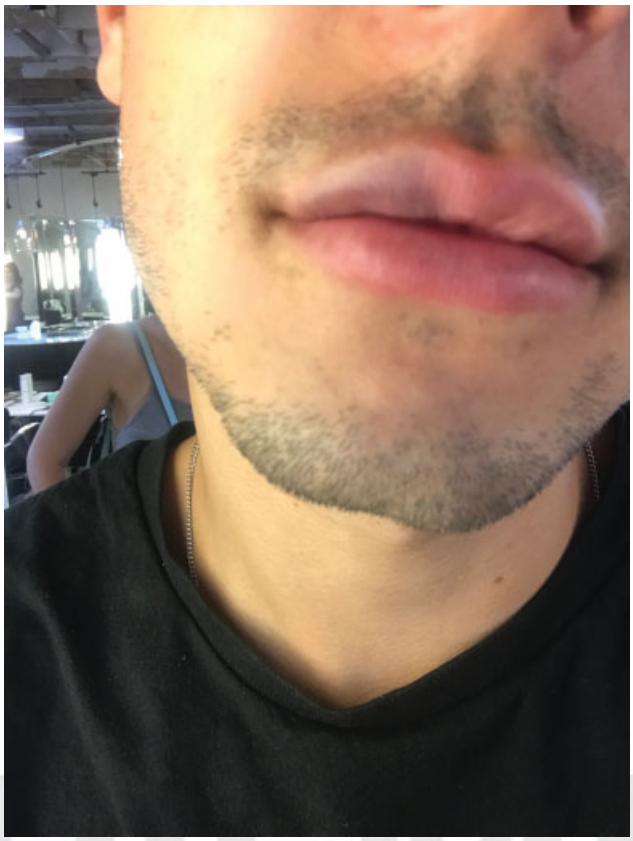

Fig. 2 Day 1—Untreated intravascular injection by another practitioner with hyaluronic acid filler.

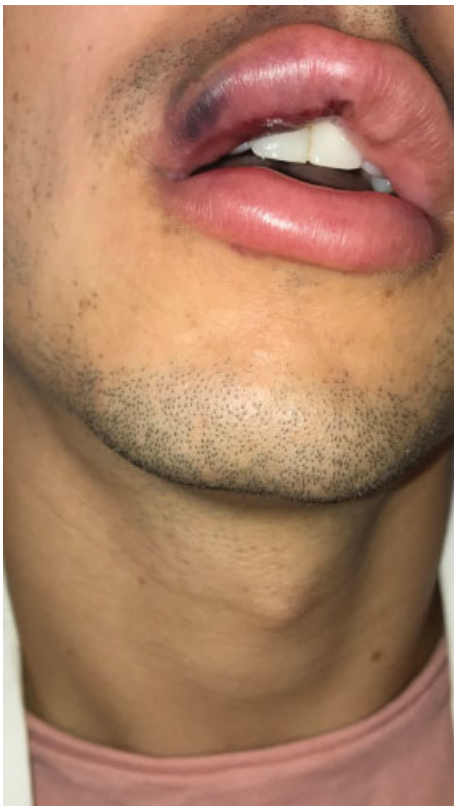

Fig. 3 Day 2—Untreated intravascular injection by another practitioner with hyaluronic acid filler.

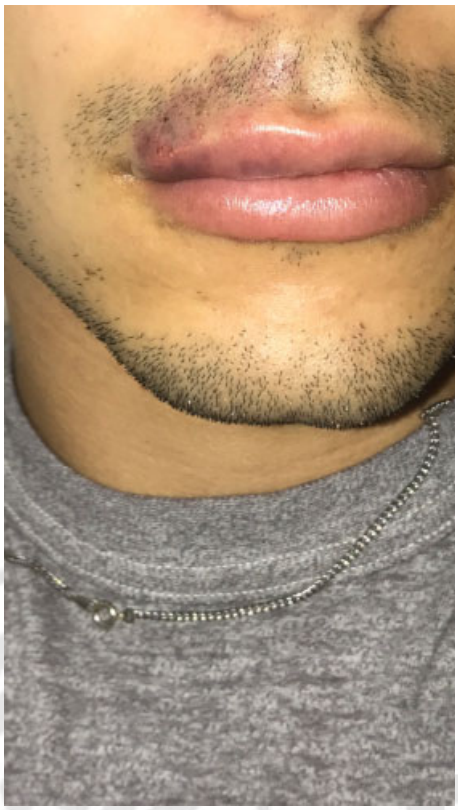

Fig. 4 Day 3—Untreated intravascular injection by another practitioner with hyaluronic acid filler.

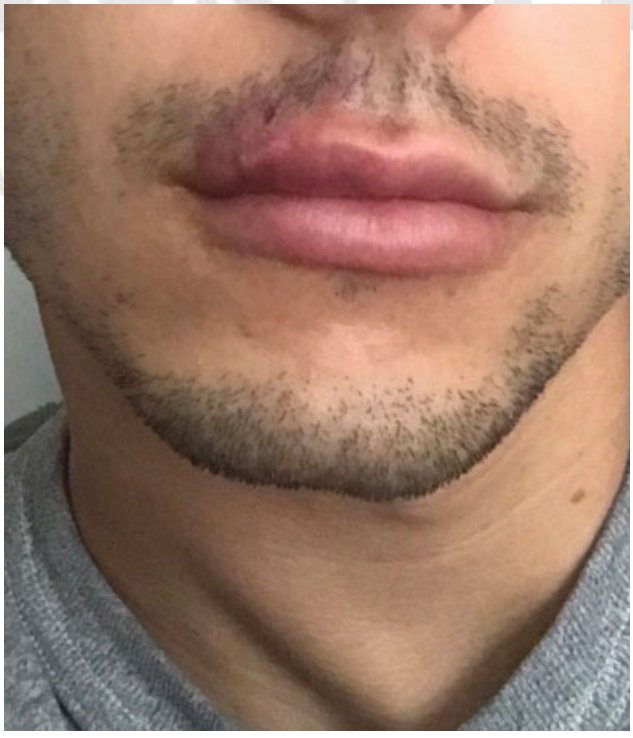

Fig. 5 Day 4—Untreated intravascular injection by another practitioner with hyaluronic acid filler.

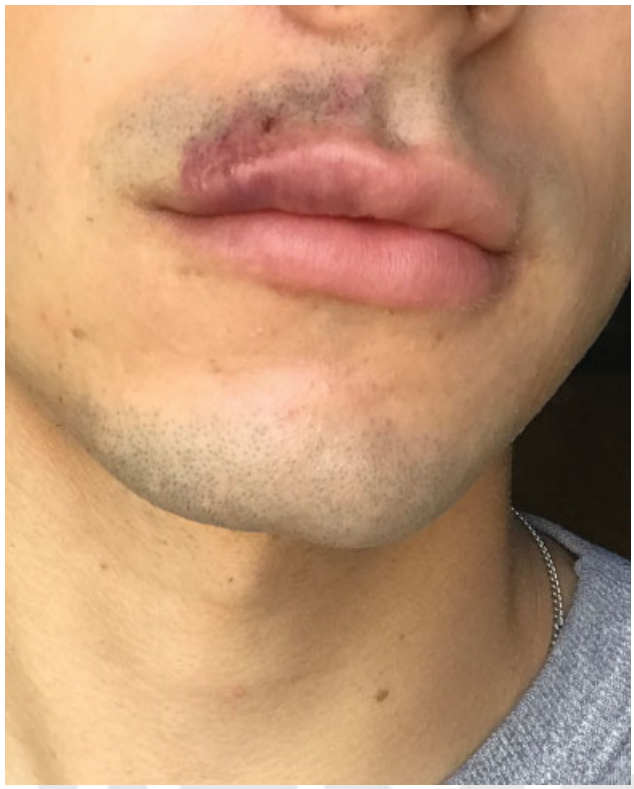

Fig. 6 Day 5—Untreated intravascular injection by another practitioner with hyaluronic acid filler.

Venous Congestion

Venous congestion may occur in conjunction with vascular compression or by itself. This would be expected to occur in areas with no dead space. Venous congestion would be suggested by continuous dark venous oozing at puncture sites. In the face, this would most likely be seen at the base of columella or nasal tip in a previously operated nose. This may also occur in areas of prior trauma, prior surgery, or tight areas such as the sulcus mentalis. There is no good way to tell the difference between dark venous oozing caused by venous congestion or other types of vascular occlusion. The treatment for all is the same: vascular compromise protocol should be initiated.

Visual Impairment

Blindness following facial injections is quite rare, but certainly not unheard of. It is important to realize that no matter how experienced the injector may be, none of us are immune to this risk. Visual impairment may result from any type of injectable, whether it is hydrocortisone suspension, fat, HLA, or PMMA. The central retinal artery occlusion may occur by anterograde or retrograde injection. It may also occur via embolization. The most likely areas at risk in the perioral region are the angular arteries and the vasculature around the lateral nasal base. Aspiration techniques and the use of a cannula in these areas may decrease risk, but do not reduce it to zero.

If the retinal artery is occluded, permanent blindness may ensure within 90 minutes. Immediate transfer to a referral center such as an academic or ophthalmologic hospital should be initiated. Conservative treatments such as ocular massage may also be utilized, although data regarding success is lacking.[8]

Nerve Damage

Damage to main sensory nerve branches in the face may occur by direct injection or via inflammation following a vascular event. If a patient complains of an immediate, severe segmental loss of sensation during an injection near the infra-orbital foramen or mental foramen, immediate dissolving of filler should be seriously considered. Notably, numbness may also be caused by lidocaine contained in injectables penetrating nearby nerves. Slower onset numbness would typically be caused by lidocaine or inflammation following filler placement.

Arterial Spasm

Arterial spasm is rare in the perioral region. This is more likely to occur in a previously operated nasal tip and may occur from filler injection or even microneedling. Presentation would entail fluctuating perfusion of an area following simple microneedling or injection of benign substances such as platelet rich plasma. The practitioner should not ignore these scenarios. Nitroglycerin past should be place along with vigorous massage and cessation of the inciting treatment.

Minor Complications

Minor complications tend to arise weeks to years following injection of dermal fillers. The most common, expected sequelae of redness, pain, bruising, temporary bumps, and numbness will not be discussed here. Often in these situations, the patient will claim that they appear worse than before receiving treatment. Preinterventional photography is of utmost importance in a cosmetic practice. You should never touch a patient with neuromodulators, fillers, or other injectables without taking high-resolution photos and getting to know the patient first. The following text provides some of the more prevalent minor complications seen with the various types of injectables.

Hyaluronic Acids

Hyaluronic acid fillers are the safest and most logical of fillers to use in the soft tissues and skin. They have properties naturally found in the soft tissue matrix, display minimal reactivity, and are reversible. As mentioned previously, injectable materials will never be fully predictable. Being able to easily fix our mistakes is a luxury.

A wide array of fillers is available, each with its own inherent characteristics. More recently, newer cross-linking technology has emerged offering an even greater selection of fillers to suit the practitioner's preference. Classic HLA choices such as Restylane and Juvederm portray a more bead-like characteristic, while newer products such as Volbella and Restylane Defyne display more linear properties.

One of the most commonly noted issues in the author's practice is migration of filler with accompanying edema. This is seen with very high frequency when classic Juvederm XC or Juvederm Ultra XC is injected into the upper lip. Juvederm XC is very hydrophilic and reactive with a tendency to migrate locally. Injections performed from above the vermillion pointing downwards to enter the vermillion have a greater tendency toward backtracking and migration, although even conservative fillers placed from below the vermillion border can migrate superiorly into the white upper lip. The appearance is a bulge and fullness with a white discoloration typically within the 10 mm above the vermillion border. This may give the patient a slightly simian appearance and cause a potential limitation in mobility due to the surrounding muscular edema. ►**Figs. 7–8** to **9** demonstrate excess fullness from Juvederm accumulation and the improvement after dissolving with hyaluronidase. The migration may also cause fullness and hooding over the lateral lip causing a joker's smile. ►**Fig. 10** demonstrates Juvederm XC hooding the lateral lip in the before photos and the alleviation of the awkward appearance after dissolving of filler. The fullness may emanate immediately or even a year later and last up to 10 years. Migration may occur with all other HLA fillers but to a significantly lesser extent. Dissolving of filler in this region is typically advised if it is causing an adverse appearance or limitation in movement.

Another common issue is the appearance of nodules, both small and large in the lips and surrounding areas. In the first few weeks, this may be considered normal and cautious intervention is advised. If the issue persists, one may consider needle aspiration with manual expression or dissolving

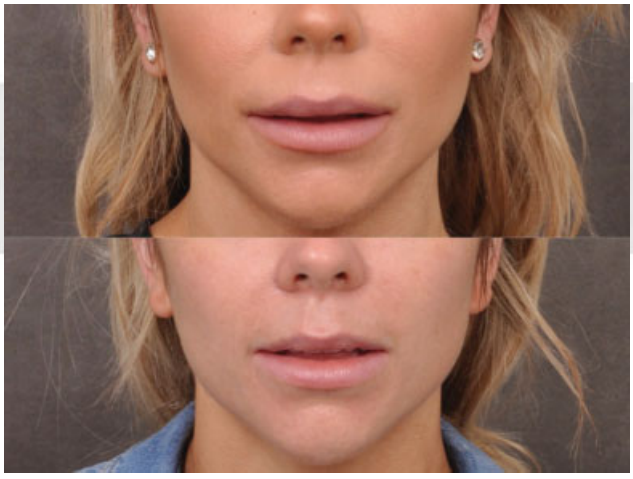

Fig. 7 A patient with Juvederm injections that had migrated while thickening and bulking the upper lip. The bottom photos show improvement after dissolution of filler.

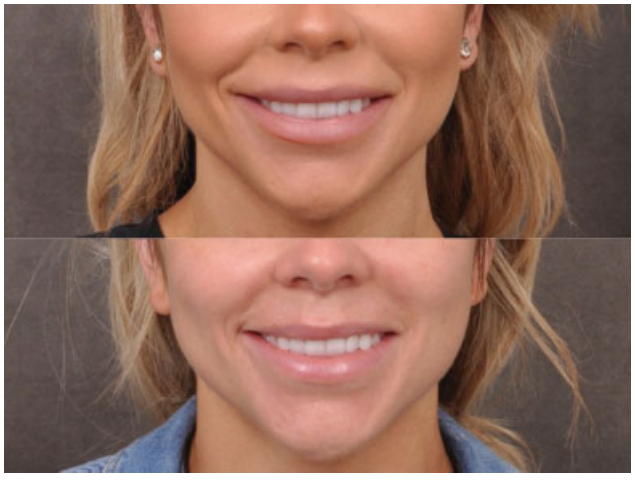

Fig. 8 Migrated Juvederm thickening and bulking the upper lip. Bottom photo after dissolving.

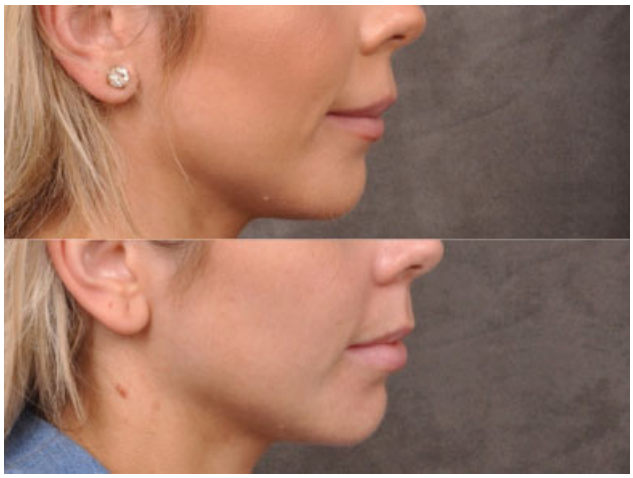

Fig. 9 Migrated Juvederm thickening and bulking the upper lip. Bottom photo after dissolving.

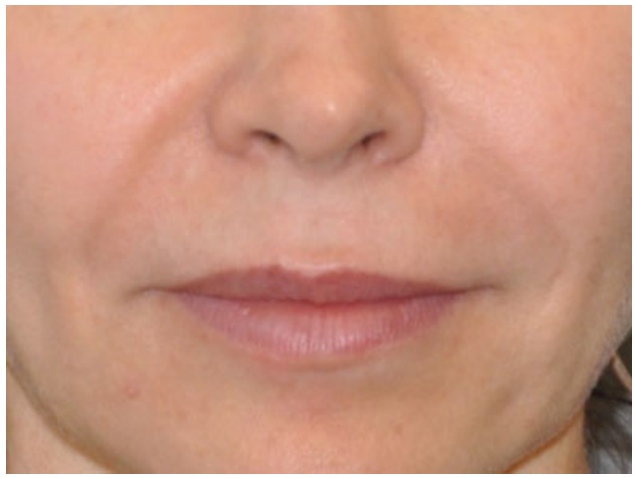

Fig. 11 A patient with broadening of the nasolabial folds from excessive injection

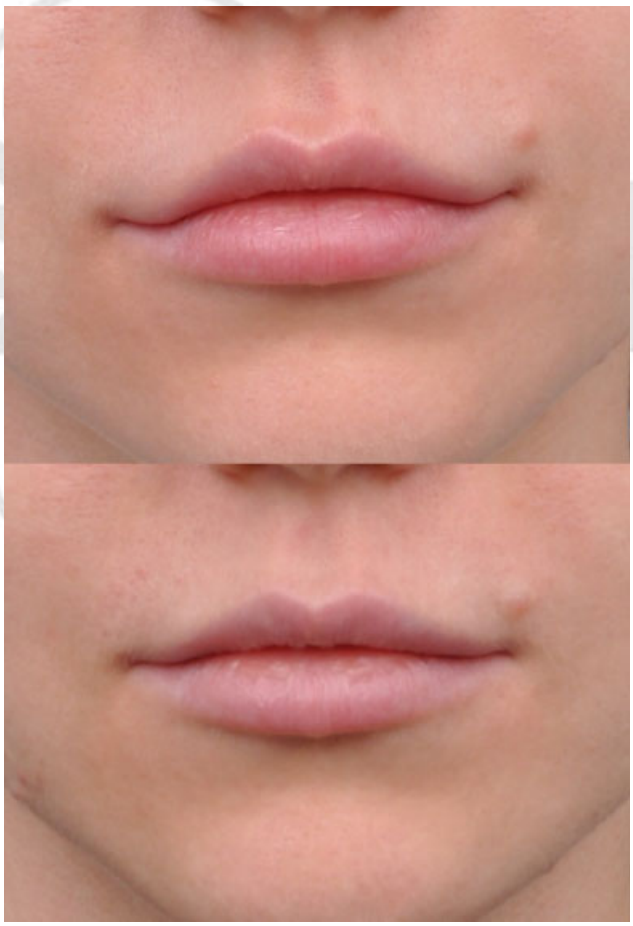

Fig. 10 Migrated Juvederm thickening and bulking the upper lip. Bottom photo after dissolving.

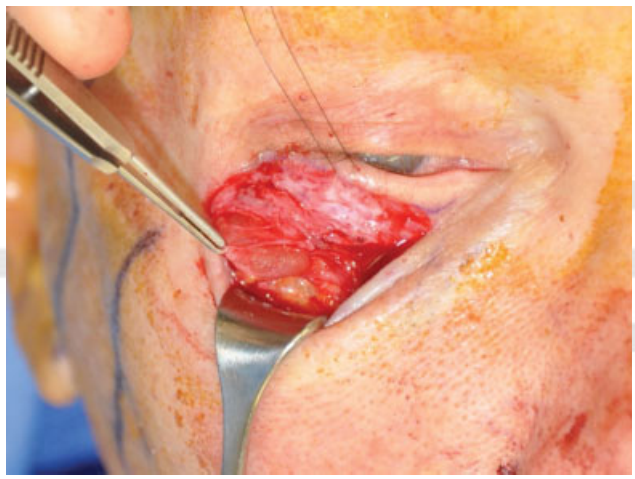

Fig. 12 Encapsulated Juvederm bolus seen intraoperatively with a clearly visible capsule.

with small amounts of hyaluronidase only as needed. This commonly occurs when HLA filler is injected near the wet-dry vermillion border or toward the wet vermillion. For this reason, HLA filler should be injected mainly in the body of the dry vermillion. Asymmetries should also be treated cautiously and only after a few weeks have passed. You may remove filler if needed or add to the opposite side. Always remain cognizant of dynamic asymmetries caused by facial dominance. The dominant resting tone on one side of the face is always greater than the other.

Broadening of the nasolabial fold (►**Fig. 11**) may occur with repeat injection creating a heavier appearance in the lower face. It is always advisable to limit injections in this area to avoid tipping the scales of beauty in the wrong direction. Large bolus injection may also result in encapsulation of the filler (►**Fig. 12**) and an overlying bulge or edema. Dissolving filler in this region is difficult to do predictably and may cause a vague distortion in patients that is quite difficult to fix. Deeper radiofrequency treatments may be used to shrink the area and variably increase the rate of filler metabolism in the face. Overfilling the marionette lines and prejowl region may similarly cause a broadened appearance and masculinize the face or perpetuate a simian appearance.

The chin, like the glabella, has a tendency to accumulate filler in the soft tissues over time and may become bulkier and heavier. For this reason, less hydrophilic fillers are used if possible and in a supraperiosteal plane preferentially over soft tissue injections. Accumulation of filler in the chin may

cause a bulky or heavy appearance while masculinizing a feminine face. Conservative dissolving may be attempted in this region or radiofrequency treatments. When dissolving in this region, the patient must be warned that the filler may be disguising an underlying peau d'orange appearance in the chin, or wrinkles in the lip that may appear once the filler is removed. This may be treated by refilling with less reactive filler or treating with small amounts of neuromodulators.

Calcium Hydroxyapatite

Hydroxyapatite, also called hydroxylapatite, is a naturally occurring mineral form of calcium apatite and is found in bone and teeth within the body. For this reason, it would be most logical to inject the substance over bony prominences for augmentation. Radiesse is a commercially available injectable calcium hydroxyapatite paste that is FDA approved for injection in the hands, for correction of human immunodeficiency virus (HIV)-related lipoatrophy, and subdermal implantation for the correction of moderate-to-severe facial wrinkles and folds such as the nasolabial folds.

The particles tend to be inflammatory with a propensity to crystallize and calcify. This type of filler is also irreversible. For this reason, the primary author strongly advises against placing this filler in the lips. The filler may calcify and remain permanently causing nodules, asymmetries, edema, and limitations in movement (►**Fig. 13**).

When injecting the nasolabial folds, great care must be taken to avoid over-injection or accidental injection to the malar fat pad or under eyes. This area is quite reactive and if placement should accidentally occur there, the resulting edema and irregularities may be permanent and severe. Injection into the marionette lines and prejowl region should be avoided in the subdermal plane. The skin is more sensitive in this area than in the nasolabial folds and adverse outcomes are very common. Nodules, rigidity, and a peau d'orange or cottage cheese appearance may occur and cannot be readily reversed.

Although various types of dissolution have been attempted, including injections with 5-fluorouracil (5-FU), hyaluronidase, or sodium thiosulfate, none have demonstrated reproducible success. Surgical removal is typically necessary should problems arise and complete removal is difficult given the integration of the crystals into the bone and skin. Intralesional injections of sodium thiosulfate may show some promise as dictated by studies treating calcinosis[9]

Poly-L-Lactic Acid

Poly-L-Lactic acid differs from other dermal fillers. Its main purpose is to volumize via stimulation and scaffolding rather than direct addition and retention of material. It is commercially available in the United States under the brand name Sculptra (Merz Aesthetics). Although PLLA is thought to simply increase collagen production, it is more accurate to describe its affect as increasing collagen production by means of inciting an inflammatory response and subsequent fibroplasia[10] What this means is that unhealthy collagen production may occur in the form of fibrosis and tissue granulation (►**Fig. 14**).

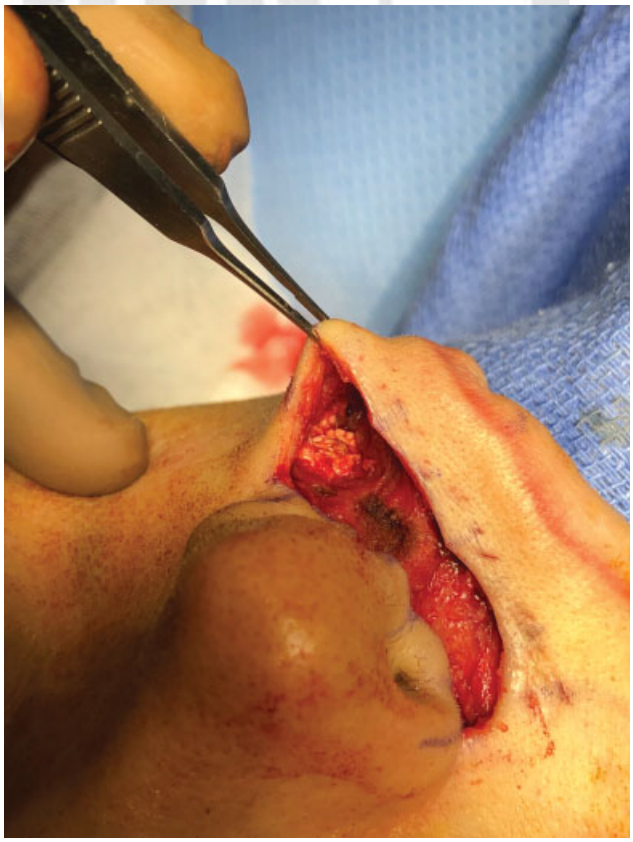

Fig. 13 Calcium hydroxyapatite crystals found in the upper lip causing chronic swelling, limitation of movement, and a palpable mass.

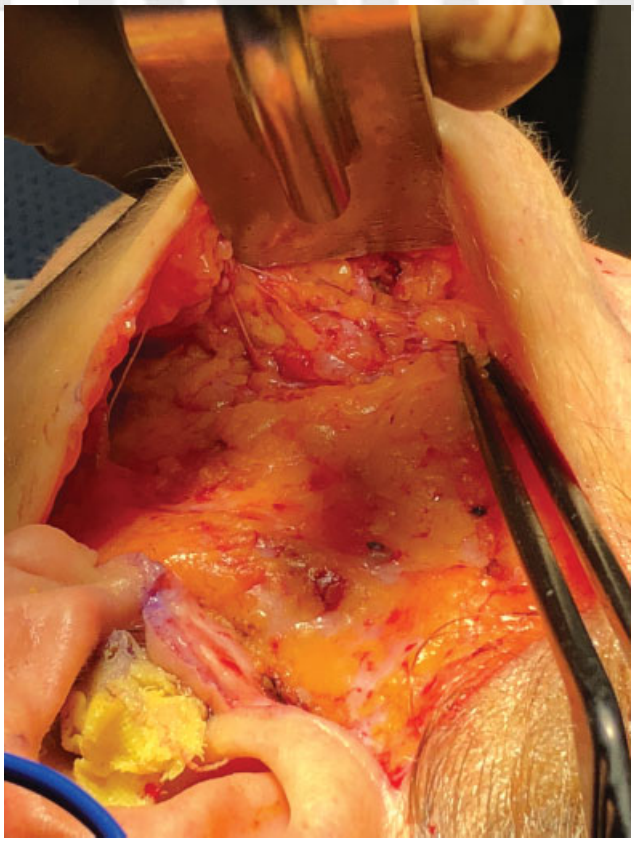

Fig. 14 Gray colored granulomas resulting from Sculptra injections seen near the nasolabial folds damaging the supple nature of the skin.

Unlike other fillers, PLLA is meant for diffuse volumization of tissues and increasing fullness, such as in patients with HIV-related lipodystrophy. When injected into the fatty or muscular layers in the face, granulomas and nodules may form. When injected in or under the dermis, nodules may form. The upper lip is particularly sensitive to these issues and Sculptra should not be injected there. Granulomas may be injected with triamcinolone or alternatively with 5-FU. 5-FU injection has a lower risk of dermal atrophy than triamcinolone, but its use is considered off-label at this point[11]

Silicone, PMMA, and Polymers

Medical grade silicone, PMMA, and other polymers are quite reactive and unpredictable. For purposes of facial injection, we have categorized them as a single group. The primary author strongly advises against use of any of these fillers in the face unless there is a compelling argument for their use, such as in acne scarring where the skin is already damaged.

Products such as Bellafill, which is considered temporary or semi-permanent, may be just as treacherous in nature as silicone causing perpetual and irreversible problems. When injected into the lips, the fillers may lay senescent for several years before becoming expansive and edematous. These fillers have a tendency to migrate into the upper lip above the vermillion and lower lip below the vermillion causing a very exaggerated appearance as they hypertrophy. Asymmetries, nodules, and granulomas typically ensue (►**Fig. 15**). It is nearly impossible to remove these fillers. In certain situations, the filler may consolidate into a larger mass, which may be expressed manually following needle puncture. Otherwise, surgical excision is more commonly needed to help fix irregularities caused by the polymers. It is important to advise the patient that complete removal is virtually impossible and they will likely have a perpetual need for corrective procedures throughout their lives.

Fat

Fat may be injected into the face in several forms. Autologous fat is most commonly used, although the use of micronized fat and allograft adipose matrix (Renuva) is slowly becoming more popular. Nanofat is very low risk and mostly intended for tissue healing purposes. Data from use of allografted fat is still lacking and the risks and benefits still remain to be seen.

Autologous fat is considered safe to use, but its risks should not be overlooked. Adverse outcomes of fat injections in the perioral region may be quite deforming and difficult to fix. Small amounts of fat injection into the lips are typically benign and the most prominent risk is formation of nodules. The nodules may be surgically excised, although asymmetries are difficult to fix. Larger injections of fat may result in a similar reaction as is seen with silicone injections. The fat may migrate above the vermillion, hypertrophy, and result in discoloration, large nodules, and edema (►**Fig. 16**). Once this occurs, it is very difficult to fix. Hypertrophy of fat around the lips can be treated by surgical excision or possibly repeated radiofrequency treatments. Deoxycholic acid has a limited role and may present some risk.

Overaggressive or superficial injection of fat in the marionette lines or prejowl region may cause broadening and masculinization of the area or a peau d'orange appearance (►**Fig. 17**). Small defects can be camouflaged with HLA fillers, while more prominent irregularities may require repeated radiofrequency treatments.

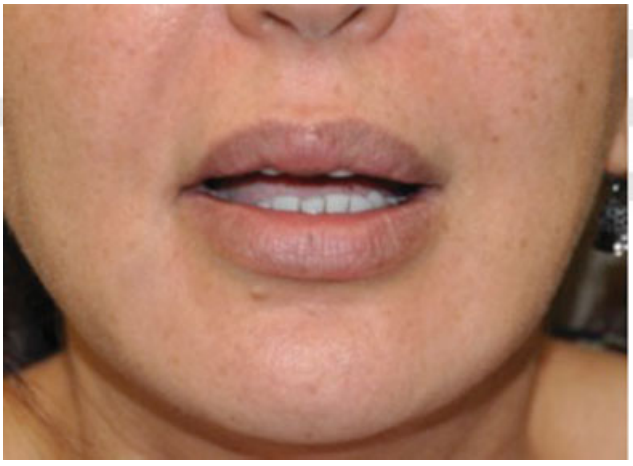

Fig. 16 Nodular hypertrophy of the tubercle of the upper lip following fat injection.

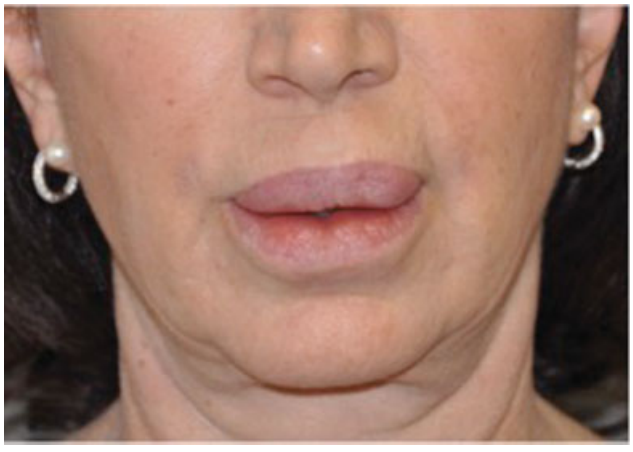

Fig. 15 Thickening and distortion of the upper lip following silicone polymer injections.

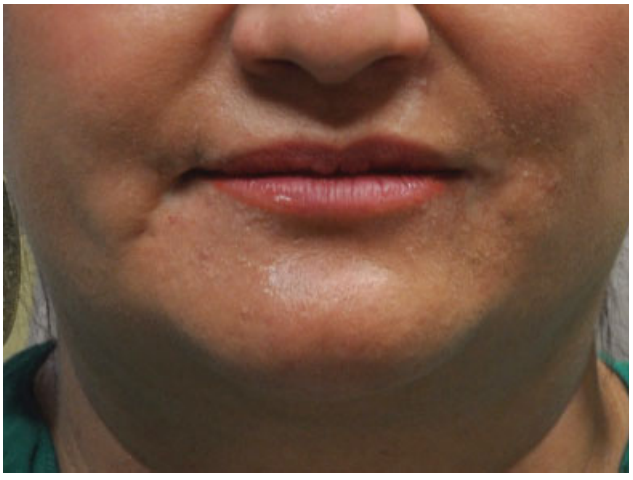

Fig. 17 Peau d'orange noted following superficial fat injections.

Threads

Injectable threads have been reintroduced to the market in recent years in the form of PDO. PDO threads have been used to simulate facelift results and more recently to try and lift the lip or improve rhytids in the upper lip[12,13] PDO threads are thought to increase collagen production. However, the formation of collagen is likely via fibrosis and replacement of type III collagen with type I collagen.[13,14] These changes are supported by the primary author's observations during facelift procedures in patients who have had prior PDO threads placed. Fibrotic collagen formation may improve rhytids, but the patient should be advised that the supple and soft nature of the skin may change and there may be temporary or permanent limitations in muscle movement.

Hyaluronidase

Hyaluronidase is an enzyme previously used to improve the permeation of local anesthetic. Its use has now been extended to breaking down HLA gels injected into the face and body. This use has yet to gain FDA approval and this type of use would be considered off-label. However, practitioners should not be dissuaded from using the product in any injectable practice. It is important to realize that it is a very effective medication but its effects are not always predictable. Even when used properly, significant soft tissue dehydration and deflation may result. Injection is most predictable when treating an obvious deformity. Hyaluronidase injected around the lower cheek, nasolabial folds, and marionette lines/prejowl sulcus carries treacherous potential. Injection into these areas may cause visible irregularities or in worse cases they may cause vague changes to tissue quality and fullness that the patient notices and the practitioner cannot visualize. It is very difficult to improve patients complaining of a gaunt, deflated appearance or of changes that cannot readily be identified in photos. Allergy testing may be performed prior to use in nonemergent situations depending on the preference of the practitioner.

Deoxycholic Acid

Deoxycholic acid (Kybella; Kythera Biopharmaceuticals) was FDA approved in 2015 for the treatment of submental fat in adults. Although Kybella may have limited off-label indications in the face, such as correction of minor irregularities from fat injection, its use should be avoided in the perioral region. Maintaining fat in the face helps support the facial structures and preserve youth. Kybella in the face has little potential for any sort of improvement. Rather, it poses almost unilateral risk to the patient as it can cause nerve paresis, skin irregularities, and indentation. Irregularities may appear months after injection. (►**Fig. 18**) Potentially traumatic interventions should be avoided until the Kybella reaction has had a chance to settle over several months.

Steroids and Antimetabolites

Triamcinolone and 5-FU are commonly used in the perioral region to treat granulomas, hypertrophic scars, nodules, and inflammatory masses[11,15] The use of 5-FU is considered off-label, but it confers a considerable advantage to triamcinolone in superficial and sensitive areas.[16] Superficial injection of triamcinolone may cause dermal atrophy, discoloration, or telangiectasia.

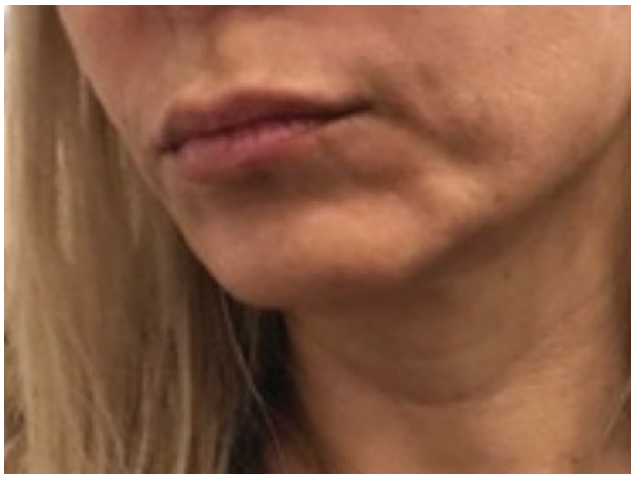

Fig. 18 Subdermal fat atrophy following perioral Kybella injection.

Conclusion

Applications for injectable treatments have increased dramatically in recent years. Injectables are inherently unpredictable in nature and limitations in their use should be respected. Given the lack of long-term control and potential for vascular compromise, reversible fillers are preferred. It would be a mistake to believe that experienced injectors are immune to these risks. Although we would love to give patients an easy, nonsurgical, permanent option, we must remember that sometimes things go wrong during injection and even years later. For this reason, we advise against the use of permanent and semi-permanent injectable such as silicone, PMMA, and other polymers. Should there be a concern for vascular compromise, treatment should be initiated immediately. Conversely, long-term and mild complications should be treated slowly and conservatively to avoid worsening of issues.

Conflict of Interest
Dr. Talei reports personal fees from Galderma and Evolus, during the conduct of the study.

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