What's New in Cosmetic Dermatology

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KEYWORDS

• Topical silicone gel • Topical triple antibiotic ointment • Vaginal laser rejuvenation
• Genitourinary syndrome of menopause • Botulinum toxins • OnabotulinumtoxinA
• DaxibotulinumtoxinA

KEY POINTS

- Topical silicone gel is preferred over petrolatum-based products as an all-purpose wound dressing for granulating and sutured wounds, regardless of cause.
- Vaginal laser rejuvenation is effective in relieving genitourinary syndrome of menopause (GSM), stress urinary incontinence (SUI), vaginal relaxation syndrome (VRS), vulvar disorders of lichen sclerosis, and other related issues.
- New cosmetic indications in the upper face for onabotulinumtoxinA have been approved by the FDA and off-label treatments for the lower face are increasing in popularity.
- Clinical trials of uncomplexed daxibotulinumtoxinA demonstrate safety and efficacy lasting more than six months.

TOPICAL SILICONE VERSUS PETROLATUM-BASED PRODUCTS AS A PREFERRED POSTSURGICAL WOUND DRESSING

The use of topical antibiotics after dermatologic surgical procedures has always been controversial in preventing surgical site infections. In the United States, dermatologists perform more than 25 million procedures yearly that result in superficial cutaneous wounds, which are low risk for postoperative infection.[1] The ever-growing routine use of topical antibiotics is unnecessary and currently not recommended. Because there is no scientific proof that the application of topical antibiotics onto a wound bed after cutaneous surgery prevents surgical site infections, the use of topical antibiotics postoperatively has become a habit without evidence.[2] This practice potentially places patients at risk for allergic or irritant contact dermatitis, contributes to delayed wound healing, produces multidrug-resistant bacterial infections, and even contributes to inflammatory chondritis and anaphylaxis.[3] Therefore, the current recommendations for wound care are to limit the use of topical antibiotics to avoid the ever-increasing incidence of bacterial resistance.[1–6] Reconsideration of the standards for postoperative wound care is highly recommended and necessary. Recently, a one question survey by the author was conducted of prospective patients presenting to a dermatologic surgical practice. (Staidle JP, Benedetto AV, Benedetto PX, et al. Comparison of a novel antibiotic-free film-forming topical wound dressing versus triple antibiotic on Mohs surgical wounds. Submitted for publication.) Before the patients were seen by their dermatologist, they were asked to respond to this question: "What is your favorite 'go to' over the counter first aid cream or ointment that you use to help heal a scratch, cut or burn?" Nearly 82% of the more than 960 responders indicated that they prefer a topical petrolatum-

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based product, of which more than 45% used some form of a triple antibiotic containing neomycin, bacitracin, or polymyxin B and another 25% admitted to using a topical bacitracin and polymyxin B product, and nearly 10% of the remaining responders used some form of topical petrolatum with or without an antibiotic component.

Other studies have shown topical silicone is safer and more effective as a postoperative wound dressing when compared with any petrolatum-based product with or without an antibiotic component.[8–11] The reason for this is silicone is inert and has no measurable pH. It is mostly bacteriostatic and for some bacteria it is bactericidal. However, petrolatum has a measurable pH and can promote microbial overgrowth. Topical silicone gel (SG) is nonocclusive, waterproof, and gas permeable. Petrolatum is a water immiscible, occlusive ointment and inhibits the exchange of gases (eg, oxygen and carbon dioxide) to occur freely from the surface of the wound. Petrolatum adheres to the wound bed and causes maceration, whereas silicone is a flexible hydrophobic barrier maintaining normal ambient wound hydration and decreases transepidermal water loss. Petrolatum, conversely, saturates and macerates cutaneous tissue and has no effect on a wound's transepidermal water loss. Because of its inherent properties, silicone protects open wounds from chemical and microbial invasion, reduces inflammation, and thereby lessens abnormal scar formation. Petrolatum is only partially protective of external chemical and microbial insults on open wounds, has no effect on reducing the extent of inflammation, nor does it have any effect on scar formation.

Because recent reports confirmed the benefits of using topical SG as a postoperative wound dressing,[8–11] we initiated a phase IV, postmarketing, prospective, open label trial to compare the use of topical SG (Stratamed, Stratpharma, Basel, Switzerland) against the popular and frequently used topical triple antibiotic ointment (TA) Neosporin, containing bacitracin, neomycin, and polymyxin B (Johnson &Johnson, New Brunswick, NJ). Neosporin ointment was used in this comparative study because of its widespread and regular use by the general public and physicians alike, which was disclosed by the internal survey conducted by the author.[7] There were two arms to the study. One cohort of 60 patients underwent Mohs surgery and the postoperative wounds were dressed with either SG (n = 30) or TA (n = 30). The other cohort of 274 patients underwent general excisional surgery or a typical dermatologic surgical procedure, such as a biopsy, curettage, or even extensive cryosurgery with liquid nitrogen. The primary objectives of this clinical study were to measure the incidence of contact or irritant dermatitis, the rate of infection, healing time, and the quality of healing as assessed by the patient and a physician observer. The secondary objectives were to document the patients' comfort level with using either product, ease of dressing changes, and overall satisfaction with either product.

The Mohs surgery arm of the study has been completed.[7] None of the patients using SG developed any sign of contact or irritant dermatitis. There was a 21.6% incidence of contact or irritant dermatitis in patients using the TA. The incidence of infection was not significantly different between either group ($P > .05$). Both the healing time ($P = .018$) and healing quality ($P < .001$) were significantly better in the SG group as compared with the TA group, measured on a scale of −4 (much worse) to +4 (much better).

Fig. 1 is an example of a patient who used the SG product and **Fig. 2** is an example of a patient who used the TA product. It was found by both the patient and physician observer that with SG there usually was less inflammation during early healing and at the time of suture removal. Because of this improved healing quality and ease of use, most patients preferred the SG product over the TA product. However, most of the Mohs wound sites at 3 months had a similar aesthetic appearance whether treated with SG or TA.

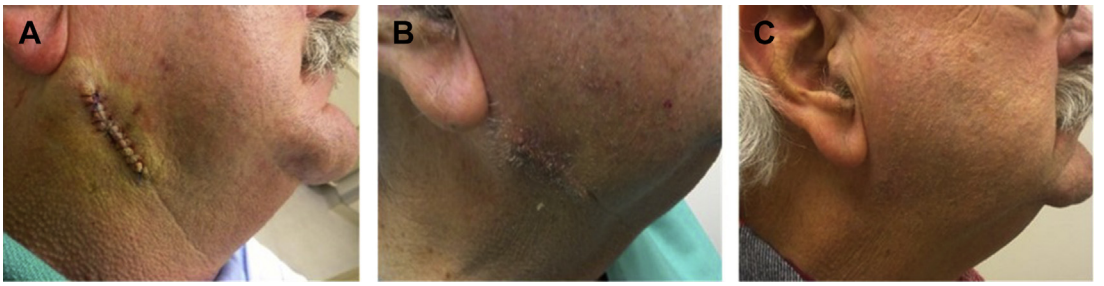

Fig. 1. This 66-year-old patient treated with silicone WD gel is shown immediately following Mohs surgery and repair (*A*), 1 week postoperatively following suture removal (*B*), and 7 months postoperatively at final assessment (*C*).

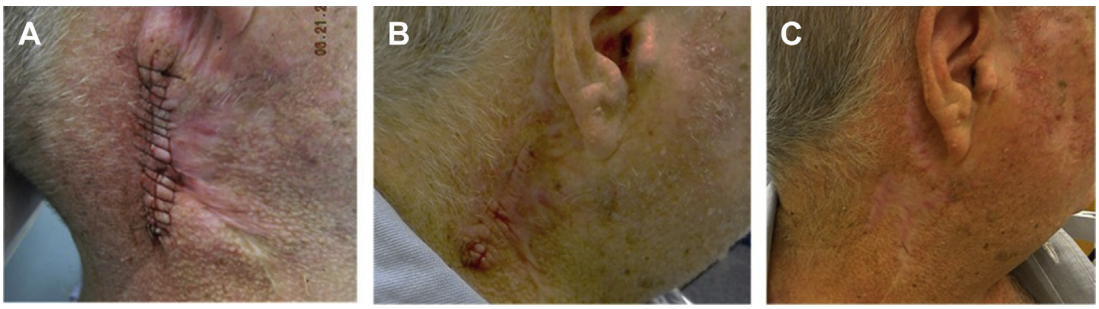

Fig. 2. This 61-year-old patient treated with TA ointment is shown immediately following Mohs surgery and repair (*A*), 1 week postoperatively following suture removal (*B*), and 7 months postoperatively at his final assessment (*C*). (Note the increased erythema at the time of suture removal.)

In conclusion, the SG film forming wound dressing demonstrated no contact or irritant dermatitis nor increased infection rate when compared with the TA. Wound healing quality was enhanced, and ease of use was better with the SG as compared with the petrolatum-based topical triple antibiotic. The SG used in this study is the first topical SG dressing indicated for the immediate application on granulating and sutured wounds. When used immediately after surgery it may also contribute to minimizing postoperative scar formation. Topical silicone is antibiotic free and can be used as an all-purpose alternative for routine wound care regardless of cause and should be preferred over any petrolatum-based product.

CARBON DIOXIDE LASER VAGINAL REJUVENATION

Women's health issues concerning urinary incontinence, vaginal dryness, vulvovaginal itching and burning, vaginal laxity, pain with intercourse, and sexual dysfunction recently have become frequent topics in the popular visual media and in print. Because of the widespread awareness of these overwhelming issues, vaginal rejuvenation has become a hot topic not only in the media, but also in doctors' offices. Treatments with laser and light-based devices to manage such devastating issues are on the rise, increasing at a rate of 26% annually and estimated to triple in 5 years. North America is expected to be the largest market for vaginal laser rejuvenation, predicted to expand by 30% each year through 2021. More than 500,000 feminine rejuvenation procedures were performed in 2016, and by 2021 more than 27,000 devices will be in operation.[12]

The most common condition that may affect women over a certain age is the genitourinary syndrome of menopause (GSM), which is caused by a diminution in estrogen production and secretion by the ovaries, causing atrophic vaginitis. Stress urinary incontinence, caused by a weakening in the suspension of the urinary bladder, can lead to involuntary loss of urine with minimal abrupt physical activities like coughing, laughing, walking, sitting down, or standing up. Vaginal relaxation syndrome (VRS), most commonly caused by vaginal childbirth, can affect younger and older women. Other vulvar issues of concern are certain dermatoses, such as lichen sclerosis and vulvodynia.[13]

Approximately 60% to 80% of postmenopausal women develop GSM, whose symptoms are caused by intravaginal mucosal atrophy, dryness, and inflammation, leading to vulvovaginal itching, burning, soreness, and discharge; dyspareunia, and postcoital bleeding. When this occurs more than 40% of women experience quality of life issues and some form of sexual dysfunction; 34% have arousal difficulties, 20% have lack of desire, and 19% have orgasmic dysfunction.[14] Of the women who have urinary issues, 50% are caused by stress urinary incontinence manifested by urgency, burning, with urination, and frequent urinary tract infections; another 20% are attributed to urinary urgency.

In the United States, atrophic vaginitis occurs in more than 50 million women, more commonly seen in premenopausal and postmenopausal women and even in those of child bearing age (25–50 years old). Of the women who have atrophic vaginitis, 26 million (59%) have given birth to children. Approximately 70% of the 3 million women (2.1million) in the United States who are survivors of breast cancer have atrophic vaginitis, and approximately 300,000 new cases of breast cancer are reported in the United States annually.[15] All these women suffering from atrophic vaginitis can benefit from some form of treatment to relieve their incapacitating symptoms. Of the women who are not at risk for breast or other endocrine cancers, but have postmenopausal hormonal issues,

hormone-replacement therapy is an option. However, for those women at risk, treatment with a laser or light-based device is a preferred therapeutic option.

Before menopause the ovaries produce sufficient amounts of estrogen, which maintains a thick and moist mucosal lining of the vagina, and blood flow to the vaginal tissue is abundant. Walls of the vagina are elastic and the moist mucosal surfaces secrete additional mucus during sexual activity. However, in postmenopausal women the ovaries produce little to no estrogen, causing the vaginal lining to become atrophic and dry. There is a decrease in blood flow to the vaginal tissues, resulting in a decrease in vaginal elasticity and a reduction in mucous secretion at all times, even during sexual activity. There also is a narrowing and shortening of the vaginal vault and atrophy of vulvar supportive structures.

The vaginal wall is composed of four layers: (1) a superficial layer of stratified squamous epithelium, (2) the lamina propria, (3) a fibromuscular layer, and (4) the adventitia. The stratified squamous epithelial lining of the vaginal vault provides protection against mechanical friction and is lubricated by glycogen-rich mucus. Vaginal walls do not contain any glandular structures. Estrogen stimulates the superficial and intermediate epithelial cells of the mucosal lining to secrete glycogen. In premenopausal women the superficial and intermediate cells predominate and are well-estrogenized, thick, and full of glycogen, secreting an abundance of mucus as needed. However, because of the diminution in estrogen secretion in GSM, there is a substantial reduction in the superficial cells of the epithelium and increase in parabasal and nonproductive intermediate cells (**Fig. 3**).

Another distressing problem for women is vaginal laxity or vaginal relaxation syndrome (VRS). The vagina can stretch up to 200% because the walls are composed of elastic soft tissue folds called rugae. VRS can occur for multiple reasons, but mostly because of multiple vaginal deliveries with or without instrumentation, advancing age, menopause, excessive sexual activity, or related trauma.[16]

Table 1 compares the different technologies of radiofrequency devices, erbium-doped:YAG lasers, and carbon dioxide (CO_2) lasers. Typically, radiofrequency treatments for vaginal rejuvenation primarily involve tissue coagulation, so therefore are somewhat painful and can take up to 30 to 45 minutes to complete. Erbium-doped:YAG lasers ablate tissue more quickly, usually within 15 minutes, but because of its high affinity for water, ablation of the vaginal mucosa is superficial. Fractional CO_2 laser treatments can take anywhere between 5 to 15 minutes to perform, depending on the proprietary laser used. Advantages of the CO_2 laser are that treatments include ablation and coagulation of the vaginal mucosa. This combined thermal effect on vaginal mucosa by CO_2 lasers can tighten vaginal laxity by improving pelvic floor support; enhance vaginal glycogen production and lubrication; and reduce symptoms of GSM, increase sexual sensation, and decrease dyspareunia. Other benefits are a reduction in stress urinary incontinence, a decrease in urinary tract infections, and symptomatic relief of lichen sclerosis and vulvodynia.

WHAT'S NEW IN THE WORLD OF THE BOTULINUM TOXINS: NEW TREATMENTS AND NEW PRODUCTS

In 2017, the Food and Drug Administration approved the cosmetic treatment of forehead

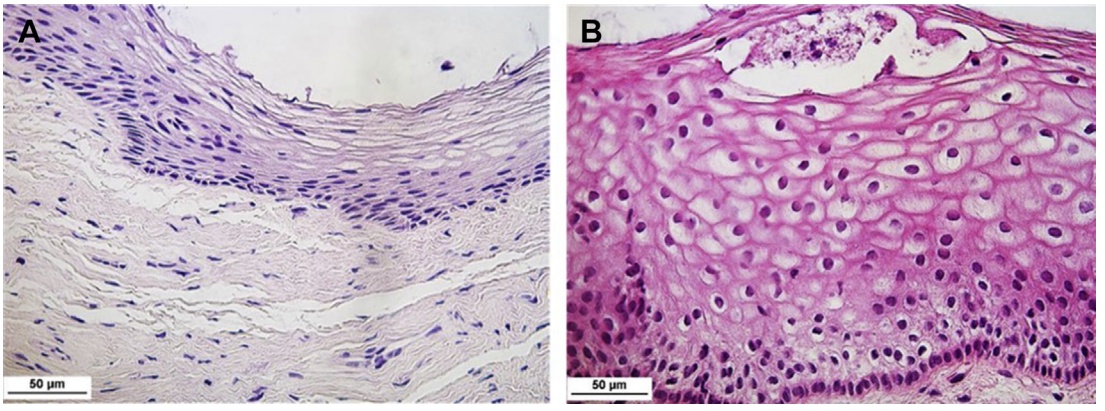

Fig. 3. Photomicrograph of a biopsy of an atrophic vaginal wall before treatment (*A*) and after the third treatment (*B*) with CO_2 laser of the same patient. Note the increase in glycogen-filled intermediate cells of the vaginal epithelium (H&E, original magnification ×40).

Table 1
A comparison of the different technologies of radiofrequency, erbium-doped:YAG and fractional CO_2 lasers

Technology	Mechanism	Procedural Time
Radiofrequency (ThermiVa; Viveve Cryo MonoRF)	Transmucosal heating tissue to 40°C–45°C, promotes prolonged edema	Up to 30 min (internal), 45 min (external) per area; multiple treatments required
Erbium-doped:YAG (Diva)	Collagen contracture from wound healing response	15–20 min; minimal thermal effect; superficial ablation
Fractional CO_2 (radiofrequency excited) super pulse only capability (FemiLift; MonaLisaTouch; Intima; GyneLase)	Ablation + coagulation induced collagen contraction, elastin production	10–20 min for internal treatments 10–15 min for external treatments (when available)
Fractional CO_2 (DC-excited) continuous wave and super pulse capabilities (FemTouch)	Ablation + coagulation induced collagen contraction, elastin production	3–5 min for internal treatments 5–10 min for external treatments

horizontal wrinkle lines with onabotulinumtoxinA. Now injections of onabotulinumtoxinA in the upper face with a total of 64 U placed in 16 sites is Food and Drug Administration approved (**Fig. 4**). Injecting forehead horizontal lines is approved for 20 U of onabotulinumtoxinA placed in five sites. Injecting glabella lines is approved for 20 U injected in five sites and lateral canthal lines is approved for 24 U in six sites.

Off-label treatments of botulinum toxin type A (BoNT-A) recently have become more popular, especially in the lower face. When treating the lower face with botulinum toxin, one must consider the directional movements of not only the levators and depressors of the lower face but also those of the platysma. The platysma has three portions (pars mandibularis, pars labialis, and pars modiolaris), which collectively interdigitate with all the peribuccal levators and depressors of the lower face (**Fig. 5**). By treating the lower face as one cosmetic unit,[17,18] a balanced and natural-appearing enhancement of the lower face is achieved. These treatments include injecting the orbicularis oris to diminish perioral vertical lip lines, the depressor anguli oris for lifting down-turned oral commissures and reducing marionette lines, and the mentalis for effacing corrugated chin lines. Direct and deliberate injections of the platysma

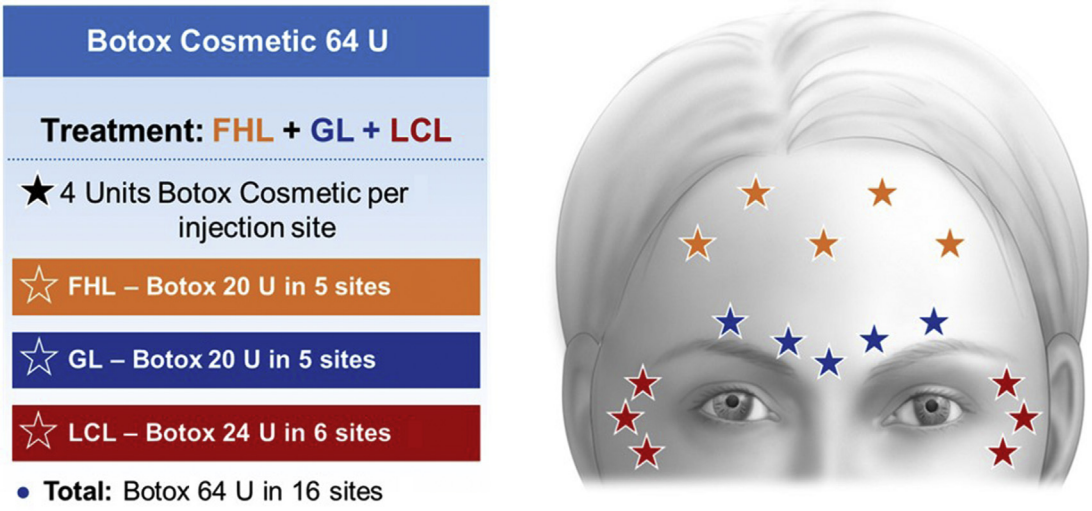

Fig. 4. Note the pattern of injections and number of units of onabotulinumtoxinA that are Food and Drug Administration approved for the cosmetic treatment of upper face wrinkles. Each star represents 4 U of onabotulinumtoxinA. FHL, forehead horizontal lines; GL, glabella lines; LCL, lateral canthal lines.

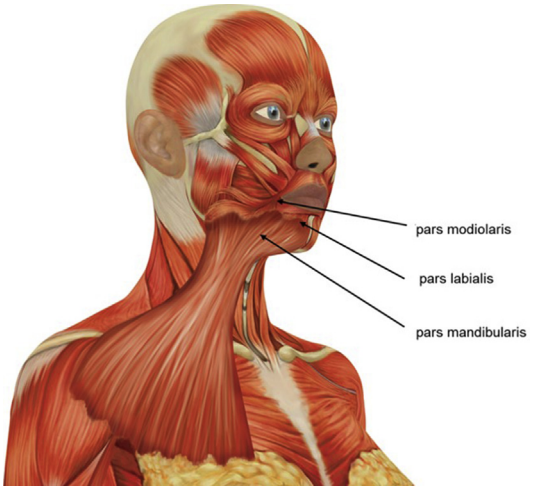

Fig. 5. Note the location of the platysma and its three portions in the lower face. (*Copyright 2018 From* Benedetto AV. Cosmetic uses of botulinum toxin A in the lower face, neck, and upper chest. In: Benedetto AV, ed. Botulinum Toxins in Clinical Aesthetic Practice Volume Two: Functional Anatomy and Injection Techniques. 3rd ed, Boca Raton: CRC Press, 2018:275; with permission. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.)

itself in different locations in the lower face and neck with BoNT-A can attenuate lower face rhytides, soften platysmal bands, and diminish horizontal neck lines. They also can eliminate wrinkling of the décolleté and uplift breasts.[17] **Figs. 6–11** illustrate the pretreatment conditions and post-treatment results of injecting onabotulinumtoxinA in the lower face musculature, including the platysma.

In 2015, the worldwide neurotoxin market reached $3.4 billion. It is expected to grow at an annual growth rate of 8% to reach $7.3 billion in 2025.[19] This escalation in treatments is attributed to the growing popularity of minimally invasive cosmetic treatments in India, China, South Korea, Japan, and other Asian Pacific countries.[20] Competition within the neurotoxin market is increasing not only in the West with Allergan, Galderma, Merz, and Revance, but also in Asia with Medytox, Lanzhou, Daewoong, Hugel, and other manufacturers and distributors based in China, Japan, and South Korea. **Table 2** identifies the major brands of botulinum toxin available worldwide for aesthetic use. **Table 3** identifies the different companies worldwide that are in the process of developing topical botulinum toxin products. **Table 4** identifies the approved BoNT products from Asia as of early 2017. Medytox, Inc is the only biopharmaceutical company in the world to have three different physical forms of botulinumtoxinA: Neuronox (900 kDa), a complexed BoNT-A; INNOTOX (900 kDa), the world's first liquid formulation of BTX-A; and Coretox (150 kDa), a noncomplexed BoNT-A. In 2013, Medytox, Inc sold to Allegan the worldwide rights to INNOTOX, a liquid BoNT-A, but still retains the rights to sell INNOTOX in Korea. Allergan is scheduled to begin phase III trials of INNOTOX shortly.

A privately held biotechnology company, Bonti, Inc (Newport Beach, CA) is in phase 2 trials evaluating a short-acting botulinum toxin type E (BoNT-E), which has a fast onset of action of about 24 hours and a short duration of effect of about 2 to 4 weeks. Their aesthetic BoNT-E product (EB-001A) is being developed to treat glabellar frown lines, and to reduce scarring at excision sites

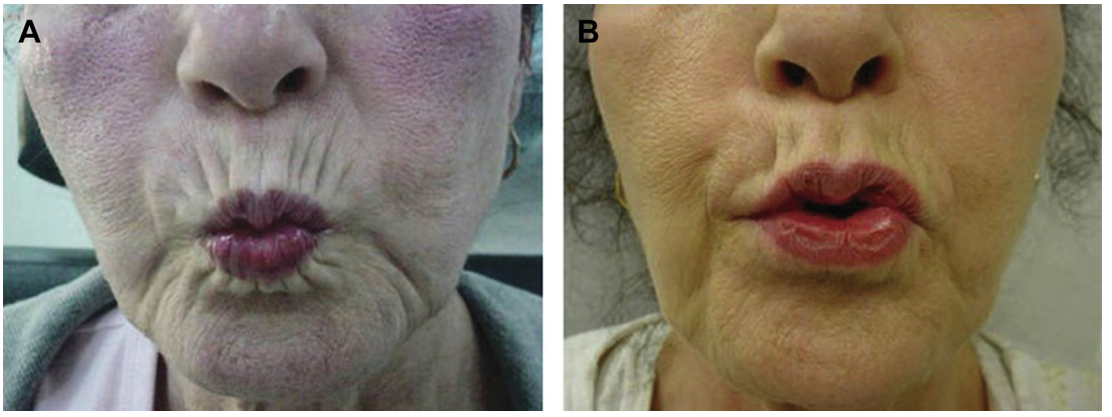

Fig. 6. Orbicularis oris. Notice the vertical lip lines before treatment (*A*) and their reduction and eversion of the vermillion with lip puckering 3 weeks after (*B*) injections of BoNT-A. (*Copyright 2018 From* Benedetto AV. Cosmetic uses of botulinum toxin A in the lower face, neck, and upper chest. In: Benedetto AV, ed. Botulinum Toxins in Clinical Aesthetic Practice Volume Two: Functional Anatomy and Injection Techniques. 3rd ed, Boca Raton: CRC Press, 2018: 249; with permission. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.)

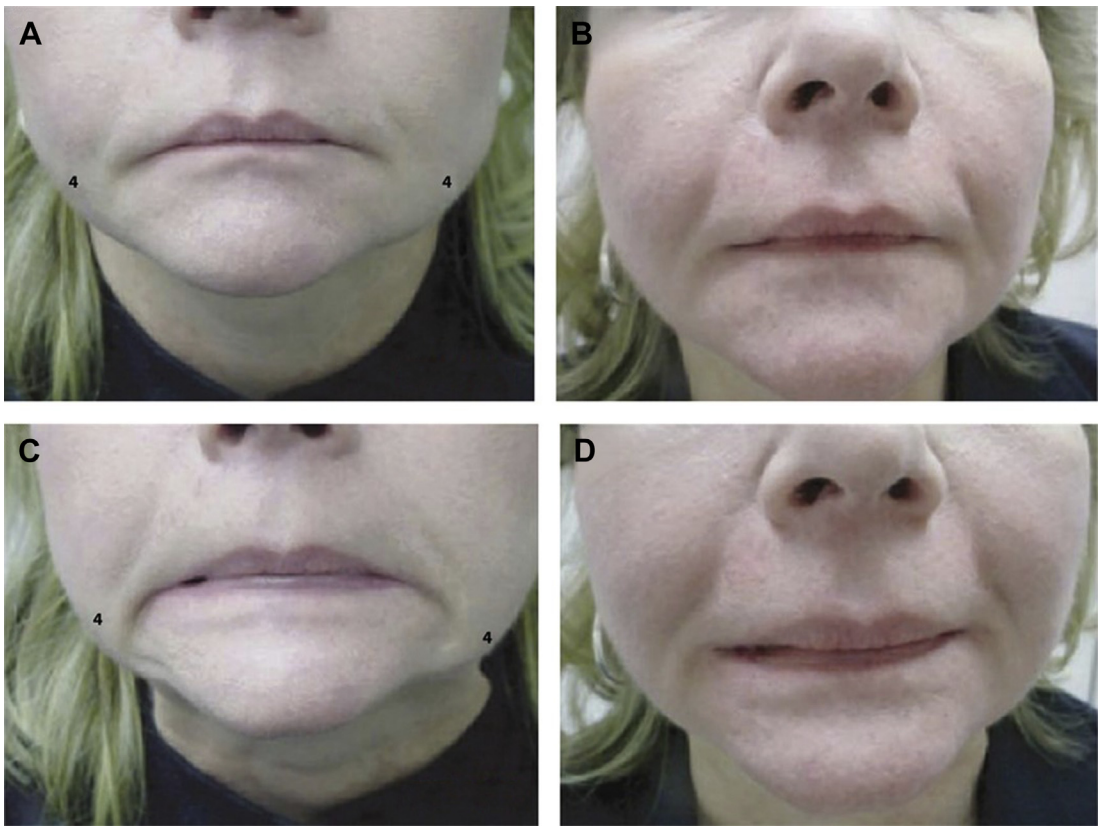

Fig. 7. Note the down-turned commissures and deep marionette lines in this 52-year-old patient at rest and with forced frowning before treatment (*A*, *C*) and the reduction in the down-turned commissures and diminution of marionette lines 3 weeks after (*B*, *D*) injections of onabotulinumtoxinA in the depressor anguli oris. (*Copyright 2018 From* Benedetto AV. Cosmetic uses of botulinum toxin A in the lower face, neck, and upper chest. In: Benedetto AV, ed. Botulinum Toxins in Clinical Aesthetic Practice Volume Two: Functional Anatomy and Injection Techniques. 3rd ed, Boca Raton: CRC Press, 2018: 263; with permission. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.)

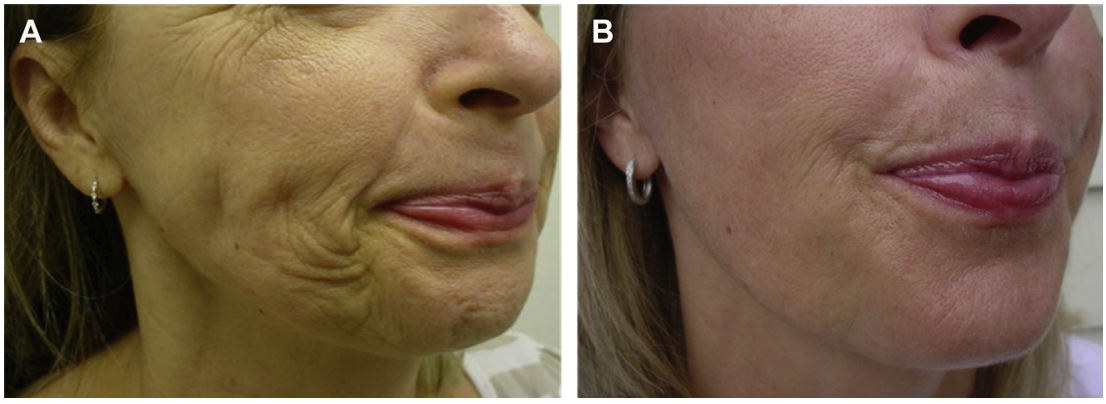

Fig. 8. Patient with wrinkling of the, pars labialis, and pars modiolaris of the platysma when smiling before (*A*) and 3 weeks after (*B*) an injection of onabotulinumtoxinA. (*Copyright 2018 From* Benedetto AV. Cosmetic uses of botulinum toxin A in the lower face, neck, and upper chest. In: Benedetto AV, ed. Botulinum Toxins in Clinical Aesthetic Practice Volume Two: Functional Anatomy and Injection Techniques. 3rd ed, Boca Raton: CRC Press, 2018: 275; with permission. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.)

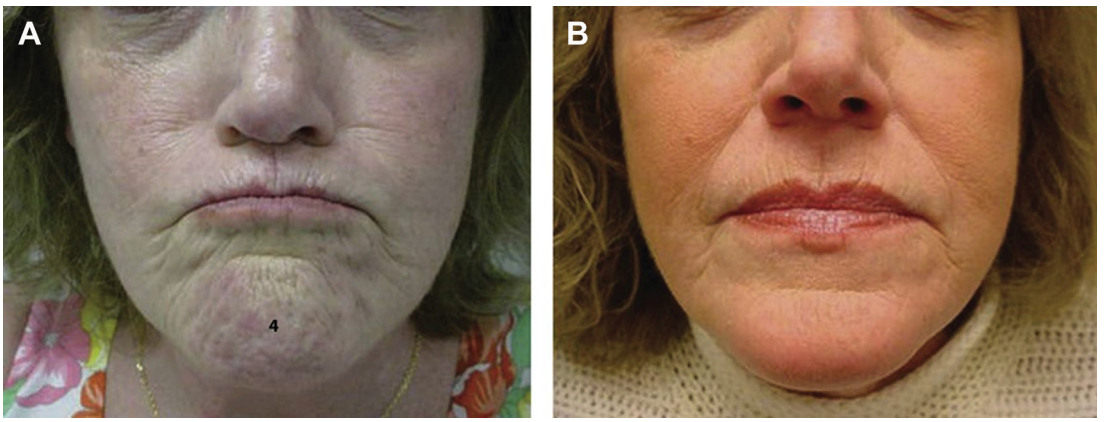

Fig. 9. Note the diminution of mental wrinkles and corrugations with the relaxation of the mentalis 6 weeks after treatment with 4 U of onabotulinumtoxinA in the center of the chin. (*Copyright 2018 From* Benedetto AV. Cosmetic uses of botulinum toxin A in the lower face, neck, and upper chest. In: Benedetto AV, ed. Botulinum Toxins in Clinical Aesthetic Practice Volume Two: Functional Anatomy and Injection Techniques. 3rd ed, Boca Raton: CRC Press, 2018: 272; with permission. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.)

following Mohs surgery and reconstruction of head and neck skin cancers. The results of their phase 2a clinical trial of moderate to severe glabellar frown lines demonstrated a favorable safety profile while confirming the expected clinical effects. Their phase 2a SHINE-1 (Scar Healing Improvement with Neurotoxin-E) clinical trial after Mohs surgery is still underway.

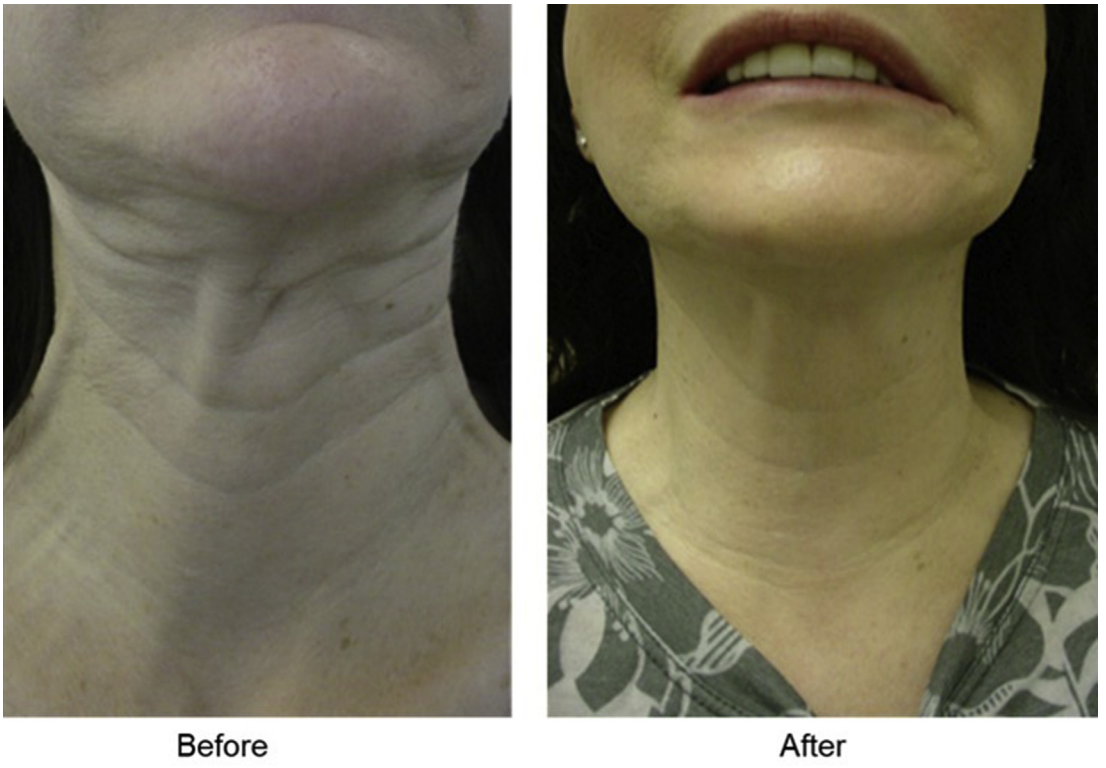

Fig. 10. Note the diminution of platysmal bands 1 month after injections of onabotulinumtoxinA. (*Copyright 2018 From* Benedetto AV. Cosmetic uses of botulinum toxin A in the lower face, neck, and upper chest. In: Benedetto AV, ed. Botulinum Toxins in Clinical Aesthetic Practice Volume Two: Functional Anatomy and Injection Techniques. 3rd ed, Boca Raton: CRC Press, 2018: 286; with permission. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.)

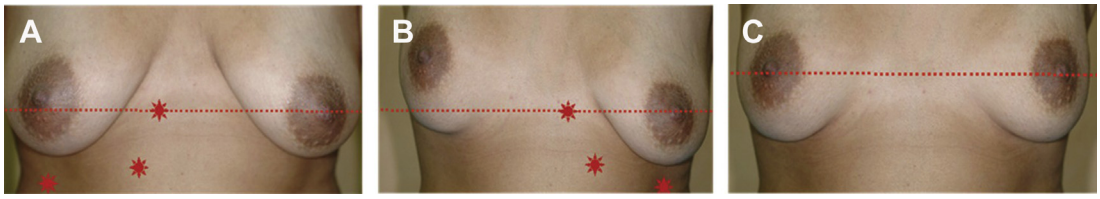

Fig. 11. Before (*A*) and 2 weeks after (*B*) 45 U of onabotulinumtoxinA injected in the right pectoralis. (*C*) One month after right pectoralis injection and 2 weeks after left pectoralis was injected with onabotulinumtoxinA. Note the 1.8-cm elevation of both breasts after treatment. (*Copyright 2018 From* Benedetto AV. Cosmetic uses of botulinum toxin A in the lower face, neck, and upper chest. In: Benedetto AV, ed. Botulinum Toxins in Clinical Aesthetic Practice Volume Two: Functional Anatomy and Injection Techniques. 3rd ed, Boca Raton: CRC Press, 2018: 296; with permission. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.)

Their therapeutic product (EB-001T) is being developed to treat surgical and nonsurgical pain by decreasing muscle hyperactivity and spasms. The first of their two therapeutic clinical trials LANTERN-1 (Long-Acting NeuroToxin-E Relief, Non-opioid-1) is a placebo-controlled, double-blind, ascending dose cohort trial to evaluate the safety and efficacy of EB-001T injected intramuscularly in subjects undergoing elective augmentation mammaplasty. EB-001T showed favorable safety results and was well tolerated in a wide dose range without reaching a maximum tolerated dose. The highest EB-001T dose tested in LANTERN-1 was eight-fold higher than the maximum dose in their successful glabellar frown lines study. LANTERN-1 was pivotal in establishing a safe dose range for use in larger muscles. LANTERN-2 is a randomized, placebo-controlled, ascending dose, double-blind clinical trial to evaluate the safety and efficacy of treating focal muscle pain with a single intramuscular injection of EB-001T administered intraoperatively into the large rectus abdominis muscle in subjects undergoing elective abdominoplasty with plication of the rectus abdominis sheath. The primary end point is a reduction of postoperative pain at rest as measured by the Numeric Pain Rating Scale over the first 96 hours. Secondary end points include Numeric Pain Rating Scale scores during activity and patient use of rescue medications, including opioids, to address unrelieved pain. Bonti predicts their BoNT-E will be an effective,

Table 2
Major BoNT brands available worldwide for aesthetic use

Product	Company	Country	Bacterial Production Strain	Process	U/Vial (Product Specific)[a]	Excipients (in Vial)
Dysport/ Dyslor/ Azzalure	Ipsen/ Galderma	France/ Switzerland	Hall NCTC 2916	Precipitation, dialysis, chromatography	125/300/350	0.125 mg HSA 2.5 mg lactose
Botox/Botox Cosmetic/ Vistabel/ Vistabex/ Vista	Allergan Plc	United States/ Ireland	Hall-hyper	Acid precipitations, dialysis	50/100/200	0.5 mg HSA 0.9 mg NaCl
Xeomin/ Xeomin Cosmetic/ Bocouture	Merz GmbH	Germany	Hall ATCC 3502	Unknown	50/100/200	1 mg HSA 4.7 mg sucrose

Note: All products are either freeze dried (Dysport and Xeomin families) or vacuum-dried (Botox family).
Abbreviation: HAS, human serum albumin.
[a] The potency units of each product are specific to that product and are not interchangeable with those for other BoNT products.
Courtesy of Pickett A, PhD, Wrexham, UK.

Table 3
Topical BoNT being developed worldwide

Company	Country	Product Name	Technology	Clinical Data Published	Comments
Revance Therapeutics, Inc	United States	RT001	TransMTS	Yes	Moved RT001 into preclinical studies
Transdermal Corp	Canada	CosmeTox	InParT (mixed micelles/ionic nanoparticles	Yes	
Anterios, Inc Allergan Plc	United States	ANT-1207 Lotion	Unknown	No	Company purchased by Allergan, PLC (January 2016)
Malvern Cosmeceuticals, Ltd	UK	MCL005	Unknown	No	

Courtesy of Pickett A, PhD, Wrexham, UK.

Table 4
Approved BoNT products from Asia as of early 2017

Product	Company	Country	Bacterial Production Strain	Process	U/Vial (Product Specific)	Excipients (in vial)[a]
BTXA/ Prosigne/ Redux/ Lantox/ Lanzox	Lanzhou Institute of Biological Products/Hugh Source Int'l	China	Hall-hyper	Crystallization, dialysis	50/100 U	5 mg gelatin 25 mg dextran 25 mg sucrose
Meditoxin/ Neuronox/ Siax/ Botulift/ Cunox	Medytox Inc	South Korea	Hall-hyper	Acid precipitations, dialysis	50/100/ 200 U	0.5 mg HSA 0.9 mg NaCl
Innotox/ MT10109 L (liquid product)	Medytox Inc	South Korea	Hall-hyper	Unknown	25/50 U	No HSA or animal products
Coretox/ MT10107 (naked toxin, no neurotoxin-associated proteins)	Medytox Inc	South Korea	Hall-hyper	Unknown	100 U	Methionine; polysorbate-20; sucrose
Botulax/ Zentox/ Regenox	Hugel Pharma	South Korea	CBFC26	Protamine sulfate diethylamino-ethanol sepharose chromatography	50/100/ 200 U	0.5 mg HSA 0.9 mg NaCl
Nabota/ Evosyal (DWP 450)	Daewoong Pharamceutical Co Ltd	South Korea	Hall?	High-Pure Technology (patented)	100 U	0.5 mg HSA 0.9 mg NaCl

Abbreviation: HAS, human serum albumin.
[a] Concentrations of excipients may depend on the number of units in vial.
Courtesy of Pickett A, PhD, Wrexham, UK.

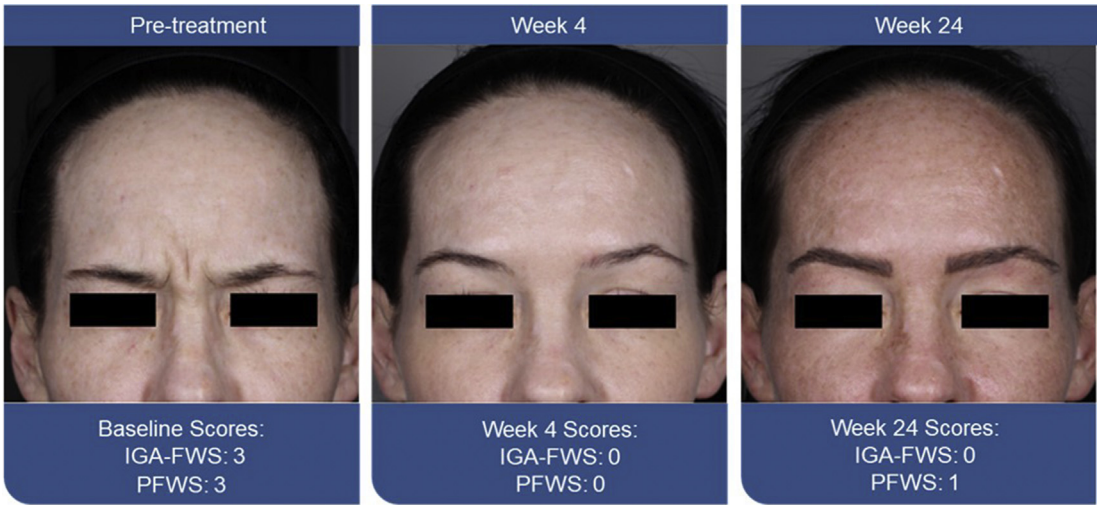

Fig. 12. A Revance study patient before and after treatment with daxibotulinumtoxinA with a three-point improvement by IGA-FWS and PFWS at Week 4 and a three-point sustained duration of effect by IGA-FWS over 24 weeks. IGA-FWS, Investigator Global Assessment Frown Wrinkle Severity; PFWS, Patient Frown Wrinkle Severity.

long-acting, nonopioid treatment of focal musculoskeletal pain, regardless of cause, which should help reduce the current demand for and abuse of opioids.

Lastly, there is a new BoNT-A under investigation for aesthetic and therapeutic use called daxibotulinumtoxinA. Produced by Revance Therapeutics (Newark, CA), it is free of accessory proteins and has a molecular weight of 150 kDa. It contains no human serum albumin or other human- or animal-derived components but contains a proprietary stabilizing excipient peptide (RTP004) that is cationic and binds to the BoNT-A molecule. Final results of their phase 3 pivotal studies, including the open label safety study, are about to be released. Preliminary results seem to indicate that patients with moderate to severe glabellar lines demonstrated a median duration of wrinkle reduction of 6 months on multiple clinically meaningful outcome measures (**Fig. 12**). Both phase 3 studies with 40 units of daxibotulinumtoxinA met their primary end point of a 2-point composite response at Week 4 and demonstrated duration of effect at more than 24 weeks. Time to return to baseline wrinkle severity, as assessed by patient and independent physician observer, exceeded 6 months and lasted up to 9 months in some subjects. Results of the clinical trials indicated that no study patient discontinued their treatment because of any adverse event.

The evolving field of cosmetic dermatology is only at the threshold of a vast array of promising innovations. Dermatologists should look to the future and eagerly embrace novel developments for the sake of improving their patients' quality of life. Reexamining antiquated therapeutic modalities is the obligation of every physician, regardless of specialty. The implementation of new treatments, such as replacing petrolatum-based products with silicone gel for more effective postoperative wound care, ablating already atrophic vaginal mucosa to regenerate glycogen-rich epithelial cells, or using a botulinum toxin to relieve pain and prevent scars, may all sound counterintuitive or even preposterous. But when evidence proves otherwise, physicians should feel reassured to incorporate such unlikely therapeutic modalities into their daily armamentarium.

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