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Botulinum Toxins in Clinical Aesthetic Practice

Volume 2: Functional Anatomy and Injection Techniques

Third Edition

Edited by **Anthony V. Benedetto**

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Series in Cosmetic and Laser Therapy

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To Dianne, my loving wife of forty years, whose encouragement and support permitted me to accomplish that which seemed at times insurmountable and unattainable.

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Preface

Because of the exponential developments in the clinical use of botulinum toxins (BoNTs), the need for a third edition quickly became a foregone conclusion. Maintaining the original mission of an instructional manual, this completely revamped and updated third edition attempts to record the phenomenal progress that has evolved in the use of BoNTs in clinical medicine over the past seven years. Updates of the literature, expanded indications, improved clinical photographs and illustrations, and newer and innovative ways to utilize the different BoNTs that are presently available worldwide are presented in this newly formatted third edition. It also has become strikingly obvious that BoNTs are injected in a variety of novel ways that differ from East to West. Therefore, a concerted effort has been made to include a profile of as many of the different BoNTs currently available around the world, including how they are utilized in a clinical aesthetic setting in both Western and Eastern cultures.

In the United States, glabellar and lateral canthal lines remain the only areas of the face that are approved by the FDA for the cosmetic use of onabotulinumtoxinA (OnaBTX-A) or BOTOX® Cosmetic. The other BoNTs available in the United States, abobotulinumtoxinA (AboBTX-A), incobotulinumtoxinA (IncoBTX-A), and rimabotulinumtoxinB (RimaBTX-B), have their own similar, but very specific, FDA indications. Consequently, except for glabellar and lateral canthal wrinkles, all the cosmetic injection techniques described in this third edition, as in the previous editions, apply to non-approved, off-label indications, which makes this book unlike most other textbooks in medicine.

It is sobering to realize that throughout human existence women and men have always sought ways to improve their appearance. To commence the in-depth and diverse discussions in this third edition on beautification and rejuvenation with BoNTs, Nina Jablonski, PhD, professor of anthropology at The Pennsylvania State University, and a world-renowned biological anthropologist and paleobiologist, provides us in her Prologue with a brief introduction to the evolutionary and anthropological perspectives on the importance of human facial attractiveness and expressivity. She cautions both patients and treating physicians in the over-use of face altering procedures that can effectively inhibit one's ability to express oneself accurately and in a completely natural manner.

Chapter 1 is written by Jean Carruthers, MD, to whom the world is indebted for her prescient identification of the cosmetic uses of the BoNTs. Dr. Jean Carruthers commences our venture through the fascinating evolving world of the BoNTs by presenting a historical account of the chronological events that led to the discovery, identification, isolation, and eventual synthesis of BoNTs for clinical use. Included is her seminal work in the development and advancement of the clinical uses of BoNT-A in ocular therapeutics, and her serendipitous discovery of its cosmetic properties. Jean describes the role she and her dermatologist husband, Dr. Alastair Carruthers, played in their provocatively sensitive introduction and promotion of the cosmetic uses of BoNT-A to the medical community.

Updates on the current advancements in the pharmacology and immunology of the different BoNTs are discussed by world-renowned scientists who are intimately involved in BoNT research and development. These include Chapter 2 by Mitchell F. Brin, MD, neurologist and one of the earliest clinical injectors of OnaBTX-A and now senior vice president of global drug development and chief scientific officer of BOTOX®, at Allergan Inc. (Irvine, CA). He presents an update on the pharmacology, immunology, recent developments, and future predictions on the use of BoNT-A. Chapter 3 by Juergen Frevert, PhD, head of botulinum toxin research at Merz Pharmaceuticals GmbH, (Potsdam, Germany), discusses the innovative pharmacology and immunology of a noncomplexed BoNT-A, and the advantages of its clinical uses.

Chapter 4 by the visionary dermatologist, Richard Glogau, MD, discusses the fascinating emerging science, development, and effective clinical uses of a new topically applied BoNT-A. Chapter 5 by Gary Monheit, MD, a dermatologist and leader in BoNT clinical research, and dermatologist James Highsmith, MD, elaborates on the recent advances of the different FDA approved BoNT-As and BoNT-B with updates on the pertinent literature and details on recent developments in their clinical use. Chapter 6 by Andy Pickett, PhD, Senior Program Leader & Scientific Expert, Neurotoxins for Galderma Aesthetic and Corrective, and Director and Founder of Toxin Science Limited, Wrexham, UK, identifies some of the different BoNTs used in clinical practice currently available in other parts of the world.

Chapter 7 by Alastair and Jean Carruthers, MD, presents updated and advanced clinical information on the adjunctive uses of the BoNTs in conjunction with injections of soft tissue fillers, and light- and energy-based devices for the aesthetic improvement of the face and body.

In Chapter 8, Arthur Swift, MD, an otorhinolaryngologist, Kent Remington, MD, a dermatologist, and Steve Fagien, MD, an ophthalmologist, add a new dimension to the aesthetic interpretation of how to use injectables when rejuvenating the face, change to including their explanation of facial proportions, geometrical Phi measurements, aesthetics, and beauty as they relate to the use of BoNTs.

For Chapter 9, dermatologists David Pariser, MD, and DeeAnna Glaser, MD, Secretary and President, respectively, of the International Hyperhidrosis Society, have comprehensively revised and updated the material on hyperhidrosis, discussing recent developments as well as new and different areas of treatment.

Chapter 10 by dermatologist Kevin C. Smith, MD, the master of novel injection techniques, along with dermatologists Irèn Kossintseva and Benjamin Barankin continues to enlighten us on unique ways to utilize BoNT-A for cosmetic and therapeutic purposes.

Chapter 11 by dermatologist and attorney David Goldberg, MD, JD, concludes the first volume with a revision and update of his chapter on the important medicolegal aspects of the cosmetic uses of BoNT.

Because of the ever-growing selection of the various BoNT products currently commercially available for clinical use in different parts of the world, the new Appendix 1 written by dermatologist Alica Sharova, MD, PhD, of Pirogov Russian National Research Medical University, Moscow, presents thought-provoking results of her metanalysis comparing consensus statements and recommendations for injecting different BoNT products in the United States, Russia, and different countries in Europe. She identifies and compares the fallacious recommendations of dose ratio equivalencies of the different available BoNTs injected, including number of injection points and dosaging for the different areas of the face and neck in males and females.

In the second volume, Sebastian Cotofana, PhD, a quintessential anatomist, has provided essential new material on functional facial anatomy in Chapter 12.

The nuclear Chapters 13, 14, and 15 on the cosmetic treatment of the face, neck, and chest with injections of BoNTs have been reorganized and expanded, assimilating many improved injection techniques by integrating updated information of recently published clinical and anatomical studies. All the anatomical figures and illustrations have been revised and enhanced throughout the text. The organization of these three chapters has remained the same. Each clinical topic is subdivided according to its facial and functional anatomy, and discussed in seven subheadings. The "Introduction" of each topic identifies the different anatomical changes acquired by men and women as they "age" and develop "wrinkles." Normal "Functional Anatomy" discusses the reasons these disconcerting changes and wrinkles occur so that a suitable plan of correction with a BoNT can be initiated. Functional anatomy is stressed and complemented by clinical photographs and detailed illustrations because the only way a physician injector can utilize any type of BoNT properly is to have an in-depth understanding of how to modify the normal and exaggerated movements of facial mimetic muscles and other potentially treatable muscles elsewhere in the body. When injections of a BoNT are appropriately performed, desirable and reproducible results without adverse sequelae are created. In the "Dilution" subheading, suggestions are given on how much diluent can be added to reconstitute a 100-unit vial of OnaBTX-A in order to arrive at various preferred concentrations per fluid volume dilutions when injecting certain muscles at different anatomical sites. The U.S. FDA-approved manufacturer's recommendation for the reconstitution of a 100-unit vial of OnaBTX-A is to add 2.5 mL of nonpreserved normal saline. This approved and recommended dilution is for injecting glabellar and lateral canthal frown lines only, since these areas on the face are the only approved indications for the cosmetic use of OnaBTX-A. However, when treating other areas of the face and body for cosmetic purposes, albeit in an off-label, unapproved manner, higher or lower dilutions of OnaBTX-A have proven to be more suitable and clinically more effective, depending on the muscles being treated. Options for "Dosing" are presented, with an emphasis placed on what to do and what not to do when injecting OnaBTX-A. Precise dosing and accurate injections of OnaBTX-A will diminish muscle movements of the face and body in a safe and reproducible way. Fastidious injection techniques are necessary to correct a particular aesthetic problem reliably, predictably, and for extended periods of time with any BoNT. "Outcomes" and results of different injection techniques are discussed to avoid "Complications" and adverse sequelae. Finally, how to inject a particular anatomical site and its projected results are summarized in the list of "Implications of Treatment".

Controversial and remarkable treatments for non-surgical breast augmentation for women and men are practiced by dermatologists Francisco Atamoros Perez and Olga Marcias Martinez and discussed in detail in Chapter 16. Their accumulated clinical evidence of the efficacy of BoNT-A injections of the pectoral area is clearly presented with an abundance of clinical illustrations.

Chapter 17, by a prominent and internationally well-known Korean dermatologist, Kyle Seo, MD, discusses the Asian perspective of the use of the different BoNTs currently available in his part of the world. Insight into the East and Southeast Asian cultural aesthetic needs and the Asian perception of aesthetics and beauty, is emphasized. He also presents a detailed description of the racial differences in the anatomy between Asians and Caucasians, which call for different indications and variations in appropriate dosing and injection points of BoNT-A treatments, necessary when treating Asian patients. He also provides some practical guidelines for the innovative use of BoNT-A in facial skin redraping and body muscle contouring injection techniques that are currently very popular in the East.

Many appendices supplying material for procedural reference conclude this second volume.

It is extremely fascinating and encouraging to understand that the cosmetic use of OnaBTX-A was initiated by the insight and convictions of two astute and courageous physicians, an ophthalmologist wife and her dermatologist husband. If it were not for the persistence of Jean and Alastair Carruthers in promoting their serendipitous observations, many other perceptive and insightful physicians would not have had the opportunity or the confidence to learn more about BoNT and its use in clinical aesthetic medicine. The challenge now being passed onto the reader is that with knowledge of how to inject a few drops of BoNT appropriately and safely, while treating patients with compassion and professionalism, additional innovative and ingenious uses of BoNT can be discovered, be they for cosmetic or therapeutic purposes.

We are all indebted to those physicians who have treated and continue to care for patients with BoNT for therapeutic and cosmetic purposes. Their commitment to the improvement of their patients' health and well-being through the advancement of sound and effective medical care is commendable and truly appreciated.

Finally, particular recognition and a special expression of gratitude is due to Kelly Heckler for her organizational skills and secretarial expertise that facilitated the completion of this book.

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Many of the anatomical drawings not otherwise attributed (e.g., Figure 10.1) have base artwork from the Shutterstock archives and are reproduced with permission under licence; the annotations and overlays have been developed by the lead author of each chapter.

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12 Functional facial anatomy, proportions of beauty, and neuromodulation

Sebastian Cotofana

DEVELOPMENT

The muscles of facial expression are derived from the second pharyngeal arch during embryologic development and thus receive their motor innervation from cranial nerve VII, the facial nerve. The primary function of these muscles is to protect the facial orifices and the organs located in their proximity from mechanical damage (orbicularis oculi), from ingestion of harmful substances (orbicularis oris), and to aid the uptake of food (levator anguli oris, levator labii superioris, depressor anguli oris, and depressor labii inferioris muscles) and air (nasalis, levator alaeque nasi, depressor septi nasi muscles). Previously important muscles for the movement of the ears, which were used, for example, during hunting or defense, can be still found as rudiments (e.g., the auricularis muscles).

During phylogenetic development, however, these muscles are progressively involved in the externalization of internal conditions and feelings (lat.: movere = emotions [= to move something out]), that is, for the expression of emotions. This was increasingly used for communication between individuals and for the coordination of social groups. A study in chimpanzees has shown[1] that the size of facial motor nucleus can be positively correlated to the group size and to the amount of time spent grooming, that is, social activity; indicating that the role of the facial muscles has been changed from rudimentary needs (food uptake and breathing) towards social interaction and group coordination. With the development of speech another important function of the muscles of facial expression was established: articulation. The perioral muscles are crucial in the formation of sounds due to their movement of the lips. These developments should be considered when trying to interfere with their primary function and effects of applied treatments should be also seen in the light of phylogenetic development. (See Prologue by N Jablonski in Volume 1.)

GENERAL FUNCTION

The muscles of facial expression are unique in their morphology as well as in their function. Regarding their macroscopic and histologic characteristics, muscles of facial expression do not contain an enveloping fascial layer, that is, epimysium, like most of the muscles in the human body. The absence of an epimysium enables these muscles to have a strong interaction with their surrounding tissues as no gliding plane is present, as opposed to having a gliding plane which reduces shear forces between neighboring structures for a frictionless and energy-efficient movement. Due to the strong interaction of the facial muscles with their surrounding tissues, distinct muscular contractions result in a minute movement of the neighboring tissues and most importantly the overlying skin. This is important for the delicate positioning of the skin during facial expressions and minute differences in contraction can result in an almost opposite effect, for example, smiling versus expression of disgust.

Another morphologic characteristic of these muscles is that they do not insert to bones, ligaments, or span joints to produce movements important for locomotion. They rather insert into the overlying skin or are of circular shape with origin and insertion being closely related. Therefore, the actions of the mimetic muscles cannot be described according to the general anatomic standards, that is, extension/flexion or abduction/adduction, but by elevation/depression with vertical, horizontal or diagonal movements resulting in facial expression on contraction.

Interestingly, histologic investigations have suggested that the muscles of facial expression have a reduced quantity of stretch receptors (as compared to regular skeletal muscles) and thus some authors have suggested that this is one of the reasons why the muscles of facial expression present with flaccid paralysis after a stroke rather than with spasticity. Recent studies revealed also that with aging the muscles of facial expression increase their muscular tone and have thus a reduced contractility. Facial exercises or the application of facial muscular training devices were less effective.[2]

ACTION MECHANISMS OF BOTULINUM TOXIN

The muscles of facial expression are classified as striated muscle fibers and are organized histologically by sequentially arranged subunits called the sarcomeres. Each sarcomere is formed by thin and thick myofilaments and receives its depolarizing signal from a cholinergic neuromuscular synapse. The ratio of recruited muscle fibers by one single lower motor neuron is 1: <100 whereas this ratio is 1: >1000 for thigh or back muscles. In regular neuromuscular transmission, an action potential is transmitted distally to the axon terminal, where neurotransmitter molecules (here acetylcholine) are stored in vesicles. On ion shift in the axon terminal, synaptic vesicles fuse with the presynaptic membrane and the vesicles' contents are released into the synaptic cleft. On the postsynaptic plate, specific receptors are present with the ability to bind the released neurotransmitter molecules and to generate a new postsynaptic potential which is then distributed across the muscle fiber and ultimately leads to muscle contraction.

The mechanism of vesicle fusion in the axon terminal requires the binding of SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) proteins that are expressed on both the vesicle (V-SNARE) and on the inner side of the presynaptic membrane (T-SNARE). Binding of these proteins to one another induces their fusion and the release of the vesicles' content into the synaptic cleft. Without the binding of the V-SNARES to the T-SNARES, the vesicles will not fuse with the presynaptic membrane resulting in a persistent but reversible inhibition of neurotransmitter release.

Botulinum toxins (BoNT) are the most potent toxins known to humankind: the lethal dose for humans is 1 μg/kg by the oral, 10–13 ng/kg by inhalation, and 1–2 ng/kg by the intravenous or intramuscular routes. In detail, these toxins consist of a heavy chain and a light chain and there are seven known serotypes (A–G) of which toxin A (BoNT-A) is used in the majority of cosmetic procedures. The toxin light chain will cleave both the V-SNARES and the T-SNARES leading to a temporary flaccid paralysis as the incoming signal cannot be transmitted via the synaptic cleft to the muscle fiber.[3]

The application of BoNT-A in the proximity of a muscle will lead to the binding of the botulinum toxin to specific receptors at the presynaptic axon terminal of the supplying nerve, internalization of the toxin into the axon, and activation of its endopeptidase activity against the V- and T-SNARE proteins. Thus, BoNT-A applications have to be applied locally and in proximity to the intended muscle in order to induce the blockage of its neuromuscular transmission. After intramuscular injection, the dose-dependent paralytic effect of BoNT can be detected within 2–3 days. It reaches its maximal effect in less than 2 weeks, lasts somewhere between 3 and 6 months and gradually begins to decline in a few months due to the ongoing turnover of synapses at the neuromuscular junction.[4]

GENERAL FACIAL ANATOMY

The anatomy of the face can be best described as a layered concept. This concept is based on the fact that facial structures are arranged in specific layers, that is, in a specific depth within the face with the surrounding structures providing rigid or soft boundaries. From superficial to deep these layers are: skin (layer 1), superficial (subcutaneous) fat (layer 2), superficial musculo-aponeurotic system (SMAS) (layer 3), deep fat (layer 4), and deep fascia/periosteum (layer 5). Once this concept is taken into consideration the third dimension is accessible and the question: "*Where is the muscle?*" is not precise enough to target the respective muscle during treatment. Moreover, the additional question: "*In which layer is the muscle?*" must be answered to achieve the best possible outcome for botulinum toxin applications.

Having in mind that the facial musculature (like any other structure in the human body) is prone to variations in location, size, and course, individualized application patterns are of crucial importance. Rigid applications "according to the book" are outdated and individualized application schemes need to be applied. Facial wrinkles, independently if dynamic or static, are to be understood as muscular contractions of underlying muscles (accompanied by social, environmental, and demographic influences) and that the vector of contraction is perpendicular to the observed facial wrinkle.

MOTOR BRANCHES OF THE FACIAL NERVE

The motor component of the facial nerve emerges at the stylomastoid foramen at the base of the skull and enters the parotid gland from deep and posterior. Within the parotid gland the nerve divides into 3–7 branches and its divisions are called parotid plexus. At the anterior boundary of the parotid gland the nerve emerges between the superficial and the deep part of the parotid gland and its branches course toward the temple (temporal branches), in proximity to the zygomatic arch (zygomatic branches), horizontally across the cheek (buccal branches), along the inferior margin of the mandible (marginal mandibular branches) and inferiorly and anteriorly toward the neck (cervical branches) (Figure 12.1). The branches are deep to layer 5, that is, deep to the parotideomasseteric fascia at the level of the masseter muscle, but change planes toward superficial at the level of the anterior boundary of the masseter muscle. There the branches can be identified superficial to the facial vein and within the roof of the facial-vein canal. From there they distribute toward the respective muscles of facial expression and provide motor supply by entering into the muscles from inferior and posterior.

In the temporal region, the temporal branches can be located within layer 4, that is, deep to the superficial temporal fascia but superficial to the deep temporal fascia; superior to zygomatic arch and inferior to the inferior temporal septum.

In the midface, the branches are located deep to the superficial musculo-aponeurotic system (SMAS).

In the lower face, the marginal mandibular branch can be identified in 100% of the cases superficial to the facial artery and vein when crossing the mandible.

ARTERIES OF THE FACE

The face is primarily supplied by branches of the external carotid artery and only in minor parts (e.g., the upper face) by branches of the internal carotid artery. The major supplying arteries of the external carotid artery are: the facial artery, transverse facial artery, buccal artery, lingual artery, superficial and deep temporal arteries. Branches of the internal carotid artery are zygomaticofacial artery, zygomaticotemporal artery, dorsal nasal, supraorbital artery, supra- and infratrochlear artery, and medial and lateral palpebral arteries. One must be aware that the arteries display a huge variation in terms of course and presence as compared to facial veins (Figure 12.2).

The facial artery courses anterior to the facial vein and can be identified within the buccal space after crossing the mandible. At the angle of the mouth the artery is connected to the modiolus via muscular and ligamentous adhesions and lies deep to the muscles of facial expression but superficial to the buccinator muscle. After giving off the superior labial artery, the name of the vessel changes toward the angular artery. The angular artery gives off branches to anastomose within the SMAS with branches of the transverse facial artery which accesses the SMAS via the McGregor's patch. The angular artery courses in the depth of the nasolabial sulcus medially and superiorly within the deep pyriform space. Deep to the levator labii superioris alaequae nasi muscle it courses superiorly at the lateral margin of the nose, gives off connecting branches to the infraorbital arteries, and pierces in general the orbicularis oculi muscle around the medial canthus. There it connects with branches from the supratrochlear, dosal nasal, medial palpebral, and supraorbital arteries.

The upper lip is supplied by the superior labial artery whereas the inferior lip receives arterial blood supply from the inferior labial artery, the horizontal mental artery, and from the mental artery.

In the temporal region, an anterior and a posterior branch of the superficial temporal artery can be identified. The superficial temporal artery emerges from the depth 1 cm anterior and 1 cm superior from the tragus and courses imbedded within the superficial temporal fascial toward the temple.

VEINS OF THE FACE

The veins of the face are in course and variation much more stable than the facial arteries and thus can serve as excellent landmarks (Figure 12.2). The blood flow is in general directed as the facial venous vessels have valves with the exception of the angular vein. Here the blood flow is not directed and thus venous blood can drain both superiorly toward the superior ophthalmic and into the cavernous sinus or inferiorly toward the facial vein and into the external jugular vein. The facial vein crosses the mandible posteriorly to the facial artery and deep to the marginal mandibular branch. It enters the facial-vein canal, which is formed by the anterior and the posterior lamina of the parotideomasseteric fascia. The vein is found anterior to the masseter muscle where it gives off the inferior and superior labial vein and the deep facial vein, which drains into the pterygoid plexus. The vein can be identified anteriorly to the parotid duct, deep to the facial nerve branches, deep to the zygomaticus major muscle, and lateral to the infraorbital foramen. At this level, the vein courses more superficial and can be found superficial to the levator labii superiors alaeque nasi muscle and forms there the lateral boundary of the deep nasolabial fat compartment. It also has connections to the infraorbital veins at this level. The angular vein then courses medially and forms the medial boundary of the deep lateral cheek fat and of the suborbicularis oculi fat (SOOF). The distance between the inferior orbital rim and the vein was measured to be in mean 4 mm and this course corresponds to the nasojugal groove which represents the inferior boundary of the tear trough. It is important to note that the vein courses inferior to the tear trough and deep to the orbicularis oculi muscle and only at the level of the medial canthus does it change toward a more superficial position. There it connects with the dorsal nasal, the supra- and infratrochlear, the supraorbital and the central forehead veins.

FACIAL MUSCLES

Upper Face Region (Figure 12.3) (See Appendix 2)

Frontalis muscle

Origin: Epicranial aponeurosis

Insertion: Orbicularis oculi muscle complex

Innervation: Temporal branches of facial nerve
Vascularization: Supraorbital artery, supratrochlear artery, lacrimal artery, anterior branch of the superficial temporal artery
Function: Elevation of the supraorbital skin and eyebrow
Depth: Layer 3
Characteristics: The muscle is the anterior part of the occipitofrontalis muscle. Together with the temporoparietalis muscle, this muscle complex is also called epicranius muscle. Approximately 2–3 cm superior to the upper margin of the superior orbital rim the muscle is connected to the periosteum via the middle frontal septum. Movements of the overlying skin during muscle contraction converge toward this septum. Interestingly, the location of this septum correlates well with the location of the central forehead line, that is, the deepest horizontal forehead wrinkle. In some individuals, wavy (as opposed to straight) forehead lines can be observed. This is due to an increased muscle fascicle angle and due to the presence of a midline aponeurosis. Histological analyses have revealed that even in the midline aponeurosis muscle fibers can be identified, underscoring the importance of central neuromodulator applications.

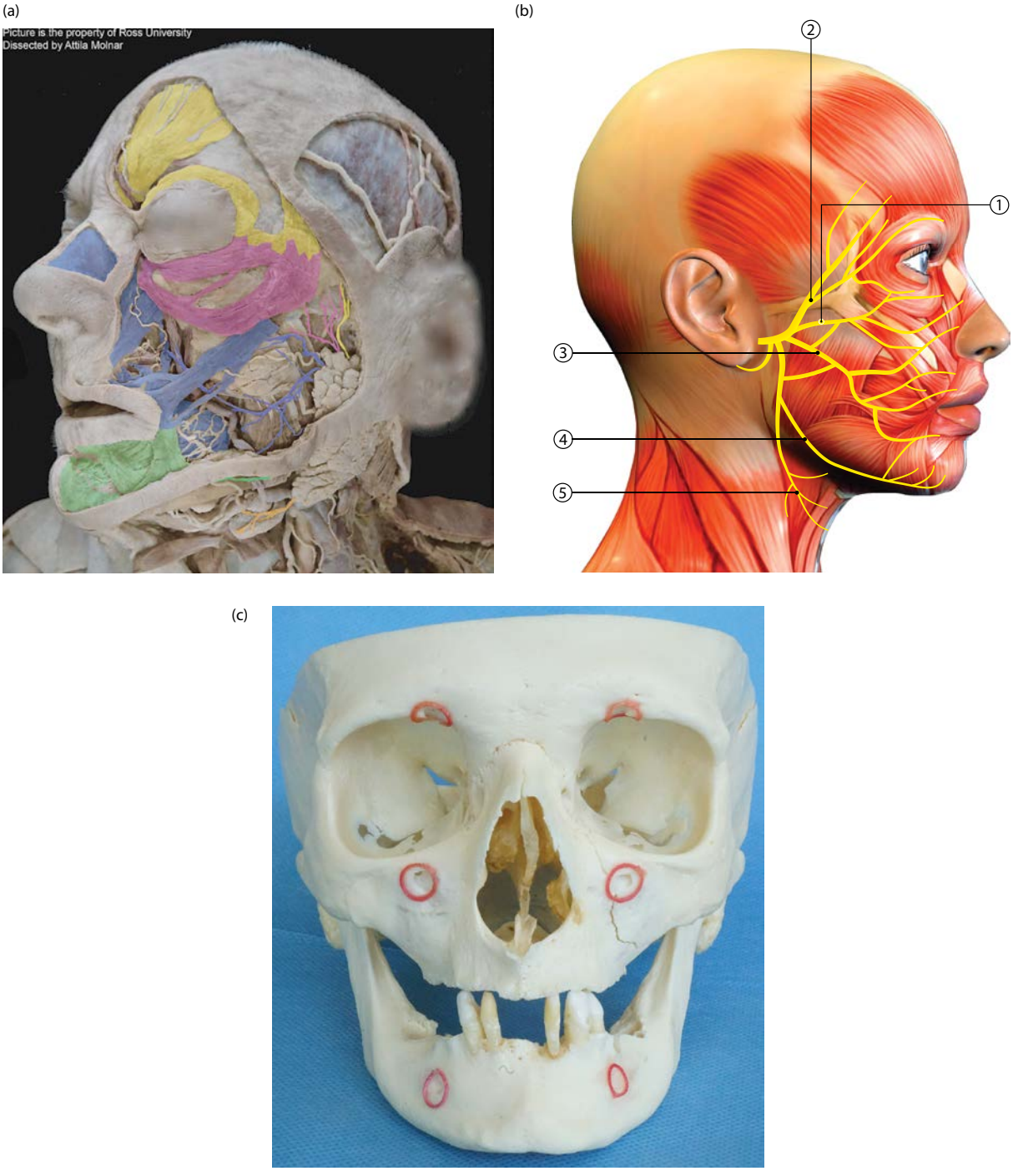

Figure 12.1 Nerves of the face. (a) Dissection. (b) The facial nerve, five motor branches: 1, zygomatic; 2, temporal; 3, buccal; 4, marginal mandibular; 5, cervical. (c) The trigeminal nerve, sensory branches (each emerging from the corresponding foramen): 1,supraorbital; 2,infraorbital; 3,mental. ([a] Courtesy of Ross University; dissection by Attila Molnar.)

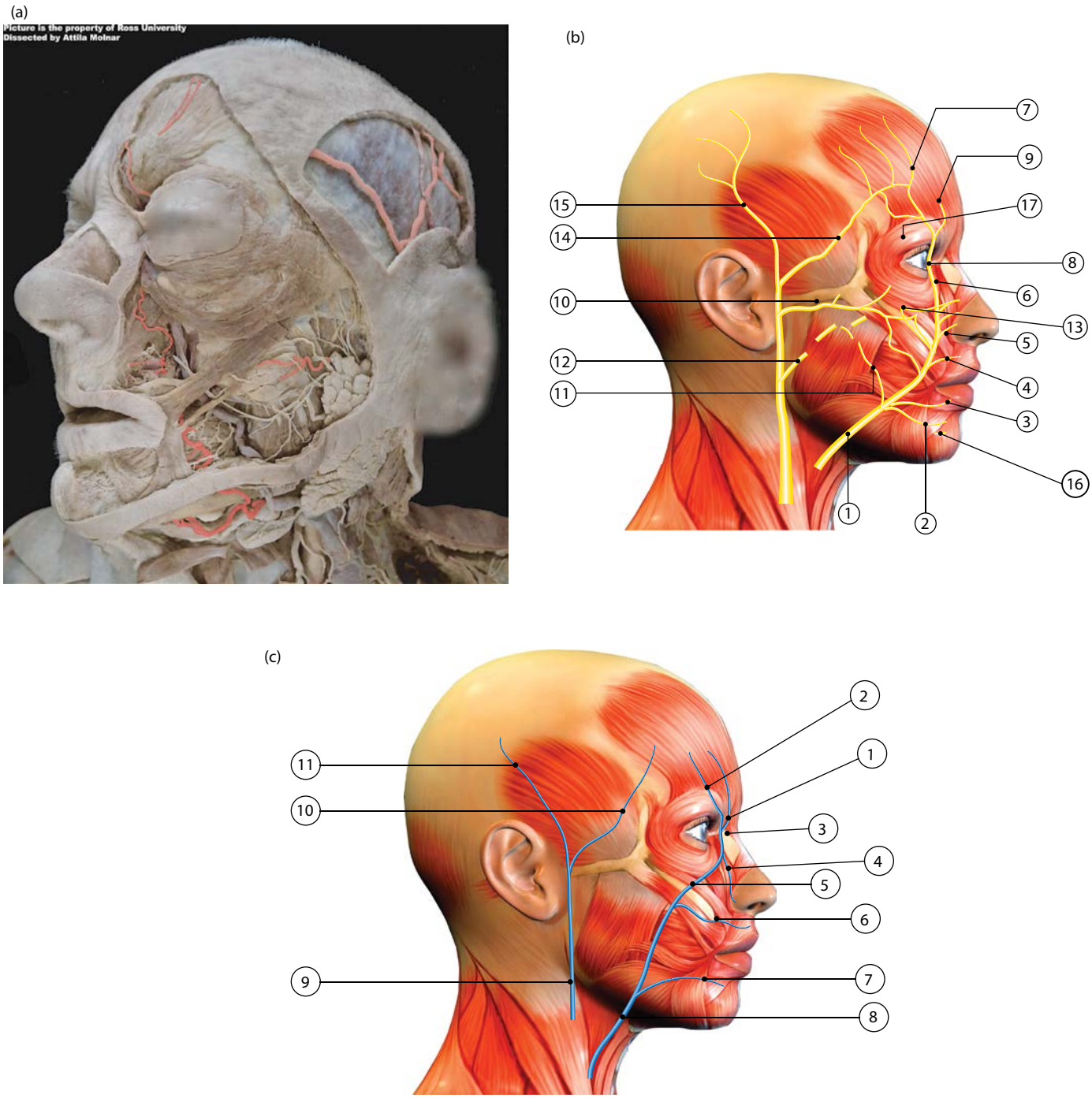

Figure 12.2 Arteries and veins of the face. (a) Dissection. (b) Arteries: 1, facial; 2, horizontal mental; 3, inferior labial; 4, superior labial; 5, alar branch of facial artery; 6, angular; 7, supraorbital artery; 8, dorsal nasal; 9, supratrochlear; 10, transverse facial; 11, lingual; 12, maxillary; 13, infraorbital; 14, anterior branch of superficial temporal artery; 15, posterior branch of superficial temporal artery; 16, mental; 17, infratrochlear. (c) Veins: 1, central forehead; 2, supraorbital; 3, dorsal nasal; 4, lateral nasal; 5, angular vein; 6, superior labral; 7, inferior labial; 8, facial; 9, retromandibular; 10, anterior branch of superficial temporal vein; 11, posterior branch of superficial temporal vein. ([a] Courtesy of Ross University; dissection by Attila Molnar.)

Orbicularis Oculi Muscle

Origin: Frontal process of the maxilla, anterior lacrimal crest, medial palpebral ligament

Insertion: Lateral palpebral ligament, lateral palpebral raphe

Innervation: Temporal branch of facial nerve, zygomatic branch of facial nerve

Vascularization: Facial artery, anterior branch of superficial temporal artery, supraorbital artery, lacrimal artery, supra- and infratrochlear artery, infraorbital artery

Function: Closure of the eye lids, depression of the eyebrow, drainage of lacrimal fluid

Depth: Layer 3 (Change of layer in the medial canthus—described as Horner's muscle at this point)

Characteristics: The orbicularis oculi muscle consists of an orbital part, septal part and a preseptal part. The latter is described as Horner's muscle at the medial canthus and facilitates the drainage of the lacrimal sack. The differentiation between the orbital and septal part is represented by the orbital margin and the separating

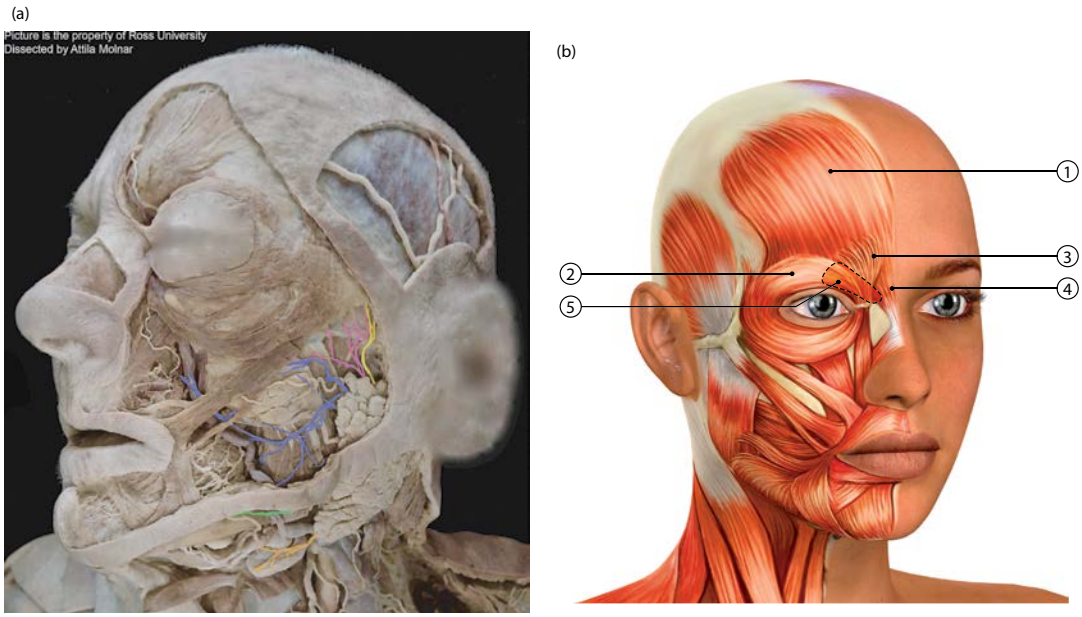

Figure 12.3 Muscles of the upper face. (a) Dissection; (b) muscles: 1, frontalis; 2, orbicularis oculi; 3, depressor supercilii; 4, procerus; 5, corrugator supercilii (deep to orbicularis oculi). ([a] Courtesy of Ross University; dissection by Attila Molnar.)

structure there is the orbicularis retaining ligament. The orbital part, however, can reach laterally and inferiorly into the midface and in dedicated cases muscular distentions (Figure 12.3) are identified, where fat from deeper structures can protrude. The laterally observed contraction at the level of the lateral canthus—also called "Crow's feet"—are arranged in perpendicular orientation to the muscular contractions in this area.

Depressor Supercilii Muscle
Origin: Frontal process of the maxilla
Insertion: Skin in the medial third of the eyebrow and into the orbicularis oculi muscle complex
Innervation: Temporal branch of facial nerve
Vascularization: Supra- and infratrochlear artery, supraorbital artery
Function: Medial and inferior movement of the eyebrow
Depth: Layer 3 (moving superficially from the medial third of the eyebrow and radiating into the skin [Layer 1])
Characteristics: The depressor supercilii muscle can be regarded as the fourth part of the orbicularis oculi muscle. This muscle is located in the same plane as the orbicularis oculi muscle and a clear separation between these two is almost impossible during gross dissections.

Corrugator Supercilii Muscle
Origin: Superciliary arch of the frontal bone
Insertion: Skin in the medial third of the eyebrow and into the orbicularis oculi muscle complex
Innervation: Temporal branch of facial nerve
Vascularization: Supra- and infratrochlear artery, supraorbital artery
Function: Medial movement of the eyebrow
Depth: Layer 5 (emerging from the bone and inserting into skin in the medial third of the eyebrow)
Characteristics: The corrugator supercilii muscle originates from the bone medial to the supraorbital foramen. However, its innervation reaches from the lateral side the muscle.

Procerus Muscle
Origin: Nasal bone, transverse part of the nasalis muscle
Insertion: Skin between the eyebrows (glabella), frontalis muscle
Innervation: Zygomatic branch of the facial nerve
Vascularization: Dorsal nasal artery, supra- and infratrochlear artery, anterior ethmoidal artery
Function: Depression of the skin superficial to the glabella between the eyebrows
Depth: Layer 5 (originating from bone and moving superficially toward the area of the glabella and radiating into the skin [Layer 1])
Characteristics: The procerus muscle originates from the bone and crosses all layers. In the central part of the muscle the dorsal nasal artery and vein can be identified, whereas in its lateral part branches of the angular vein, as well as of the supra- and infratrochlear artery, and supraorbital artery are coursing in a vertical direction. Its fibers are radiating into the superficial fatty tissue, that is, the glabellar fat body, and are anchored there. The most cranial fibers connect with the central part of the frontalis muscle and can pull the central part of the forehead inferiorly.

The interaction of the frontalis muscle, orbicularis oculi muscle, procerus, depressor, and corrugator supercilii muscle can be classified as the orbicularis occuli muscle complex in the periorbital region. All muscles show their effect on the movement of the eyebrows as well as the skin movement in this area. Also, the orbicularis oculi muscle complex must be balanced against the cranial pull of the frontalis muscle, which in turn is the only elevator of the eyebrow.

Midface Region (Figure 12.4): Nose (See Appendix 2)
Nasalis Muscle
Origin: Alveolar canine jugum, canine fossa
Insertion: Aponeurosis of the dorsal nose, skin of the nasal wing
Innervation: Zygomatic branch of facial nerve
Vascularization: Internal carotid: dorsal nasal artery, external nasal artery, anterior ethmoid artery; external carotid artery: facial artery, maxillary artery, lateral nasal artery, superior labial artery, septal artery, alar artery
Function: Elevation of the nasal wings and nasal tip, opening of nasal nares
Layer: Dorsal nose (layer 3, part of the superficial musculo-aponeurotic system)

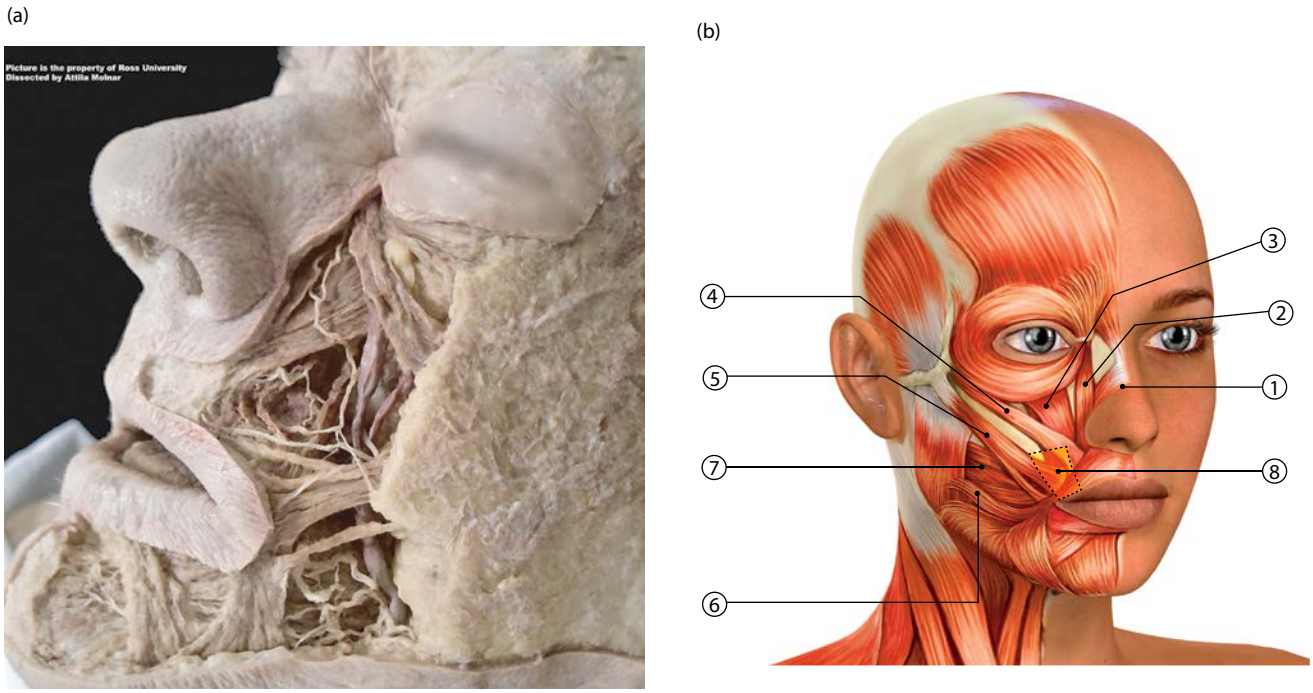

Figure 12.4 Muscles of the midface. (a) Dissection; (b) muscles: 1, nasalis; 2, nasal part of the levator labii superioris alaeque nasi; 3, labial part of levator labii superioris alaeque nasi; 4, zygomaticus minor; 5, zygomaticus major; 6, risorius; 7, buccinator; 8, levator anguli oris (deep to all others except buccinator). ([a] Courtesy of Ross University; dissection by Attila Molnar.)

Characteristics: The nasalis muscle is composed of a transverse and an alar part. Contraction of the nasalis muscle leads to the formation of nasal lines, also called "bunny lines."

Depressor Septi Nasi Muscle
Origin: Processus alveolaris incisivus
Insertion: Nasal septum
Innervation: Zygomatic branch of facial nerve, buccal branch of facial nerve
Vascularization: Superior labial artery, septal artery, alar artery
Function: Depression of the wings and nasal tip
Depth: Layer 5 (variation: layer 3)
Characteristics: The depressor septi nasi muscle originates in certain cases from the orbicularis oris muscle. On contraction, the muscle reduces the lip-nose distance and thus creates the impression of a short upper lip.

Levator Labii Superioris Alaeque Nasi Muscle
Alternative name: Angular head of the quadratus labii superioris muscle
Origin: Frontal process of the maxilla, medial infraorbital margin
Insertion: Skin of the nasal wings, lateral part of the nasolabial sulcus, medial part of the modiolus
Vascularization: Infraorbital artery, superior labial artery, external nasal artery, angular artery
Function: Elevation of nasal wings and upper lip
Innervation: Zygomatic branch of facial nerve
Depth: At its origin layer 5, the further caudally the more superficial (layer 1)
Characteristics: The muscle can be subdivided into a labial part (alternative name: infraorbital head of the quadratus labii superioris muscle) and an alaequae nasi part. The latter is located more medially toward the nose whereas the labial part is located more laterally with its fibers inserting into the modiolus. The angular vein can be identified superfial to this muscle whereas the infraorbital foramen is located deep to this muscle.

Zygomaticus Major Muscle
Origin: Zygomatic bone (anterior to the zygomaticotemporal suture)
Insertion: Modiolus, orbicularis oris muscle, skin of the nasolabial sulcus
Innervation: Zygomatic branch of facial nerve
Vascularization: Zygomaticofacial artery, anterior branch of superficial temporal artery, angular artery, infraorbital artery
Function: Supero-lateral movement of the lip, causes a deepening of the nasolabial sulcus
Depth: At its origin layer 5, the further inferomedial the more superficial (layer 1)
Characteristics: The origin of the zygomaticus major can be found in close proximity to the McGregor's patch, which also represents the beginning of the zygomatic ligament. The zygomaticus major muscle forms with its broad-based origin the lateral boundary of the deep lateral cheek fat compartment. In its medial third the muscle can be identified superficial to the facial vein and may thus cause compression during contraction. Its terminal muscle fibers radiate into the skin of the nasolabial sulcus and form the floor of the superficial (subcutaneous) nasolabial fat compartment.

Zygomaticus Minor Muscle
Alternative name: Zygomatic head of the quadratus labii superioris muscle
Origin: Zygomatic bone, medial to the zygomaticus major muscle
Insertion: Modiolus, orbicularis oris muscle, nasolabial sulcus
Innervation: Zyomatic branch of facial nerve
Vascularization: Zygomaticofacial artery, anterior branch of superficial temporal artery, angular artery, infraorbital artery
Function: Supero-lateral movement of the lip, causes a deepening of the nasolabial sulcus

Depth: At its origin layer 5, the further inferomedial the more superficial (layer 1)
Characteristics: The zygomaticus minor muscle originates from the zygomatic bone and its fibers intermingle with the fibers of the orbital part of the orbicularis oculi muscle, which can be found in layer 3. As the orbicularis oculi muscle is discontinuous in some anatomical variations, the zygomaticus minor muscle can be listed as a part of the orbicularis oculi muscle or even as a part of the levator labii superioris muscle.

Levator Anguli Oris Muscle
Alternative name: Caninus muscle
Origin: Canine fossa, inferior to the infraorbital foramen
Insertion: Modiolus, orbicularis oris muscle
Innervation: Zygomatic branch of facial nerve
Vascularization: Infraorbital artery, angular artery, superior labial artery
Function: Supero-medial movement of the lip and of the labial angle
Depth: At its origin layer 5, the further inferomedial the more superficial (layer 1)
Characteristics: The levator anguli oris muscle originates inferior to the infraorbital foramen and forms the floor of the deep medial cheek fat compartment and the deep pyriform space.

Risorius Muscle
Origin: Masseteric fascia, SMAS, skin (very variable)
Insertion: Modiolus
Innervation: Buccal branch of facial nerve
Vascularization: Facial artery
Function: Lateral movement of the labial angle
Depth: Layer 5 (when originating from the parotideomasseteric fascia), layer 3 (when originating from the SMAS), layer 2 (when originating from the subcutaneous tissue)
Characteristics: The risorius muscle displays a high variation regarding origin and course and in some dedicated cases, it is absent during gross dissections.

Buccinator Muscle
Origin: Alveolar process of the maxilla, buccinator crest, pterygomandibular raphe
Insertion: Modiolus, orbicularis oris muscle
Innervation: Buccal branch of facial nerve
Vascularization: Buccal artery, lingual artery, facial artery
Function: Assisting during chewing via creating tension of the cheeks
Depth: Layer 6 (muscle is covered by extension of buccopharyngeal fascia, which can be regarded as deep fascia)
Characteristics: The buccinator muscle can be subdivided into three main muscle fascicle bundles: upper, medial, and lower, which crisscross each other at the modiolus and thus form the deep component (layer) of the orbicularis oris muscle. The parotid duct pierces the muscle anterior to the masseter muscle, but posterior to the facial vein. In its covering fascia, the juxtaoral organ is embedded, which is postulated to have a function either as a stretch receptor or as a neuroendocrine organ.

Masseter Muscle
Origin: Deep aspect of zygomatic bone (deep part) and inferior aspect of zygomatic bone (superficial part)
Insertion: Lateral aspect of the ramus of the mandible (deep part) and mandibular angle (superficial part)
Innervation: Masseteric nerve of mandibular nerve of trigeminal nerve
Vascularization: Maxillary artery
Function: Elevation and protrusion of the mandible
Depth: Layer 6 (deep to the parotideomasseteric fascia, which is considered layer 5)
Characteristics: The masseter muscle plays an important role in the lateral shaping of the face and its volume contributes significantly to the overall facial appearance. The branches of the facial nerve run on its surface medially.

Lower Face (Figure 12.5) (See Appendix 2)
Orbicularis Oris Muscle
Alternative name: Incisivus labii superioris muscle/incisivus labii inferioris muscle for its part originating at the upper and lower jaw
Origin: Alveolar jugum caninus of the maxilla (superiorly) and of the mandible (inferiorly)
Insertion: Same as origin and skin of the upper and lower lip
Innervation: Zygomatic branch of facial nerve, buccal branch of facial nerve, marginal mandibular branch of the facial nerve

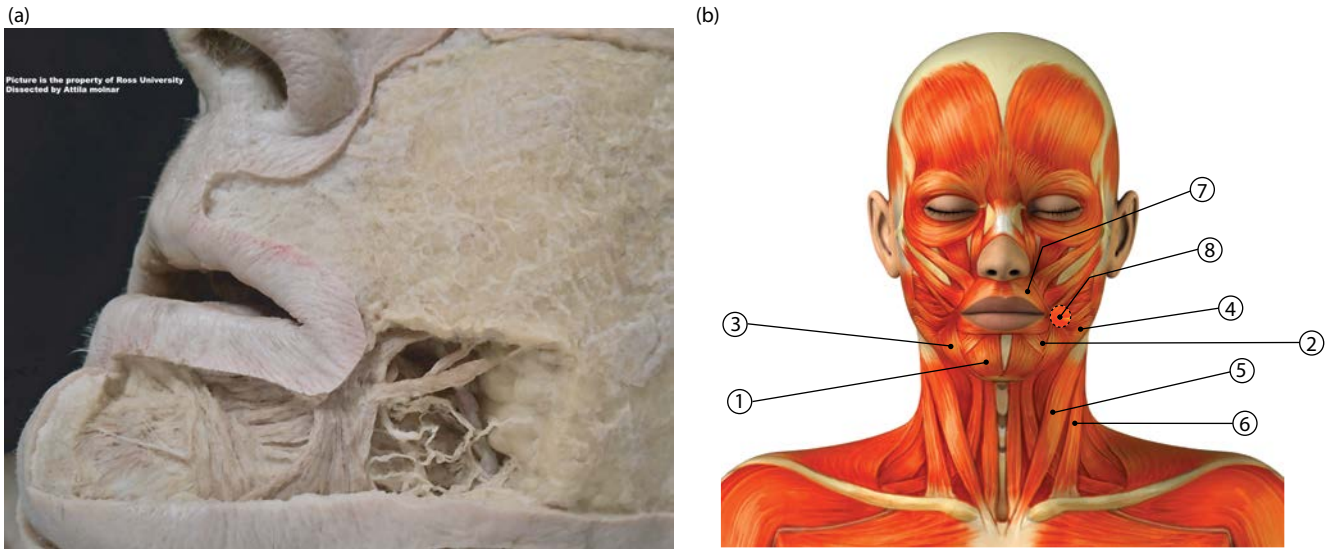

Figure 12.5 Muscles of the lower face. (a) Dissection; (b) muscles: 1, mentalis; 2, depressor labii inferioris; 3, depressor anguli oris; 4, platysma; 5, sternal part of the sternocleidomastoid muscle; 6, clavicular part of the sternocleidomastoid muscle; 7, orbicularis oris; 8, modiolus. ([a] Courtesy of Ross University; dissection by Attila Molnar.)

Vascularization: Superior labial artery, inferior labial artery, horizontal mental artery
Function: Closure of the oral cavity, internal torsion of the vermilion
Depth: Layer 3
Characteristics: The orbicularis oris muscle consists of a superficial and a deep part. The deep part is formed by the fibers of the buccinator muscle, whereas the superficial part is formed by the fibers of the muscles of facial expression. The modiolus is the hypomochlion of the peri-oral musculature as here a total of three layers of muscles merge together to form a muscular pillar of 1 × 1 × 2 cm in extent. The modiolus can be found 0.7–1.5 cm laterally to the labial angle and spans from layer 2–6. The facial artery is firmly attached to the modiolus, but can vary in its course along the upper and lower lips with three potential positions: subcutaneous, intramuscular, and submucosal.

Depressor Anguli Oris Muscle
Alternative name: Triangularis muscle
Origin: Inferior mandibular margin
Insertion: Modiolus, lower lip (lateral end)
Innervation: Marginal mandibular branch of facial nerve, buccal branch of facial nerve
Vascularization: Inferior labial artery, horizontal mental artery, mental artery
Function: Depression of the lower lip and labial angle
Depth: Layer 3
Characteristics: The depressor anguli oris muscle originates from the bone in layer 5 but becomes more superficial toward its course to the modiolus. The muscle can be identified superficial to the depressor labii inferioris muscle and its lateral fibers merge with those of the platysma (layer 3).

Depressor Labii Inferioris Muscle
Alternative name: Quadratus inferioris muscle
Origin: Inferior mandibular margin, but cranial to the depressor anguli oris muscle and inferior to the mental foramen
Insertion: Modiolus, lower lip (lateral third)
Innervation: Marginal mandibular branch of facial nerve
Vascularization: Inferior labial artery, horizontal mental artery, mental artery
Function: Depression of the lower lip
Depth: Layer 3
Characteristics: The depressor labii inferioris muscle can be identified deep to the depressor anguli oris muscle having a fiber direction perpendicular to the orientation of those of the depressor anguli oris muscle. Medial to a vertical line passing through the angle of the mouth the depressor labii inferioris muscle and lateral to this imaginary line, the depressor anguli oris muscle can be identified.

Mentalis Muscle
Origin: Alveolar jugum of the mandible inferior to the transverse mental septum
Insertion: Skin of the chin
Innervation: Marginal mandibular branch of facial nerve
Vascularization: Inferior labial artery, horizontal mental artery, mental artery
Function: Cranial movement of the skin of the chin, creating a prominent labiomental sulcus

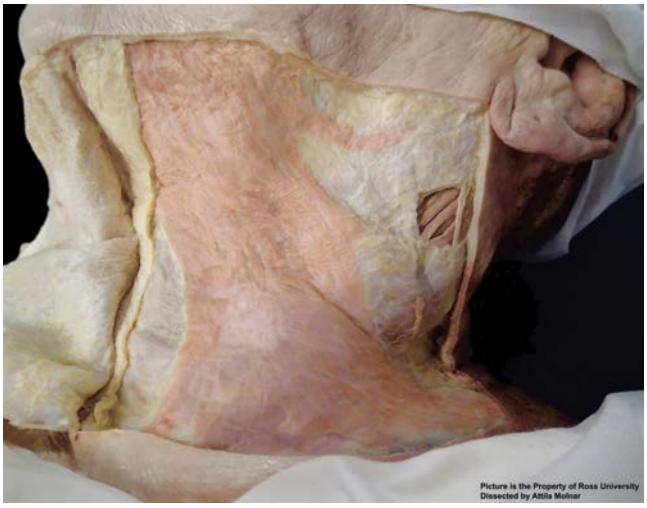

Figure 12.6 Platysma: dissection. (By courtesy of Ross University; dissection by Attila Molnar).

Depth: Layer 5 to layer 1
Characteristics: The mentalis muscle can originate as a two-headed or one-headed muscle from the mandibule, and the difference in the muscle morphology can be inspected by the presence of a mental fovea, which is more prominent if a two-headed variation is present.

Platysma (Figure 12.6)
Origin: Modiolus, subcutaneous plane with adhesions at the level of the inferior mandibular margin
Insertion: Skin of the neck
Innervation: Cervical branch of facial nerve
Vascularization: Superficial branch of transverse cervical artery, mental artery
Function: Depression of the labial angle, movement of the skin of the neck
Depth: Layer 3
Characteristics: The platysma is continuous with the SMAS in the midface and with the superficial temporal fascia in the upper face. It is discontinuous in the midline which can be observed in the aging neck or during forced muscular contractions. The longitudinal bands of the neck result from adhesions to the overlying skin but also from projections of the mandibular ligament and from the submental septum.

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13 Cosmetic uses of botulinum toxin A in the upper face

Anthony V. Benedetto

INTRODUCTION

In the United States, injections of botulinum neurotoxin (BoNT) to diminish horizontal forehead wrinkle lines, glabellar (central brow) frown lines and lateral canthal rhytides (crow's feet) are the only cosmetic and aesthetic indications approved by the Food and Drug Administration (FDA) in the United States of America (USA).[1–3] Injecting BoNT for cosmetic purposes in any other part of the face or body is not approved in the United States (US) by the FDA and therefore is considered off label use.[1–3] It remains to be seen whether the FDA and other governmental regulatory agencies of other countries will ever approve every single indication for which the BoNTs have proven to be effective in clinical practice. The fact remains that BoNTs are extremely reliable, nontoxic, and safe.[1–6] BoNTs provide reproducible results when administered as prescribed. Consequently, BoNTs have now become a major component of the armamentarium of any physician who practices aesthetic medicine in any capacity and who wants to produce the best cosmetic results for their patients.

In the early 1980s, botulinum neurotoxin serotype A (BoNT-A), known at that time as Oculinum™, was found to be effective for the treatment of strabismus in humans as an alternative to surgery.[7] Soon thereafter, Oculinum™ was acquired by Allergan, Inc. and renamed BOTOX®. In 1989, BOTOX® was approved by the FDA for the therapeutic treatment of strabismus and blepharospasm.[7] By 2000, BOTOX® was approved by the FDA for the therapeutic treatment of cervical dystonia. In April 2002, the FDA approved BOTOX® for the cosmetic treatment of glabellar frown lines. This resulted in the manufacturer's redesignation of the additional brand name of BOTOX® Cosmetic.[1] Both BOTOX® and BOTOX® Cosmetic are exactly the same product: they contain the same active ingredient in the same formulation, are manufactured by identical methods, and are only distributed under different names for different labeled indications and usage. BOTOX® is to be used for therapeutic purposes, whereas BOTOX® Cosmetic is to be used for cosmetic purposes.[1,8]

Subsequently, new and different formulations of BoNT-A other than BOTOX® and BOTOX® Cosmetic were approved for use in the US for both therapeutic and cosmetic purposes. The first of these was DYSPORT®,[2,9–11] which was approved by the FDA in May 2009 (see Chapter 5 by Monheit and Highsmith). In July 2011, XEOMIN®, a non-complexed BoNT-A was approved by the FDA for therapeutic and cosmetic purposes[3,12–14] (see Chapter 3 by Juergen Frevert).

To distinguish the current and future different formulations of BoNT from one another without mentioning their trade names, the FDA has assigned nonproprietary names, a type of "generic" name, to the different formulations of the currently approved BoNTs. (OnaBTX-A) was assigned to BOTOX® and BOTOX® Cosmetic, also known as Vistabel® in certain countries in Europe, and Vistabex® in Italy. AbobotulinumtoxinA (AboBTX-A) was assigned to DYSPORT®, also known as Azzalure® in Europe and Reloxin® elsewhere. IncobotulinumtoxinA (IncoBTX-A) was assigned to XEOMIN®, otherwise known as XEOMEEN® in Belgium and Bocouture® in Europe and elsewhere. Botulinum neurotoxin type B (BoNT-B) known as Myobloc® in the United States and Neurobloc® in Europe was given the designation of RimabotulinumtoxinB (RimaBTX-B) (see Chapter 5). Other BoNTs currently available for use in other parts of the world are discussed in Chapter 6 by Andy Pickett.

Chapters 13 through 15 discuss cosmetic injections of BoNT for the face and body. It is of particular importance to understand that in order to avoid ambiguity and confusion with the injection of appropriate and effective doses of BoNT, any reference to BoNT-A in these three chapters will indicate specifically BOTOX® Cosmetic and explicitly onabotulinumtoxinA or OnaBTX-A. The reason for this is not preferential usage by the author, but because OnaBTX-A was the first BoNT-A to be used for cosmetic purposes worldwide, and for many years a multitude of patients have been treated with OnaBTX-A before any of the other BoNT-As were available. Consequently, most of the patients illustrated in these next three chapters were treated with OnaBTX-A with the preferred dosages indicated. Therefore, for the sake of clarity and uniformity, all dosage units specified throughout Chapters 13 through 15 are expressed in units of OnaBTX-A.

Some may criticize the "cookbook" approach to Chapters 13 through 15. This systematic detailing of why, where, and how much OnaBTX-A to inject in a particular area of the face and body, however, is necessary to understand when correcting a certain aesthetic problem, and, therefore, was done intentionally. Moreover, it is important to note that the face is the only area of the body where there is no deep subcutaneous membranous fascia beneath the skin, thus allowing slips of muscle fibers that are attached to the facial skeleton at their origin to insert directly into the undersurface of the skin. But not all facial muscles have their origins attached to bone. Some arise from aponeuroses, but then they still insert onto the undersurface of the skin. Consequently, when these muscles contract, they move the skin of the face, producing folds and wrinkles always in a perpendicular orientation to the direction of muscle contraction. Nowhere else in the body are there similar types of muscles that contract voluntarily or involuntarily, pulling on the skin and expressing an emotion.

The face can be divided topographically into three segments using anatomical and cosmetic unit boundaries: the upper, mid, and lower part of the face. In these segments of the face there are either single or multiple muscles, that when contracted, move mostly in one direction. Depending on their location on the face and the anatomic position of their fibers, these mimetic muscles can move the skin in an upward, oblique, or downward direction. For example, this allows one to either raise or lower the eyebrows, smile or frown, open or shut the eyes, and so on. This difference in the direction of skin movement is done by muscles in a complementary, opposing fashion, that is, by elevating (levator) or lowering (depressor) muscles. These competing movements by agonistic or antagonistic muscles contracting intentionally or unintentionally cause horizontal, radial, or vertical wrinkling of the face. Consequently, nonverbal communication can be expressed with the slightest contraction of one or a combination of facial muscles (hence the designation "mimetic facial muscles").

The reader must never lose sight of the fact that every single individual patient is different and he or she should never be treated in an identical fashion without justification. These Chapters 13 through 15 strive to provide both the learning and experienced physician injector, the rationale for why and how a patient should be treated with a particular dose of OnaBTX-A in one area or another for a distinct and reproducible outcome. The reader also must understand that the explicit injection techniques, described with their indicated preferred dosages of OnaBTX-A, are only the author's perception of a given aesthetic problem. The reason for the particular pattern of wrinkles and the interpretation of a potential solution is this author's approach to the management of that specific problem for that particular patient, who may or may not present again in the future in exactly the same

way. Therefore, when a physician is evaluating a patient prior to a treatment with a BoNT, it does not matter if the patient has or has never been treated previously with BoNT. The physician should approach that patient as if he or she were receiving BoNT for the very first time. Prior to commencing with injections of a BoNT, the physician must evaluate the patient's current aesthetic problem completely and have a comprehensive understanding of the patient's current concerns. The physician injector should not necessarily rely on past treatment dosing or on instructional photographs that address injection techniques and dosing for similar problems. With a substantial understanding of functional anatomy, the physician injector should be flexible enough to evaluate correctly and treat appropriately the patient's concerns and specific offending changes which are visible at the time of presentation. An expert injector utilizes BoNT to improve a patient's excessively dynamic muscle movements—thus treating the patient, not a picture.

The "before and after" clinical photographs of patients treated with OnaBTX-A presented in Chapters 13 through 15 are pictures not of study subjects, but of actual patients treated on a regular basis with effective and different doses of OnaBTX-A in a long-standing dermatologic clinical aesthetic practice. Hence, the reason for the lack of standardization in the quality of the photographs. These before-and-after clinical photographs are presented here only as examples of reasonably acceptable clinical outcomes. The reader in turn, after some personal experience with treating patients, should be able to use these examples of injection techniques and treatment outcomes to develop a preferred approach with his or her own personal injection techniques and produce comparable results when treating patients with similar clinical problems.

It is extremely important to understand that the specific units and dosages of BoNT-A discussed in Chapters 13 through 15 are only for OnaBTX-A (i.e., BOTOX® Cosmetic) unless explicitly stated otherwise. The same number of units specified in detail in these chapters for OnaBTX-A should absolutely not be used with an identical unit dose of another source or manufacturer, to treat patients with BoNT-A, even if a dose ratio of equivalency is provided as being 1:1.[1] The confusion with dose equivalencies using OnaBTX-A as the standard to which, regardless of serotype, all other BoNTs are measured, will only become more apparent and less reliable when different formulations of BoNT-A or other BoNT serotypes are utilized in the future.[15,16] The reason for this interchangeable indecipherability of dosing of the different brands of BoNTs is because currently the proprietary cell-based potency assay used by Allergan is different from other manufacturers' proprietary potency assays of their own BoNT and varies according to vehicle, dilution scheme, and laboratory protocols. Therefore, when using any type of BoNT including OnaBTX-A (i.e., BOTOX® Cosmetic), it is imperative that one learns how to administer that particular brand of BoNT independently of any conversion ratio because individual muscles may respond in a distinctly different manner to certain formulations and specific serotypes of BoNT (see Appendix 1).[15] Understanding the pharmacokinetics and pharmacodynamics of BoNT is still only in its early stages, and the possibilities for future developments are limitless[17–19] (see Chapter 2 by Mitchell Brin).

In 2002, the muscles of the central brow or "glabellar complex" were the first muscles of the face or body into which OnaBTX-A could be injected for cosmetic purposes that were approved in the United States (US) by the FDA.[1] Then in 2013, the FDA approved injections of OnaBTX-A for the cosmetic reduction of lateral canthal wrinkles or "crow's feet."[1] In 2017, OnaBTX-A was approved by the FDA for the temporary reduction of moderate to severe forehead wrinkles lines. Treatment of all other muscles in any other part of the face or body with injections of OnaBTX-A or any other BoNT for cosmetic reasons is done solely and expressly in an off-label, non-approved manner.

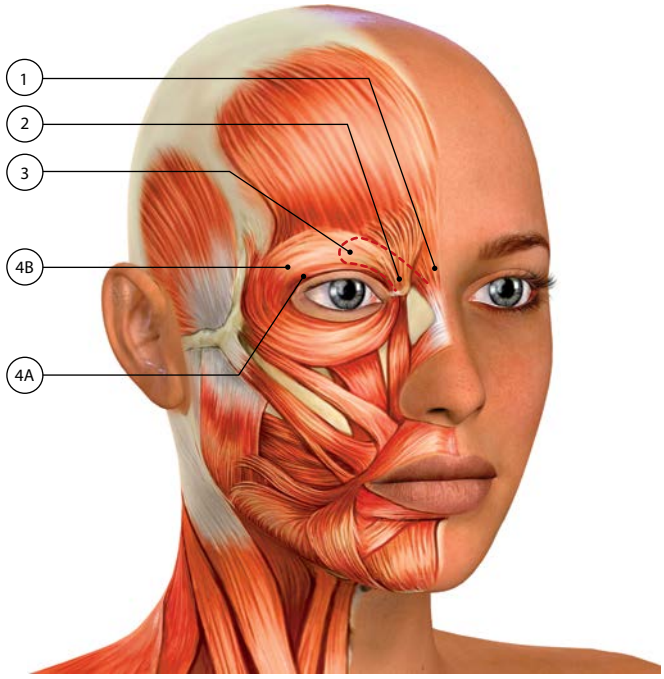

Figure 13.1 The upper third of the face consists of a single brow elevator (the frontalis) and four brow depressors: 1, procerus; 2, depressor supercilii; 3, corrugator supercilii (its path underlying orbicularis oculi is shown here); 4A palpebral and 4B orbital fibers of orbicularis oculi. (See Appendix 2—muscle attachments.)

CENTRAL BROW (GLABELLAR) FROWN LINES

Introduction: Problem Assessment and Patient Selection

The area most frequently treated with BoNT is the central brow or glabella and its frown lines.[20–26] On the skin surface, the glabella is the space between the eyebrows. There are four depressor muscles of the brow that cause the horizontal and vertical creases of the glabella (Figure 13.1). These muscles allow one to squint to protect the eyes from projectiles, gusts of air, and the elements (i.e., glaring light, wind, dust, sand) by lowering the eyebrows and adducting them medially. However, resting hyperkinesis of these depressor muscles can cause persistent, unintentional adduction and lowering of the medial aspect of the eyebrows, causing vertical and horizontal wrinkles between the eyes. This central brow frowning during moments of intense concentration, for example, can be misinterpreted by others as a veritable frown, which usually expresses negative feelings of concern, fatigue, disappointment, frustration, anger, pain, suffering, advanced age, and so on. (Figure 13.2a). Weakening the four depressors of the glabella with injections of BoNT can raise and slightly abduct the eyebrows and virtually eliminate the frown lines of the glabella. This allows a person to appear more relaxed, expressing a positive demeanor, even when in reality one might be frowning and attempting to convey a negative sentiment (see the Prologue from Nina Jablonski) (Figure 13.2b and c). An elevated brow generally expresses a positive attitude, whereas a depressed brow is indicative of a negative one. In addition, low-set eyebrows that progressively appear with age, eventuate in the formation of upper eyelid and lateral canthal hooding (Figure 13.3). Arched or peaked eyebrows usually are more attractive in women (Figure 13.2c), whereas men in general possess more horizontal eyebrows (Figures 13.4 and 13.5). However, be aware of women who pluck or have had permanent tattooing of their eyebrows, because the natural position of their brows may be altered (see Figure 13.42).

The brow has both static qualities of beauty and dynamic quantities of expressiveness that change with advancing age. As one ages,

Figure 13.2 (a) A 53-year-old patient with unintentional frowning during intense concentration. An OnaBTX-A treatment was subsequently given. (b, c) 3 weeks after OnaBTX-A injections in the forehead and glabellar area seen here (b) with and (c) without frowning.

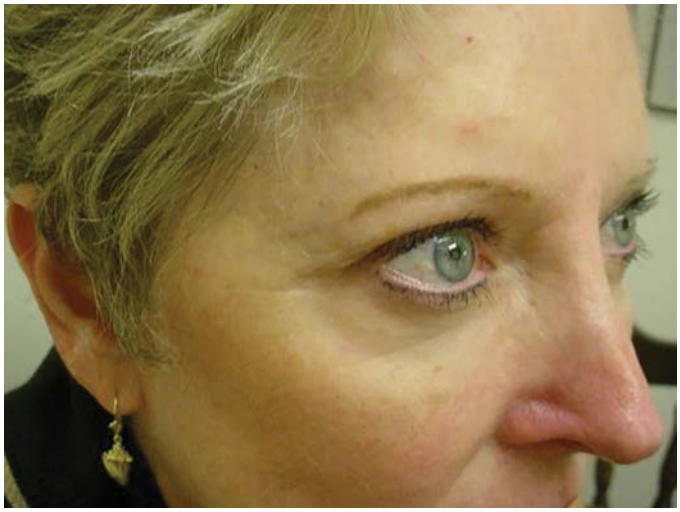

Figure 13.3 Low set eyebrows and upper eyelid and lateral canthal hooding in a 59-year-old patient.

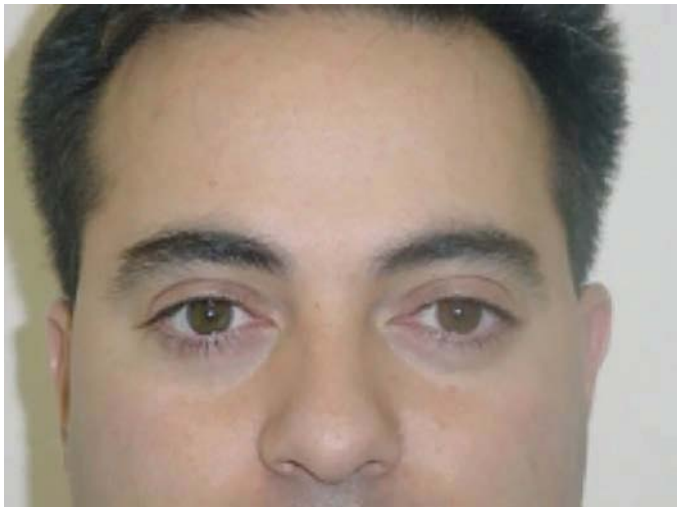

Figure 13.4 The ideal eyebrows for a man are less arched and lower set than a woman's.

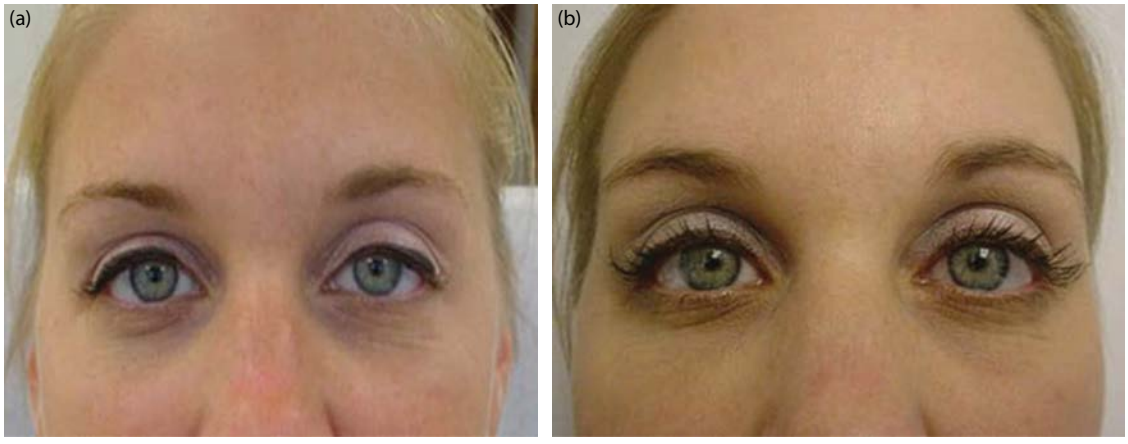

Figure 13.5 (a) A 28-year-old patient with relatively flat eyebrow arches before treatment. (b) After treatment with strategically placed OnaBTX-A, the eyebrows are elevated and arched. Note the right eyebrow also is slightly lifted and more symmetrical with the left.

the skin of the face and the rest of the body become inelastic and redundant. In the periorbital area, the skin of the eyebrows and forehead becomes lax and can drop inferiorly to lie over the superciliary bony ridge of the brows. This is recognized as brow ptosis of varying degrees of severity. Brow ptosis can alter the shape and position of the eyebrows, thereby compromising a person's youthful appearance and aesthetic attractiveness.

Trindade de Almeida et al. have classified glabellar frown lines into five distinct patterns[27] (see Figures 13.20 through 13.24). Although the muscular anatomy is by and large alike in most patients, individual skeletal morphology and idiosyncratic muscular movements can produce unique variations in the pattern of wrinkles in the glabellar area during intentional animation and spontaneous expression. The same is true anywhere else on the face for exactly the same

reasons. The differences in glabellar wrinkle patterns indicate that the strength of each of the four glabellar muscles are not identical or uniform in size and strength in every patient and one set of muscles may be stronger or weaker than its codepressor set of muscles. Their response to neurostimulation also is uniquely different in every individual. Therefore, the pattern of glabellar frowning is dependent on which muscles are idiosyncratically stronger or weaker, and the injected dose of OnaBTX-A must vary accordingly. Some glabellar wrinkle patterns are observed more frequently than others according to Trindade de Almeida et al.[27]

Functional Anatomy of the Central Brow (Glabella) (See Appendix 2)

On the skin surface, the center of the brow, that is, the space between the eyebrows is referred to as the glabella. In the area of the central brow or glabella in some individuals, both vertical and horizontal lines may develop, which frequently can project unintended negative social cues when one frowns. The bony glabella is the smooth, flat, triangular elevation of the frontal bone superior to the nasal radix positioned between the two superciliary ridges or arches. Contracting any of the mimetic muscles of the face will cause wrinkling of the skin perpendicular to the orientation of those muscle fibers and in the direction of their movement. The muscles that produce the *vertical* lines of the glabella do so because their fibers are oriented more or less horizontally and they move in a horizontal direction when contracted. They are the corrugator supercilii and the adjacent medial horizontal fibers of the upper eyelid orbicularis oculi.[28–30] The horizontal lines between the eyebrows across the root and bridge of the nose result from the contraction of the vertical fibers of the "medial" brow depressors, which move in a vertical direction when contracted. They are the procerus, depressor supercilii, and the adjacent medial vertical fibers of the orbicularis oculi (Figure 13.1). All four brow depressor muscles, corrugator supercilii, orbicularis oculi, depressor supercilii, and procerus oppose the contractions of the single brow levator muscle, the frontalis, in an agonistic/antagonistic fashion which is functionally characteristic of all the mimetic muscles of the face and anterior aspect of the neck (Figure 13.1).

The corrugator supercilii is a small, pyramidal, deeply situated paired muscle that arises from the frontal bone just inferior to the medial aspect of the bony superciliary arch approximately 4 mm lateral to the nasion[31,32] (Figure 13.6). The nasion is the point of juncture of the nasofrontal bony sutures with the internasal bony sutures (Figure 13.7). Clinically, the nasion can be palpated as the center of the concavity at the nasal radix (or root). The corrugator supercilii lies directly against the frontal bone just beneath the interdigitating muscle fibers of the superior orbicularis oculi, procerus, depressor supercilii, and frontalis medially and travels upwardly and laterally at an oblique angle of approximately 30°, to emerge from beneath the interdigitating fibers of the frontalis and superior orbicularis oculi and inserts underneath the skin into the soft tissue and dermis above the middle of the eyebrow in the vicinity of the midpupillary line and the supraorbital notch. The insertion point of the corrugator is approximately 4.2–4.5 cm lateral to the midline and is often seen as a dimple in the skin just above the medial brow ("corrugator dimple") (see Figure 13.8).

In anatomical dissections, the medial aspect of the corrugator can be seen partially interdigitating with the frontalis superiorly, procerus medially, and orbicularis oculi inferiorly.[29,33] The bulk of the corrugator supercilii usually is found overlying the inferior aspect of the superciliary arch (Figure 13.7).[31] Anatomic studies have demonstrated that the thickest portion of the belly of the corrugator is at or just above a horizontal plane drawn through the middle of the eyebrow and approximately 2.0–4.0 cm from the nasion (Figures 13.6 and 13.7).[28,29,31–35] In some individuals the corrugator can be shorter and more oblique or even bifid with a *transverse* and an *oblique* head,[33] which is one of the reasons why there are different patterns of glabellar frown lines[27] (see the frown lines in Figures 13.20 through 13.26). The supratrochlear neurovascular bundle passes through the corrugator supercilii, while the supraorbital nerve runs underneath the muscle and divides into two upward running branches: the medial *superficial* and the lateral *deep* nerve branches.

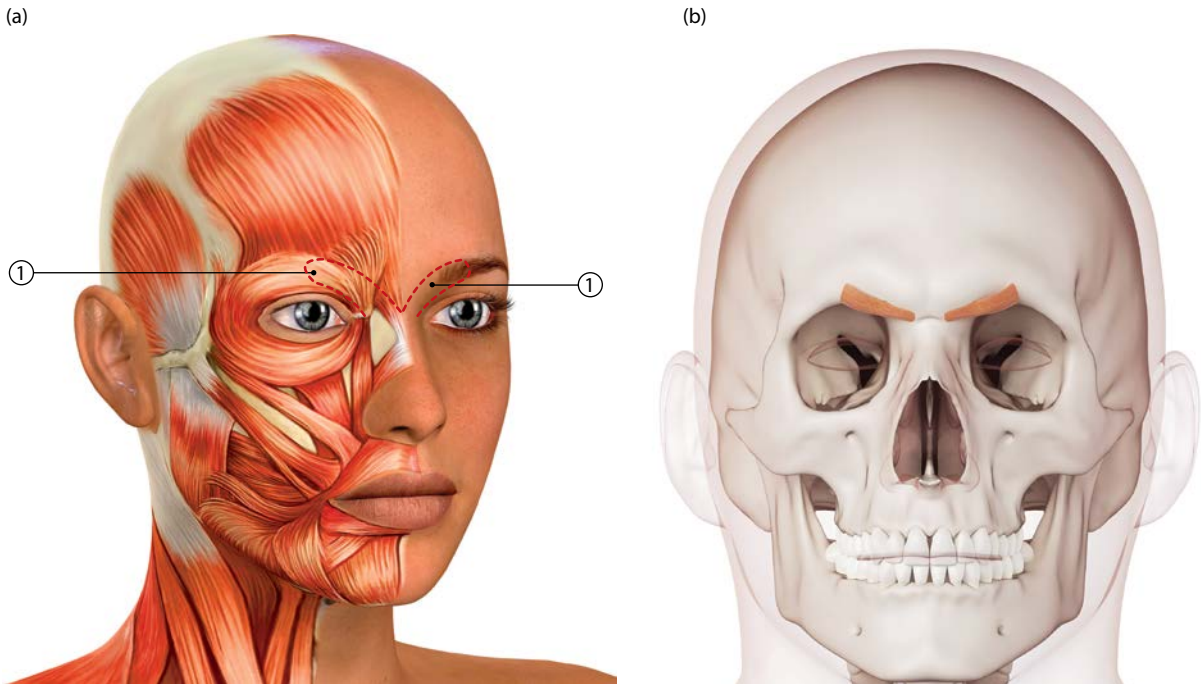

Figure 13.6 (a) The corrugator supercilii lies on the bone and deep beneath the other glabellar muscles; its course is shown here. (See Appendix 2—muscle attachments.) (b) The origin and insertion of the corrugators.

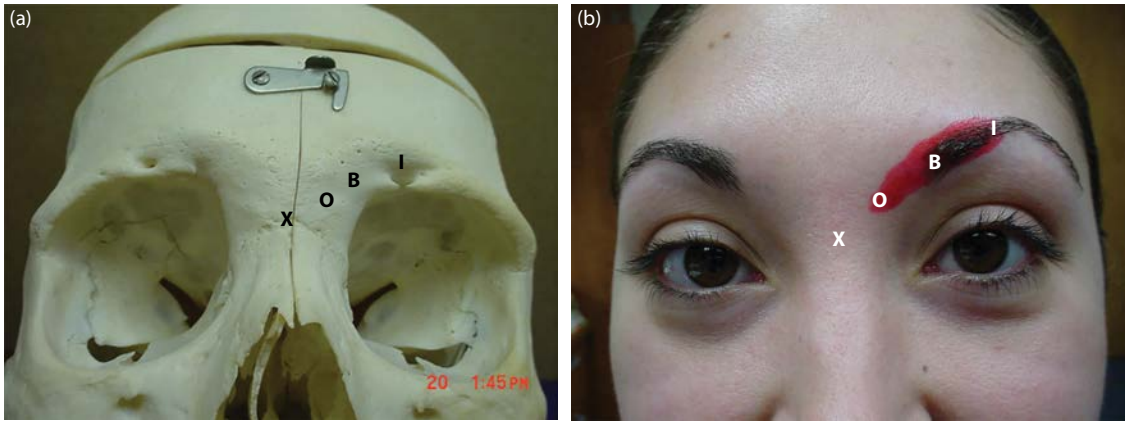

Figure 13.7 The corrugator supercilii. (a) Skull with view of the corrugator supercilii superimposed with letters. The thickest part of the belly of the muscle is approximately 2.0 cm from the nasion. (b) A patient with representation of corrugator supercilii drawn in red with superimposed lettering. *Abbreviations*: X, naison; O, origin; B, belly; I, insertion of corrugator supercilii.

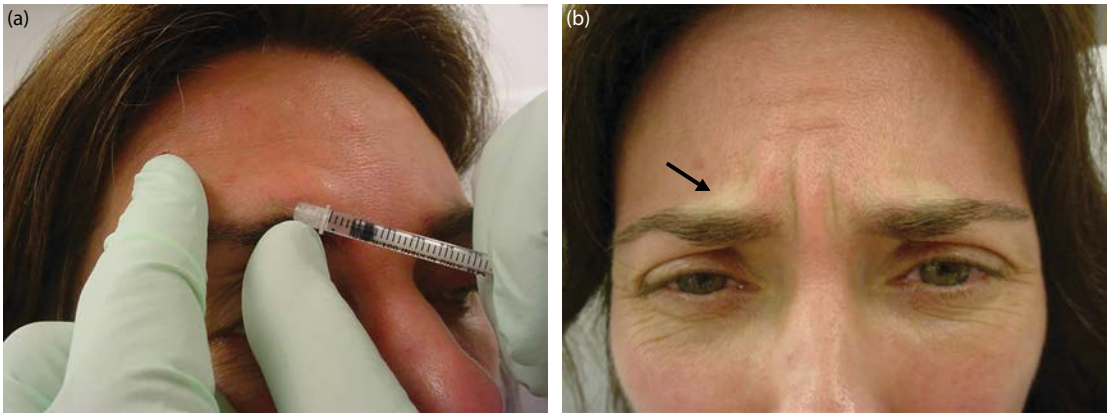

Figure 13.8 (a) Injection just above the middle of the eyebrow where the lateral aspect of the corrugators insert into the undersurface of the midbrow, just medial to the supraorbital notch or midpupillary line. (b) Note the obvious dimpling of the skin as the patient forcibly frowns.

The supraorbital artery and vein travel alongside the deep branch of the supraorbital nerve.[29]

The orbicularis oculi is a thin, broad, flat muscle whose fibers form a concentric ring over the eyelids and around the orbit. This sphincteric muscle can be divided into three parts. The outermost fibers of the orbicularis oculi are called the *orbital* portion of the orbicularis oculi. The orbital orbicularis oculi arises from the bony structures of the lateral nose and medial orbit, including the medial canthal ligament. Its fibers then run superiorly and inferiorly, forming a wide sphincteric ring surrounding and extending beyond the edges of the bony orbital rim and also into the eyelids (Figure 13.9).[28–30] A portion of the medial aspect of the orbital orbicularis oculi, whose fibers have a more distinctly vertical orientation, is occasionally referred to as the "depressor supercilii" by some authors (Figure 13.10).[33,36] Contraction of the medial aspect of the orbital orbicularis oculi lowers the eyebrow downward and medially and slightly depresses the lateral aspect of the brow. The inner portion of the orbicularis oculi which overlies the eyelids is identified as the *palpebral* portion of the muscle. The palpebral orbicularis oculi is further subdivided into the *preseptal* and *pretarsal* portions (Figure 13.10).[28–30] Contraction of the palpebral orbicularis oculi approximates the upper with the lower eyelids, either deliberately or involuntarily.

The horizontal lines of the glabella and nasal root are produced by the contraction of the vertically oriented fibers of the procerus, depressor supercilii, and the medial vertical fibers of the orbital orbicularis oculi. These three muscles also are referred to as the "medial brow depressors."[33]

The procerus is a thin (≤1 mm thick), paired muscle, pyramidal in shape and centrally located in the midline of the glabella between the two eyebrows. It overlies the nasion and the bony origin of the corrugator supercilii. Inferiorly at its origin, the paired muscle bellies of the procerus are joined together but can separate in the form of a V superiorly at their attachments into the skin.[29] The shape, size, and strength of the procerus will determine the different types of frown lines that are created across the nasal radix (see de Almeida's glabellar frown lines, Figures 13.20 through 13.26). Its location 2–4 mm beneath the surface of the skin makes it an easy target for injections of BoNT[32] (Figure 13.10). The procerus arises from the fascial aponeurosis attached to the periosteum covering the lower caudal part of the nasal bridge (i.e., the upper portion of the nose overlying the nasal bone), the perichondrium covering the upper cephalic part of the upper lateral nasal cartilages, and the aponeurosis of the transverse part of the nasalis. It inserts superiorly into the skin and subcutaneous tissue at the nasal radix and lower part of the forehead between the two eyebrows. Superiorly, muscle fibers of the upper border of the procerus also interdigitate with muscle fibers of the lower central frontalis. Inferiorly, muscle fibers of the procerus interdigitate with fibers of the transverse nasalis. Laterally, the procerus interdigitates with the corrugator supercilii, depressor supercilii, and the medial fibers of the orbital orbicularis oculi. Contraction of the procerus pulls the medial aspect of the eyebrows downward, creating the horizontal

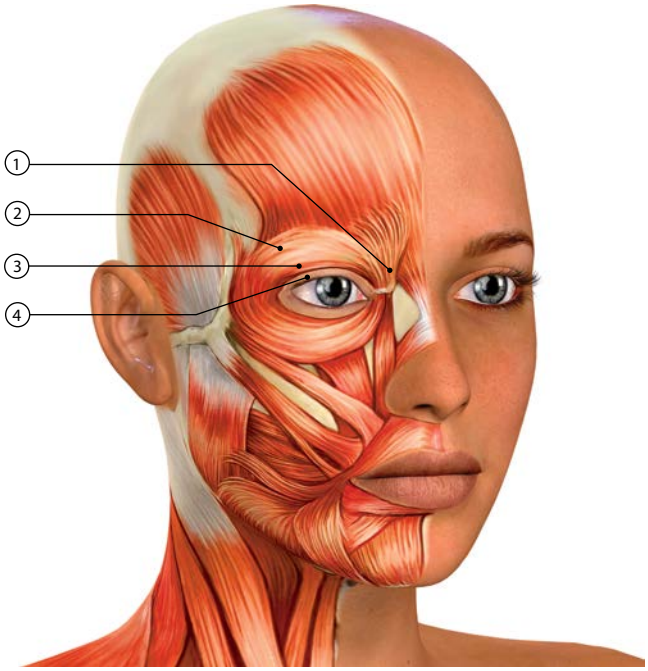

Figure 13.9 The orbicularis oculi has different subdivisions and interdigitates with the other depressors and elevator of the glabella: 1, depressor supercilii; 2, orbicularis oculi, *orbital* portion; 3, orbicularis oculi, *palpebral* portion *preseptal*; 4, orbicularis oculi, *palpebral* portion, *pretarsal*. (See Appendix 2—muscle attachments)

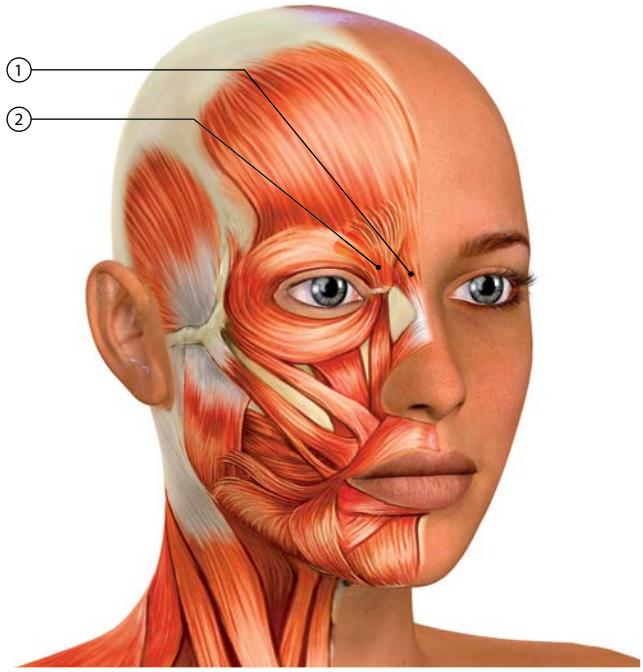

Figure 13.10 The depressor supercilii is the diminutive muscle of the glabella. The procerus is the midline, deep muscle of the glabella. 1, procerus; 2, depressor supercilii. (See Appendix 2—muscle attachments)

frown lines across the root and bridge of the nose. Anatomic studies also have demonstrated that the procerus can be longer in women than in men and, at times, bifid similar to the frontalis.[29,34]

The depressor supercilii is considered by many a component part of the medial, vertical fibers of the orbital orbicularis oculi (Figure 13.10).[28–30,34] Yet others consider it a separate and distinct muscle from the orbicularis oculi and corrugator supercilii.[33,36] The depressor supercilii is a small, vertically oriented muscle that has been found to originate directly from bone as one or two distinct muscle heads from the frontal process of the maxilla roughly 2–5 mm below the fronto-maxillary suture line, and the nasal process of the frontal bone slightly posterior and superior to the posterior lacrimal crest. Clinically, the depressor supercilii can be located approximately 10–15 mm above the medial canthal tendon.[36] In cadaver dissections where the depressor supercilii originated as two separate heads, the angular vessels passed in between the two bundles of muscles. In cadavers where there was only one muscle head originating at the medial canthus, the angular vessels were found coursing anteriorly to the muscle before traveling deeper into the glabellar area.[29] The depressor supercilii then passed vertically upward and over the origin of the corrugators to insert into the undersurface of the skin at the medial aspect of the eyebrow, approximately 13–16 mm superior to the medial canthal tendon. It overlies the corrugator supercilii and the medial aspect of the orbital orbicularis oculi, but interdigitates with some of the more superficial fibers of the orbital orbicularis oculi.[28,31,34] Not only does it help move the eyebrow downward and close the eyelid, but the depressor supercilii also participates in the functioning of the physiological lacrimal pump by compressing the lacrimal sac (see page 174).

Opening and shutting the eyes is partially accomplished by the contraction of the accessory muscles of the upper eyelid: one is a cholinergic, striated muscle, the levator palpebrae superioris; the other is an adrenergic, nonstriated, smooth muscle called the superior tarsal muscle of Müller. The levator palpebrae superioris is the main retractor of the upper eyelid. It is a thin, flat, triangular sheet of striated muscle originating at the apex of the bony orbit at the common tendinous ring or annulus of Zinn on the lesser wing of the sphenoid behind the globe and just above the origin of the superior rectus (Figure 13.11a).[28,30] The levator palpebrae superioris is positioned above the superior rectus as they both pass over the superior aspect of the eyeball within the bony orbit. Approximately at the level of Whitnall's transverse suspensory ligaments, the superior rectus attaches to the superior aspect of the globe at the level of the superior-conjunctival fornix, while the levator palpebrae superioris continues anteriorly as a wide aponeurosis. As the aponeurosis continues forward, some of its tendinous fibers attach to the anterior surface of the tarsus, and the rest of the fibers pass in between the muscle fibers of the pretarsal orbicularis oculi and attach to the undersurface of the eyelid skin.[28,30] Its tendinous attachments in the upper eyelid are responsible for the formation of the superior eyelid crease (Figure 13.11a).

Dilution for Injecting the Central Brow (Glabella) (See Appendix 3)

Different clinicians have their favorite patterns of injecting the glabella with varying doses of different concentrations of OnaBTX-A. The manufacturer's package insert recommends reconstituting the 100 U vial of OnaBTX-A with 2.5 mL of unpreserved normal saline, thus yielding 4 U of OnaBTX-A for each 0.1 mL of solution.[1] However, since the brow depressors interdigitate with each other in close proximity in a very small and confined area, it is extremely important to inject accurately precise amounts of OnaBTX-A in this area. Therefore, many seasoned injectors still reconstitute the 100 U vial of OnaBTX-A with only 1 mL of normal saline. This provides 1 U of OnaBTX-A in every 0.01 mL of solution, which is easily injected using a 0.3 mL Becton-Dickinson insulin U-100 syringe with a 31-gauge needle directly attached (Becton, Dickinson and Company, Franklin Lakes, NJ).[37] The advantage of using an insulin syringe is that the needle is directly swaged onto the hub of the syringe barrel, so there is little or no additional wastage of product in the hub of the needle or in the neck of the syringe (Figure 13.12). In addition, each

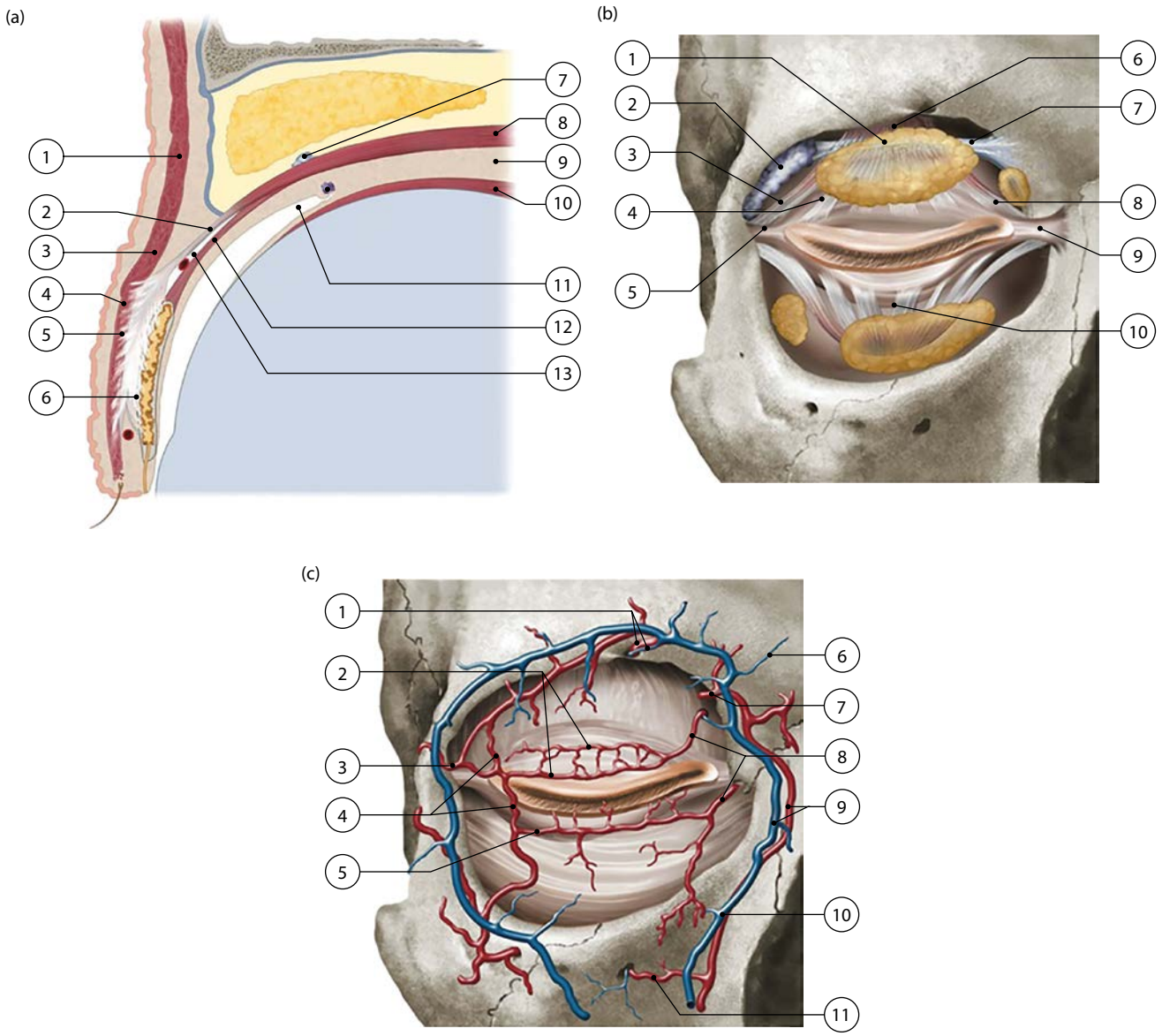

Figure 13.11 (a) Close-up view of the upper eyelid anatomy and muscle attachments. The levator palpebrae superioris is the main retractor of the upper eyelid; it is a striated muscle. Mueller's superior tarsal muscle is not striated, but a smooth muscle. 1, orbicularis oculi (orbital); 2, levator aponeurosis; 3, orbicularis oculi (preseptal); 4, orbicularis oculi (pretarsal); 5, levator aponeurotic insertion into orbicularis; 6, levator aponeurotic insertion into superior tarsus; 7, Whitnall's ligament; 8, levator palpebrae superioris; 9, common sheath; 10, superior rectus; 11, superior conjunctival fornix; 12, superior tarsal muscle; 13, post-aponeurotic space. (b) Anterior view of the upper orbit with the attachments of the levator aponeurosis and lower lid retractors. 1, pre-aponeurotic fat pad; 2, lacrimal gland; 3, lateral horn of levator aponeurosis; 4, levator aponeurosis inserting into superior tarsus; 5, lateral canthal tendon; 6, levator muscle; 7, Whitnall's ligament; 8, medial horn of levator aponeurosis; 9, medial canthal tendon; 10, lower lid retractors inserting into inferior tarsus. (c) Anterior view of the orbit showing the complexity of the vascular arcades and other vascular structures. 1, supra-orbital artery and vein; 2, tarsal arcade upper lid; 3, lacrimal artery; 4, lateral palpebral artery; 5, tarsal arcade lower lid; 6, frontal vein; 7, supratrochlear artery; 8, medial palpebral artery; 9, angular artery and vein; 10, facial artery and vein; 11, infraorbital artery and vein.

unit line marked on the syringe barrel corresponds to 0.01 mL or 1 U of OnaBTX-A when a 100 U vial of OnaBTX-A is reconstituted with 1 mL of saline. In this way, only minimal volumes of OnaBTX-A will be needed to produce the desired cosmetic results. Moreover, most practitioners now have switched to using preserved saline with 0.9% benzyl alcohol.[38–41]

Dosing: How to Correct the Problem (See Appendix 4) (What to Do and What Not to Do) When Treating the Central Brow (Glabella)

The pretreatment evaluation should include examining the patient at rest and in full motion. Lightly palpate the muscles of the glabellar area with the palmar surface of the fingertips of the nondominant hand as the patient squints and frowns. This will help determine the location, size, and strength of the individual muscles of the glabella (Figure 13.1). A frequently used and standardized technique for treating the glabella is to inject OnaBTX-A into five different sites with doses that range anywhere from 4 to 10 U or more at each site (Figure 13.13).[16,41–43] Electromyographic guidance in this area has not particularly improved treatment outcomes because these facial muscles are superficial and easily localized by palpation and topographical landmarks.[3,21,34,44]

Patients who possess thinner, less sebaceous skin with finer wrinkles and shallower skin furrows and folds that can be spread apart and reduced with the fingers ("glabellar spread test") seem to have better, longer-lasting results.[45] There are, however, some patients who are

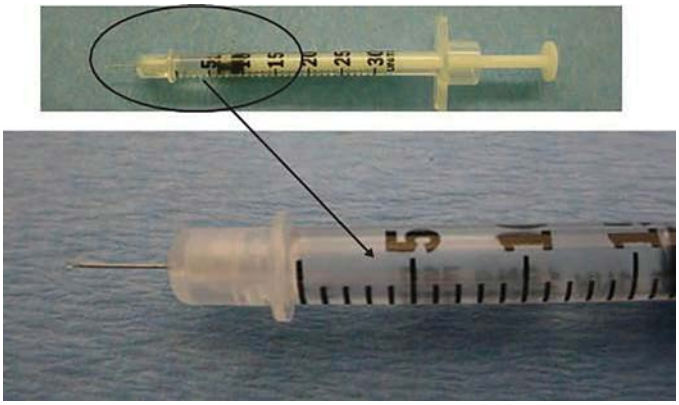

Figure 13.12 A 3/10 mL Becton-Dickinson insulin U-100 syringe with a 31-gauge needle swaged directly onto the syringe barrel. Note the absence of any dead space between the hub of the needle and the neck of the syringe. Each unit notch on the barrel corresponds to 0.01 mL or 1 U.

Figure 13.13 Standard five injection points for treating glabellar frown lines.

more difficult to treat because they are less responsive to the effects of OnaBTX-A. In this group of patients who are more difficult to treat, there is one type of patient who possesses thick sebaceous skin with deep, intractable wrinkles whose furrows are difficult to pull apart with the fingers. Usually these turn out to be men and sometimes women who spend a lot of time outdoors or constantly in front of a computer screen. The other type of patient is the one who possesses the inelastic, redundant skin seen with dermatochalasis and whose furrows also are deep but very easy to pull apart. These patients characteristically are older (>65–70 years old) and unfortunately are not ideal candidates for glabellar chemodenervation. Typically, in these patients, after having OnaBTX-A injected with impeccable technique, the resultant relaxation of the glabellar muscles causes a drop in the brow and infolding of the inelastic, redundant glabellar skin. Consequently, brow ptosis and persistent frown lines and wrinkles are the only outcome, even if higher doses of OnaBTX-A are subsequently injected.

Generally, glabellar frown lines in women can be satisfactorily treated with a total dose of about 20–30 U of OnaBTX-A injected into the standard five injection sites (Figure 13.14).[46–48] Men, on the other hand, usually require a significantly higher dose of OnaBTX-A (40–80 U) injected at seven or more sites across the glabella and medial brow to produce a reasonable effect that lasts at least 3–4 months (Figure 13.15).[49–53] When glabellar lines are deeper, longer, or thicker on one side of the midline, that set of medial brow depressor muscles (e.g., procerus, depressor supercilii, and medial aspect of the orbital orbicularis oculi) should receive a slightly higher dose of OnaBTX-A than the medial brow depressors on the contralateral side. Especially when treating men and those patients who have the "V" and deep "parallel lines" patterns of glabellar wrinkles (see Figure 13.21), the two additional injection points can be given along with the standard five injection points to reduce these deep glabellar lines effectively (Figure 13.13). The two additional injections usually are given *superficially* as one injection over the midpupillary line, bilaterally, which is in the vicinity where the lateral fibers of the corrugator supercilii pass upward and through the interdigitating fibers of the frontalis and orbicularis oculi and attach to the undersurface of the skin. Superficial injections avoid weakening the interdigitating fibers of the frontalis and orbital orbicularis oculi thereby avoiding brow ptosis, while injections given at least 3–4 cm above the bony orbital rim or 2–3 cm superior to the superciliary arch or ridge at the midpupillary line prevent, blepharoptosis (Figure 13.14).

At one time, there were some injectors who preferred treating the glabella separately in one session first, before injecting the frontalis in a different, later session, especially with first-time patients.[41,54] This concern might have been justified in the earlier years when injection techniques were just being developed, especially since high doses of

Figure 13.14 Standard five injection points for treating glabellar lines in a female frowning (a) before and frowning (b) 3 weeks after an OnaBTX-A treatment.

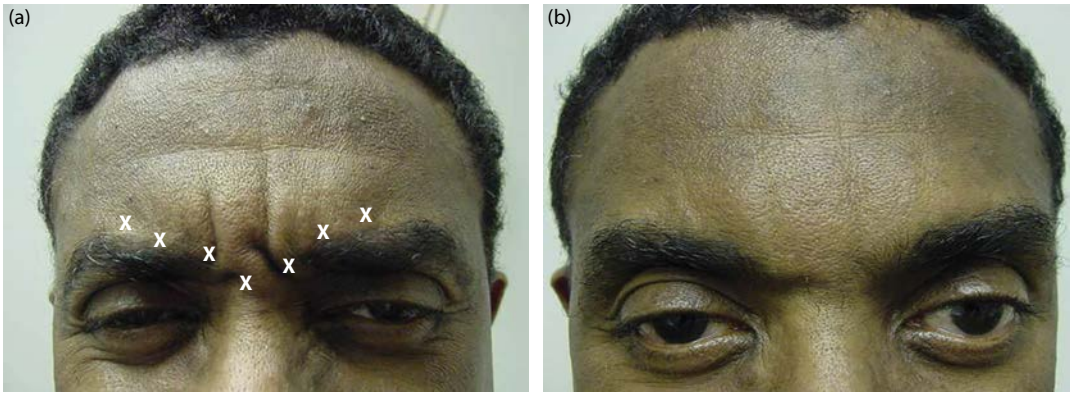

Figure 13.15 Standard seven injection points for treating stronger glabellar muscles causing deeper furrows and frown lines in a 51-year-old male (a) before and (b) 1 month after an OnaBTX-A treatment in a forced frown.

OnaBTX-A were being injected into the forehead. By injecting both the glabellar depressor muscles at the same time as the one brow elevator muscle, overdosing with total immobility of the forehead and glabella frequently was seen. At times, even brow ptosis was inevitable with those previously recommended doses.[41] With the evolving aesthetics and appeal of a "less frozen" look to the forehead, along with the recent FDA approval of injecting OnaBTX-A into the frontalis to reduce the appearance of horizontal forehead lines and into the lateral orbital orbicularis oculi to reduce the appearance of crow's feet, most injectors are now treating the entire upper one-third of the face during the same session effectively and safely (Figure 13.1).[42,55,56]

Treating glabellar lines with OnaBTX-A and producing optimal results are not simple tasks. There have been many injection patterns reported in the literature over the years, and they all produce optimal results when the ideal patient is treated appropriately with a given injection pattern. This leads one to believe erroneously that any injection pattern will work and so injecting OnaBTX-A is easy. However, this is not quite the case (see the glabellar patterns in Figures 13.20 through 13.26).

What is most important for a successful treatment outcome is for the physician injector to evaluate the patient comprehensively prior to treatment and to understand why certain wrinkles are formed and which muscles are creating them. Once a sound assessment is made and a justifiable treatment approach is designed, it does not matter which of the injection patterns one uses. Patients should be treated individually according to their idiosyncratic pattern of muscle movements and the resultant wrinkles they produce. A three, five, seven, or even more injection-point pattern can be used if it is appropriate for that particular patient.[57,58] However, the novice injector needs a point of reference; a standard of injection patterns to guide him or her during their initial treatment sessions. As the neophyte injector acquires a better understanding of the functional anatomy and its responses to different patterns of injections with OnaBTX-A, then a more directed and personalized approach to OnaBTX-A injections will automatically develop. The physician injector should also not forget to identify, photograph, and indicate to the patient prior to all OnaBTX-A injections any variation in the anatomy that might be present and cause the patient's eyebrows to be asymmetric. It appears that as much as 45%–65% of the general female and male population has some form of brow asymmetry prior to ever being treated with a BoNT (author's personal observation). The patient's permanent clinical record should contain photographic documentation along with a written summary of the physician's clinical assessment and conversation with the patient addressing any idiosyncrasies and asymmetries the patient may possess. It is absolutely necessary to include in the record, the patient's response to the conversation, including acknowledgment of any particular anatomical differences, in addition to a written and signed consent for treatment before initiating treatment with any BoNT.

The pretreatment position and symmetry or asymmetry of the eyebrows and eyelids will dictate the technique with which one will need to treat the glabellar frown lines (Figure 13.16). In women whose eyebrows

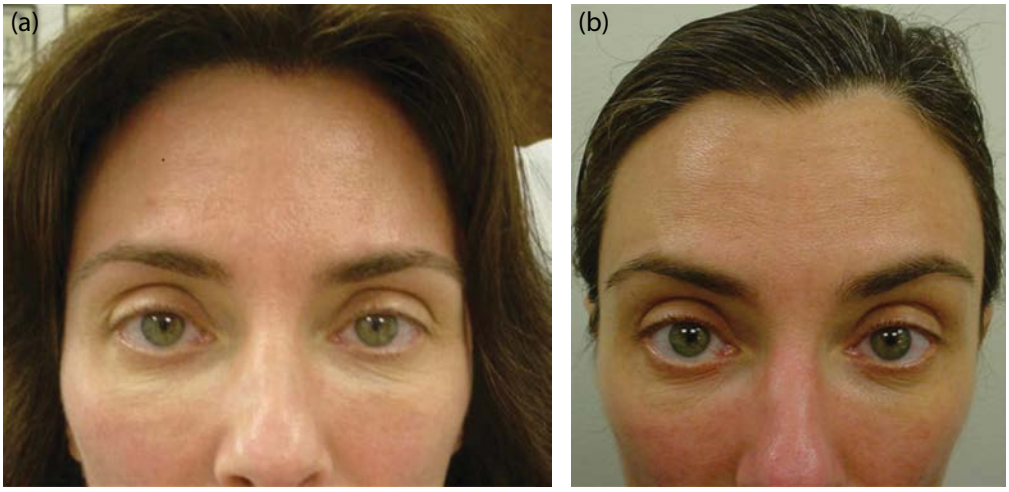

Figure 13.16 Woman with eyebrows barely arched (a) before strategically placed injections of OnaBTX-A were placed into the brow depressors. Same patient (b) after treatment with eyebrows more highly arched.

are barely arched, strategically placed injections of OnaBTX-A into the brow depressors can elevate the eyebrows by allowing the untreated lower fibers of the frontalis to raise the eyebrows unopposed by the weakened interdigitating fibers of the corrugator supercilii, procerus, orbicularis oculi, and depressor supercilii (Figures 13.17 and 13.18).

To treat the glabellar frown lines with optimal, reproducible results and the least amount of complications, precise injections of relatively concentrated doses and low volumes of OnaBTX-A must be used on both sides of the midline whether the doses are equal. With the patient sitting up or in the semireclined position, gently palpate the medial aspect of the eyebrows as the patient squints and frowns. After locating the belly of the corrugator supercilii with the second and third fingertip pads of the nondominant hand, ask the patient to raise the eyebrows as high as possible, while keeping the tip of the index finger positioned over the thickest part of the belly of the corrugator supercilii (Figure 13.17). Prior to inserting the needle, the index finger of the nondominant hand should be advanced slightly cephalad and above the point of maximal muscle thickness. This usually is just above the eyebrow. The thumb is placed at the margin of the supraorbital bony rim. The bore of the needle tip should be pointed upward and away from the globe. The needle is inserted into the skin at a 60°–90° angle and allowed to glide over the upper edge of the thumb between it and the index finger. The needle is slowly advanced into the belly of the corrugator supercilii in an oblique direction, slightly upward and lateral, until penetration into the belly of the corrugator can be felt. Entry into a muscle usually is detected when, after passing through the dermis and subcutaneous tissue, an abrupt release of resistance is felt as the needle penetrates fascia and muscle fibers. At this point, the needle may or may not impinge on the bone. If it strikes a bone, the patient will sense sharp pain. The needle should then be withdrawn gently enough to move away from the bone, but not far enough to exit the belly of the corrugator. The needle should always remain deep within the muscle, medial to the supraorbital notch and approximately 2–2.5 cm superior to the supraorbital bony margin during injections of the BoNT. The physician injector must refrain from striking the frontal bone with the needle tip, so as not to inflict any additional pain to the patient, which occurs when the periosteum is pierced. However, this may not be avoidable when first learning how to find the deeply seated corrugators and effectively inject them at the proper depth.

Figure 13.17 Technique of injecting the medial corrugator supercilii (note the position of the thumb and index finger of the nondominant hand).

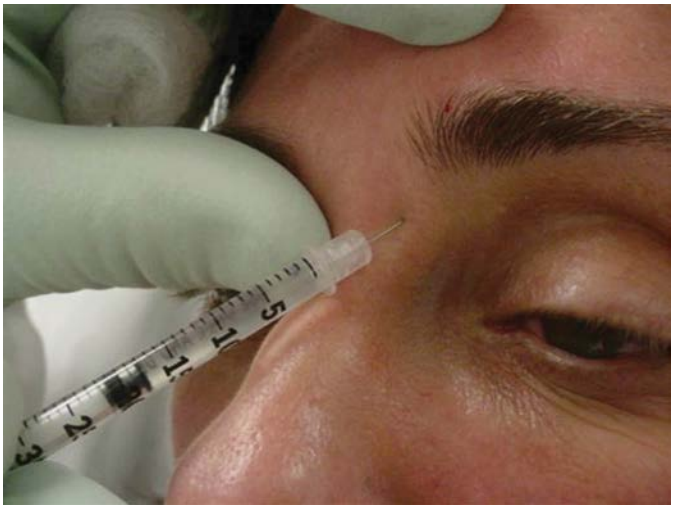

Figure 13.18 Technique of injecting the medial aspect of the orbicularis oculi and depressor supercilii starting at the most infero-medial aspect of the superciliary arch. Note the 60° angle and superficial placement of the needle, approximately 2 cm directly above the ocular caruncle.

Placing the nondominant index finger and thumb on the brow just above and below the eyebrow prior to injecting OnaBTX-A serves many purposes. It prevents injecting OnaBTX-A too low and close to the orbital rim. When direct pressure is applied with the thumb inferior to the border of the supraorbital bony rim, Binder et al. felt they could reduce the migration of OnaBTX-A behind the orbital septum and avoid blepharoptosis.[59] This maneuver also helps identify the location and position of the corrugator supercilii because the muscle can be felt between the index finger and thumb with light palpation. *Slow*, *deliberate*, and *gentle* injections prevent OnaBTX-A from dispersing into surrounding, nontargeted muscle fibers. While in position, inject 4–10 U of OnaBTX-A into the strongest portion of the muscle, which is located approximately 10–15 mm superior and 15–20 mm lateral to the nasion or the center of the concavity at the nasal radix.[31–35,57–59]

Next, watch as the patient frowns again, and notice to what extent the midbrow adducts toward the glabella. Stronger corrugators will visibly pull the skin medially toward the midline just above the eyebrows in the vicinity of the mid-pupillary line. In some patients, additional vertical corrugations along the brow parallel to the central vertical glabellar lines also will be formed (see Trindade de Almeida's glabellar "converging lines" in Figures 13.24 through 13.27). These corrugations can be reduced by injecting 2–4 U of OnaBTX-A *intradermally* into the skin just above the middle of the eyebrow where the corrugators insert into the undersurface of the midbrow, which is just medial to the supraorbital notch or midpupillary line. This point is identified by an obvious dimpling (corrugator dimple) of the skin as the patient forcibly frowns (Figure 13.8b). These more lateral injections over the midbrow should be applied first by asking the patient to raise their eyebrows and then physically raising the center of the eyebrow with the thumb of the nondominant hand. Then approach the skin at a 45°–60° angle and injecting *superficially*, confirmed by raising a wheal. The fibers of the corrugators in this location are superficial and insert into the under surface of the skin. These injections should reduce the adduction of the brow and eliminate brow corrugations adjacent to glabellar frown lines and along the central brow (see Figures 13.25, 13.26a and b). If the injections are too deep, then fibers of the frontalis also will be affected and brow ptosis can result. If the injections are too low and close to the bony orbital rim, blepharoptosis will result.

Next withdraw the needle out of the skin and redirect the tip of the needle medially in the direction of the head of the eyebrow. Insert the needle 60°–90° to the skin surface at, or adjacent to the most medial aspect of the superciliary arch and eyebrow, approximately 2 cm

directly superior to the ocular caruncle at the inner canthus (Figure 13.18). Injections should be given superficially, and confirmed by raising a wheal. Approximately 2–6 U of OnaBTX-A at this point of maximum muscle contraction will treat the vertical muscle fibers of the medial orbital orbicularis oculi and the depressor supercilii. Because the fibers of the orbicularis oculi and depressor supercilii are closely adherent to the overlying skin at this location, injections can be given either intradermally or in the superficial subcutaneous plane. Superficial injections at this location also avoid puncturing the supratrochlear vessels and nerve. A pleasing vertically upward lift to the medial brow can be accomplished by this technique, if fibers of the frontalis are not inadvertently affected.[60,61] Gentle massage in an upward and lateral direction for a few seconds immediately after the injection helps relieve the typical acute pain of a transcutaneous injection. Heavy-handed massage will definitely disperse the OnaBTX-A beyond the target area and into muscle fibers not intended for treatment, that is, into the fibers of the lower frontalis, which can result in brow ptosis.

Next, treat the procerus with an injection of approximately 4–10 U of OnaBTX-A given between the eyebrows at the nasal root into the belly of the procerus (Figure 13.19). Some spread of the onaBTX-A into the interdigitating fibers of the depressor supercilii and medial fibers of the orbital orbicularis oculi often occurs, potentiating the weakening effect on all three muscles. The dose needed for this injection of OnaBTX-A will depend on the overall muscle strength and depth of the horizontal glabellar wrinkles that are present. The strength of the procerus can be determined by gently palpating the mid-glabellar area with the pads of the second and third fingertips of the nondominant hand, while the patient repeatedly squints and frowns. Glabellar wrinkles can be deeply fixed in the skin, especially the horizontal ones. Those that are more resistant to treatment with OnaBTX-A commonly are found in men and women who spend a lot of time outdoors or in front of a computer screen, because their glabellar muscles are significantly hypertrophied from frequent squinting. Intramuscular instead of subcutaneous injections of OnaBTX-A into the procerus should be performed by gently grasping the skin and soft tissue of the root of the nose between the thumb and the index finger of the nondominant hand. Then elevate the skin and muscle before placing the needle between the two fingers and injecting OnaBTX-A into one or two sites in the center of the nasal radix. This maneuver also will avoid the needle puncturing the nasal bone and causing additional unwarranted pain on the patient. The site of injection should be anywhere from 1 to 3 mm above or below the center of the nasion. The weaker muscle fibers of the procerus are injected with at least 2 U of OnaBTX-A, while the stronger ones usually can be injected with up to 10 U and possibly even more in one, two, or more injection points. The depressor supercilii already will have been partially treated by the injections given at the medial aspect of the superciliary arch and eyebrows when the medial orbital orbicularis oculi and the depressor supercilii are treated. Likewise, gentle massage performed in and around the nasal radix immediately after injecting the procerus also will result in some spread of the OnaBTX-A into the interdigitating fibers of the depressor supercilii and medial orbital orbicularis oculi.

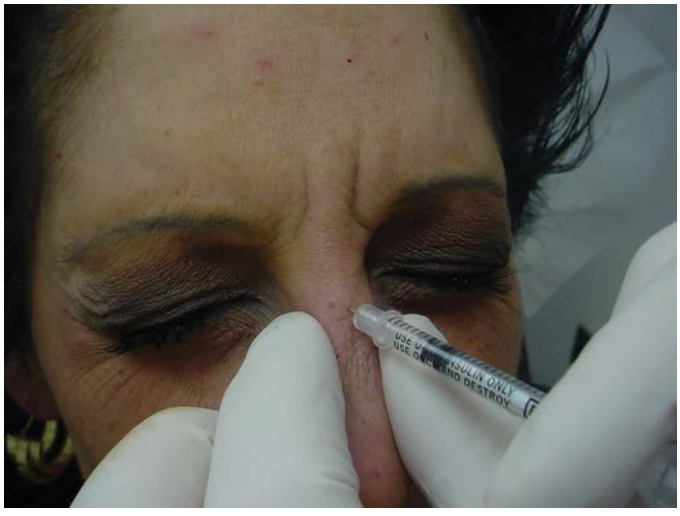

Figure 13.19 Technique of injecting the procerus (note the position of the index finger and the thumb of the nondominant hand).

Some patterns of glabellar frowning are seen more frequently than others.[27] The most common pattern observed by Trindade de Almeida and colleagues were those produced by the simultaneous adduction and depression of the skin of the glabella (64%). This occurs when the corrugators contract and parallel vertical lines are formed in the center of the glabella as the skin of the brow moves toward the midline. At the same time, the procerus pulls the skin of the brow inferiorly, forming horizontal lines across the root of the nose. There are two distinct variations of this most commonly seen pattern of glabellar frowning. The less frequently observed pattern (27%) of the two is what Trindade de Almeida et al. call the "U" pattern (Figure 13.20).[27] In these patients, the 5-point injection technique is corrective with 4–10 U of OnaBTX-A given at each injection point.[27] Stronger, more hyperkinetic corrugators and procerus produce a similar pattern of glabellar frown lines but they are deeper and more acute, resulting in a pattern that better resembles a "V." This was seen in 37% of the patients studied (Figure 13.21). Higher doses of OnaBTX-A in the 7-point injection pattern are usually necessary to diminish these lines.[27]

Another, less frequently observed pattern, named the omega pattern, was seen in only (10%) of patients. When these individuals frown, their eyebrows initially adduct centrally and glabellar skin drops slightly forming deep parallel vertical lines. Then with continued forceful frowning the upper part of the center of the glabella will slide upward toward the frontal hairline, forming deep horizontal furrows and folds. The medial end of the brows continues to move inferiorly producing slight horizontal lines along the lateral sides of the nasal radix to create an overall wrinkle pattern that outlines the Greek letter omega (Ω) (Figure 13.22).[27] In these individuals the corrugators and fibers of the medial brow depressors seem to contract in unison with the muscle fibers of the lower to mid central frontalis. Injections of 4–8 U or more of OnaBTX-A at multiple sites into the corrugators and medial brow depressors, while 2–6 U of OnaBTX-A into the procerus and 2–6 U into the lower medial frontalis in divided doses at multiple sites will diminish the omega pattern of glabellar frowning.[27]

The "inverted omega" pattern was the least encountered (6%) of all the five patterns identified by the Trindade de Almeida group and was attributed to individuals with a flat nasal radix, which is commonly found in the Asian population (Figure 13.23).[27] When these individuals frown the center of their glabella drops inferiorly along with their eyebrows, creating deep horizontal wrinkle lines across the nasal radix but minimal to no vertical glabellar lines.[27,62] In such individuals, treat the procerus with 6–10 U of OnaBTX-A and the depressor supercilii and medial orbital orbicularis oculi with 4–8 U of OnaBTX-A and the corrugators with 4–8 U of OnaBTX-A.

Another less commonly seen glabellar frown pattern (20%) is the one where there is just adduction of the mid-to-lateral brow toward the center of the glabella. There is minimal vertical movement of the glabella either inferiorly or superiorly because there seems to be a neutralizing balance of movements between the procerus and the frontalis that produces barely perceptible or no horizontal glabellar frown lines in this "converging arrows" (or "parallel lines," the author's preferred term) pattern (Figure 13.24).[27] In these individuals, the extent and depth of the lateral-to-medial brow corrugations are dependent on the

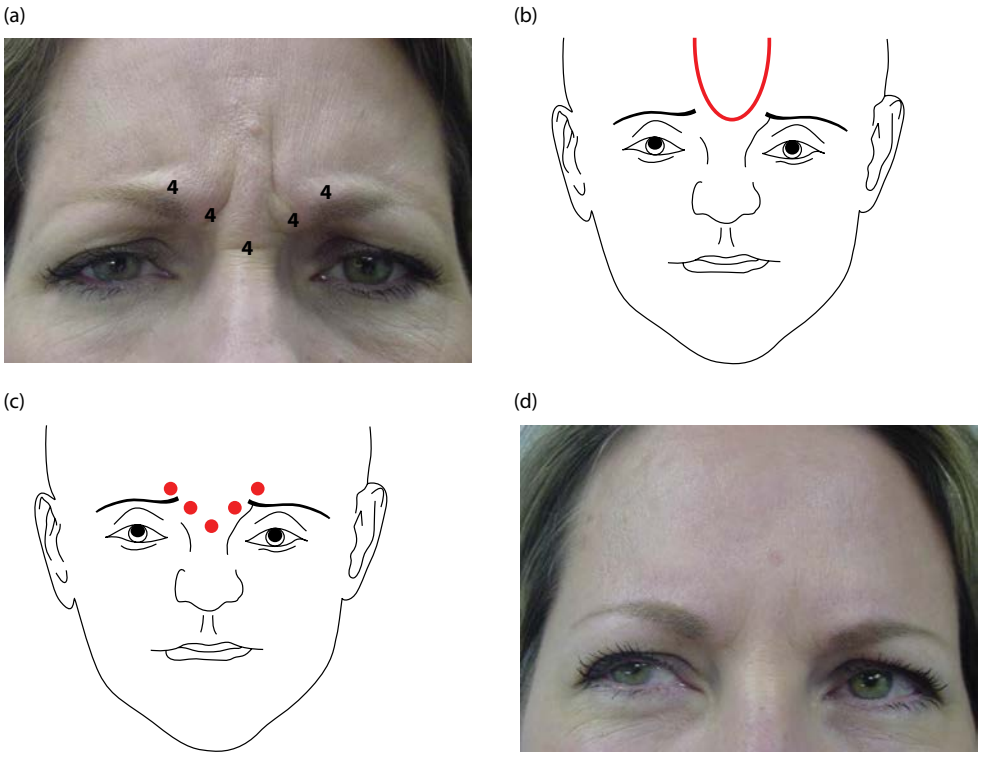

Figure 13.20 (a) Mild to moderate approximation and depression of the medial brow forming the typical and one of the most commonly seen patterns of glabellar frown lines (the "U" pattern). (b) Commonly seen "U" type of glabellar contraction and resulting pattern of frown lines. Muscles involved: predominantly the corrugators and procerus (see Reference 26). (c) Five-point pattern of injection for this commonly encountered glabellar "U" pattern (see Reference 26). (d) Same patient frowning 2 weeks after an OnaBTX-A treatment.

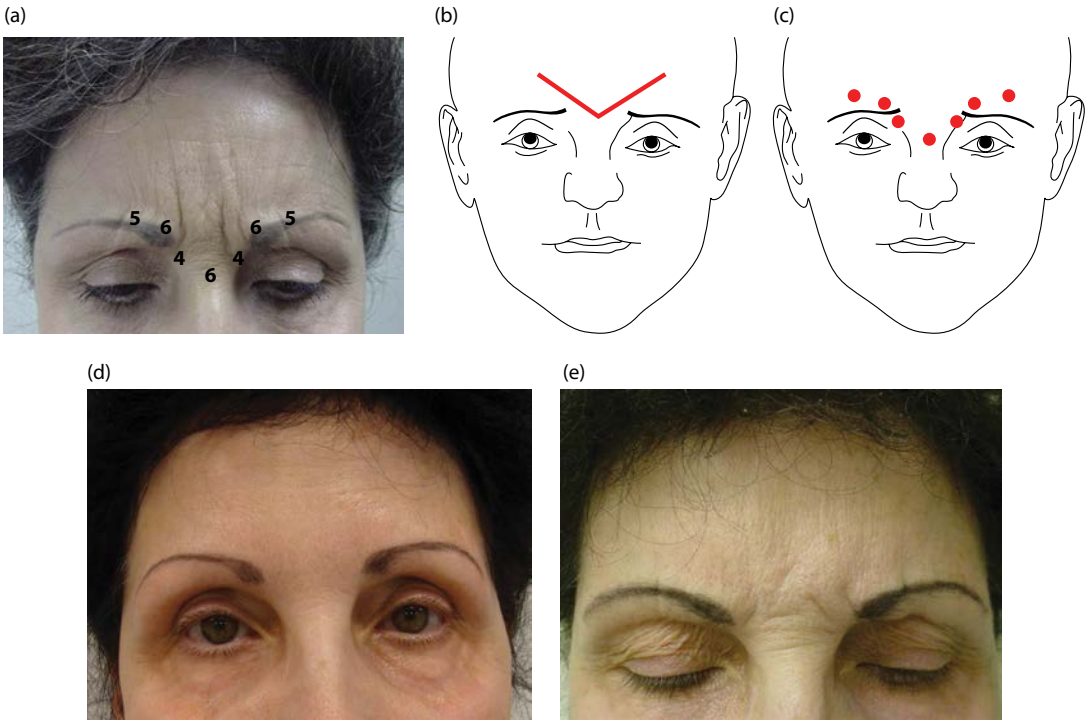

Figure 13.21 (a) Moderate to severe approximation and depression of the medial brow forming the more commonly seen pattern variation identified by very deep glabellar frown lines (the "V" pattern) in a 62-year-old woman. (b) Vigorous glabellar contraction and resulting "V" pattern of frown lines. Muscles involved: strong corrugators, procerus, and medial aspect of the orbicularis oculi (see Reference 26). (c) Seven-point pattern of injection for this exaggerated glabellar "V" pattern. Higher doses of OnaBTX-A are usually needed for treatment (see Reference 26). (d) Same patient at rest and (e) frowning 2 weeks after an OnaBTX-A treatment.

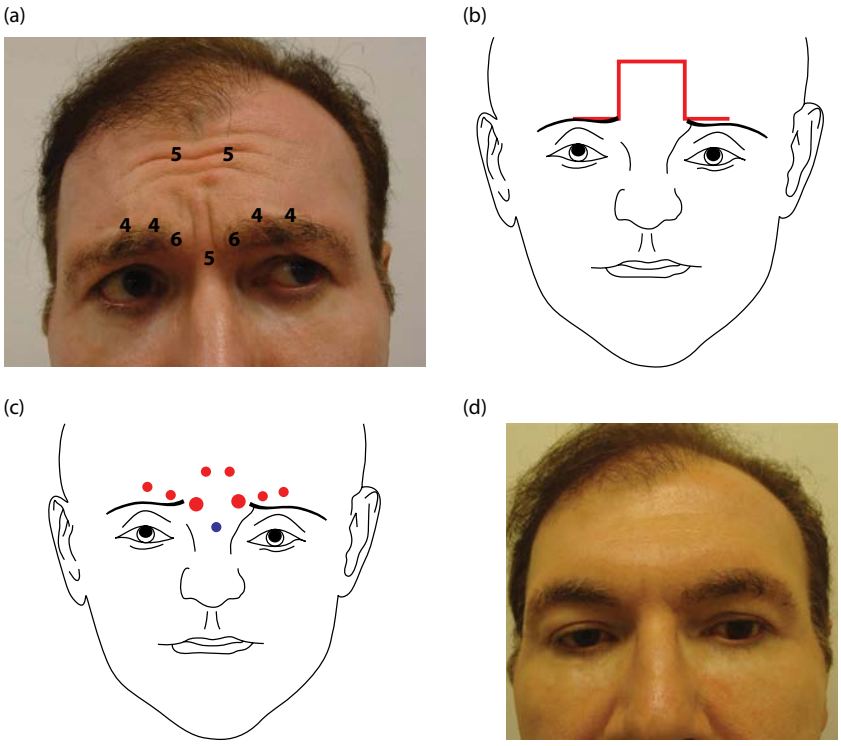

Figure 13.22 (a) Adduction of the medial eyebrows and elevation of the center of the glabella along with depression of the mid and lateral brow forms the "omega" pattern of glabellar frowning. (b) This type of glabellar contraction results in the "omega" pattern of frown lines. Muscles involved: corrugators and lower central frontalis (see Reference 26). (c) This eight-point pattern of injection is used for the glabellar "omega" pattern. Higher doses of OnaBTX-A are needed for the corrugators and lower central frontalis and usually none for the procerus (blue, author's modification). (d) Same patient frowning 2 weeks after an OnaBTX-A treatment. ([c] From Trindade de Almeida AR et al. *Dermatol Surg* 2012; 38(9): 1506–15.)

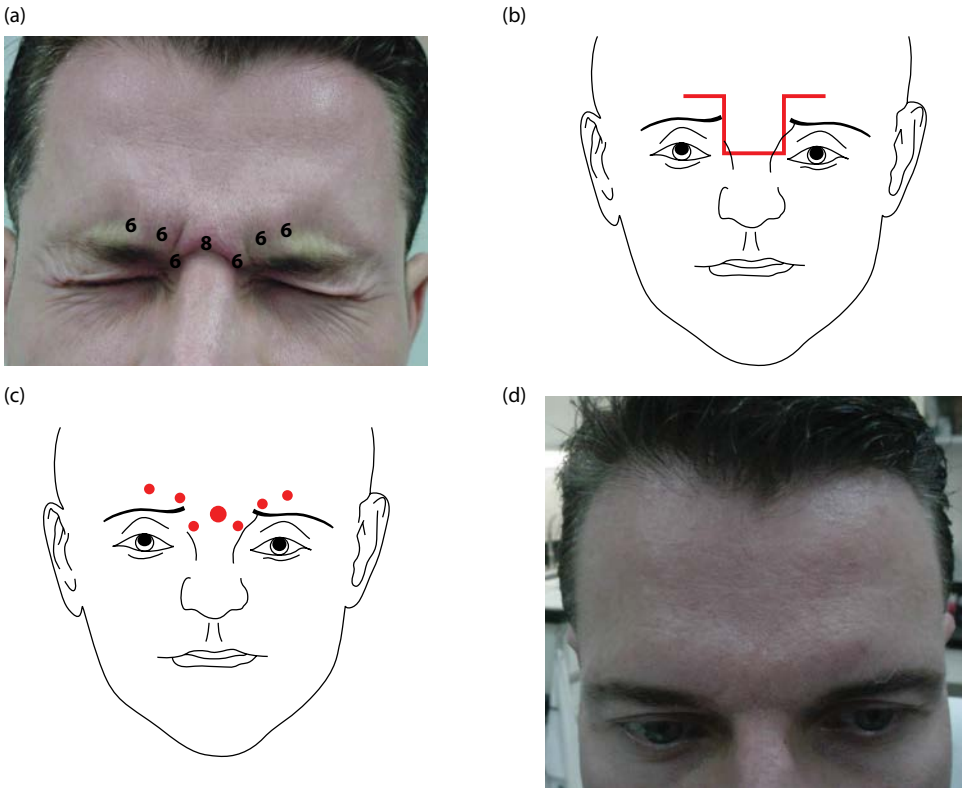

Figure 13.23 (a) More depression than adduction of the medial brow forms the "inverted omega" pattern of glabellar frowning. Note the deep horizontal line at the root of the nose. (b) Less frequently seen type of glabellar adduction producing an "inverted omega" pattern of frown lines. Muscles involved: mostly the procerus and depressor supercilii (see Reference 26). (c) A different seven-point pattern of injection for this uncommon glabellar "inverted omega" pattern. Higher doses of OnaBTX-A are needed for the procerus (see Reference 26). (d) Same patient frowning 2 weeks after an OnaBTX-A treatment.

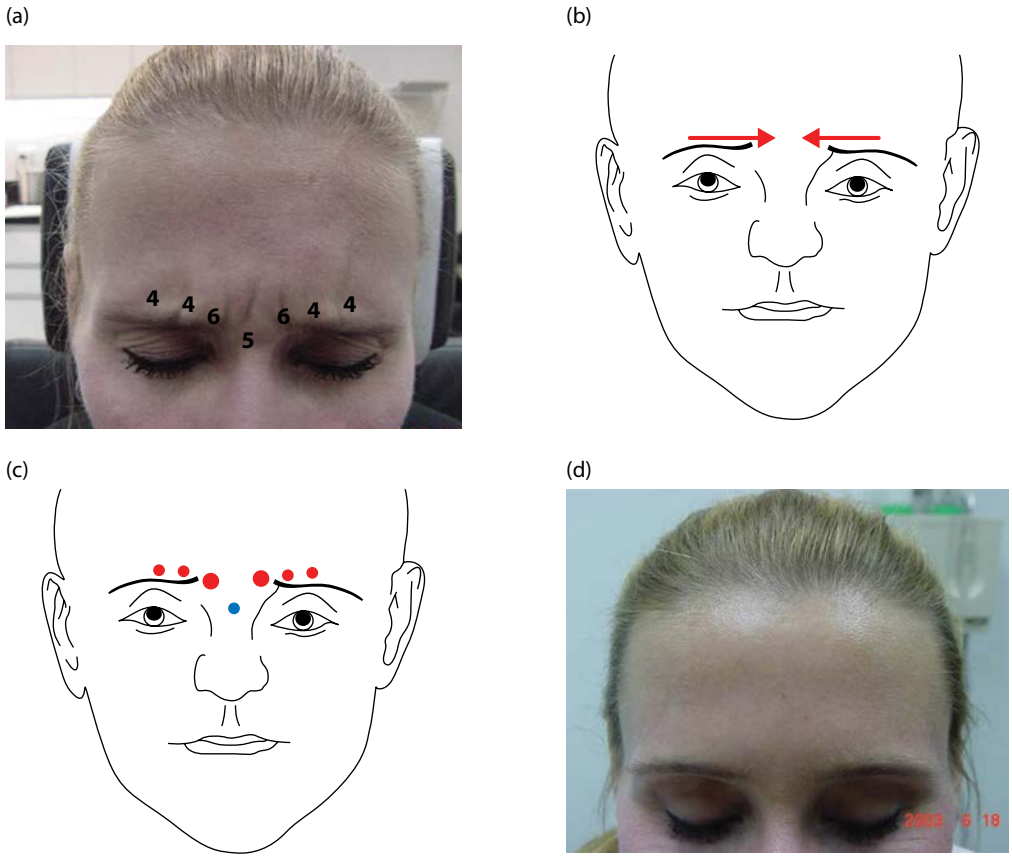

Figure 13.24 (a) Adduction and approximation mainly of the eyebrows form this "converging arrows" pattern of glabellar "corrugated" frowning. There is little to no depression or elevation of the medial brow. (b) This is an uncommon type of glabellar contraction resulting in a "converging arrows" or "parallel lines" (author) pattern of frown lines. Muscles involved: mainly the corrugators and the upper mid horizontal *orbital* orbicularis oculi. (see Reference 26). (c) This six-point pattern of OnaBTX-A injections targets mainly the corrugators and the mid-section of the upper orbital orbicularis oculi (blue, author's modification). (d) Same patient frowning 3 weeks after an OnaBTX-A treatment. ([c] From Trindade de Almeida AR et al. *Dermatol Surg* 2012; 38(9): 1506–15.)

person's age and the amount of skin laxity present. Increased skin laxity promotes an increased number of vertical corrugations along the medial brow. Injections of a higher than usual dose (6–10 U or more) of OnaBTX-A into the belly of the corrugator supercilii, along its body and into the tail, will nicely relax the excess wrinkling across the brow (Figures 13.25 and 13.26). The medial horizontal muscle fibers of the upper orbital orbicularis oculi also may play a role in the brow corrugations, which would then require one or more *intradermal* injections of 2–6 U of OnaBTX-A, approximately 2–3 cm above the supraorbital bony rim at the midpupillary line and medially along the supercilliary arch if corrugations persist after treatment. The procerus also can be treated with 4–10 or even more U of OnaBTX-A when indicated (author's preferred technique) (see Figures 13.22 and 13.24).[27]

Outcomes (Results) When Treating the Central Brow (Glabella) (See Appendix 4)

A clear and accurate record of all the units and where they were injected must be maintained of each treatment session on all patients. Meticulously detailed clinical records facilitate reproducible results. Consequently, when proper injection techniques are followed, results are predictable and reproducible. The vertical lines between the eyebrows and the horizontal ones across the root of the nose will diminish and eventually disappear. Glabellar and midbrow corrugations if treated appropriately also will be reduced and temporarily eliminated.

There can be a noticeably high arching of the eyebrows of approximately 2–3 mm, caused by the levator action of the frontalis in those patients whose glabellar depressors have been substantially weakened, when the interdigitating muscle fibers of the frontalis immediately above the brow have not (Figure 13.27).[60–64] There also can be an increase in the horizontal distance between the eyebrows along with an elevation of the medial aspect of the eyebrows when glabellar frown

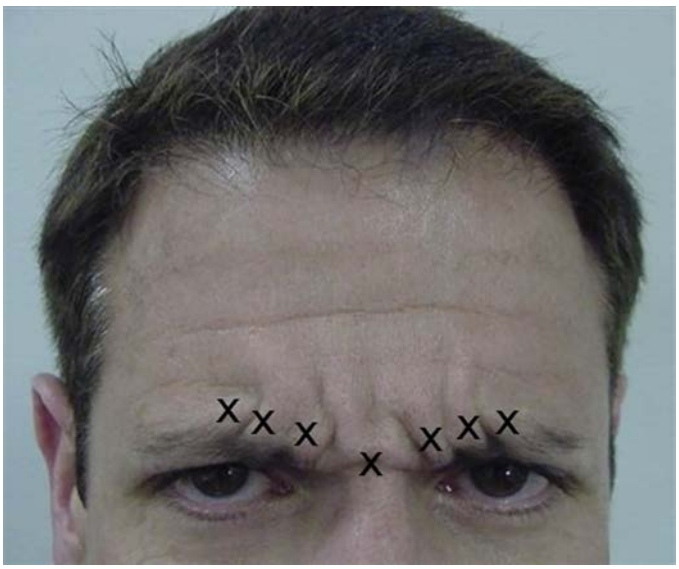

Figure 13.25 Converging arrows or parallel lines pattern of glabellar wrinkling before treatment in a 48-year-old male. Note the strong procerus contraction producing the deep horizontal line across the nasal radix.

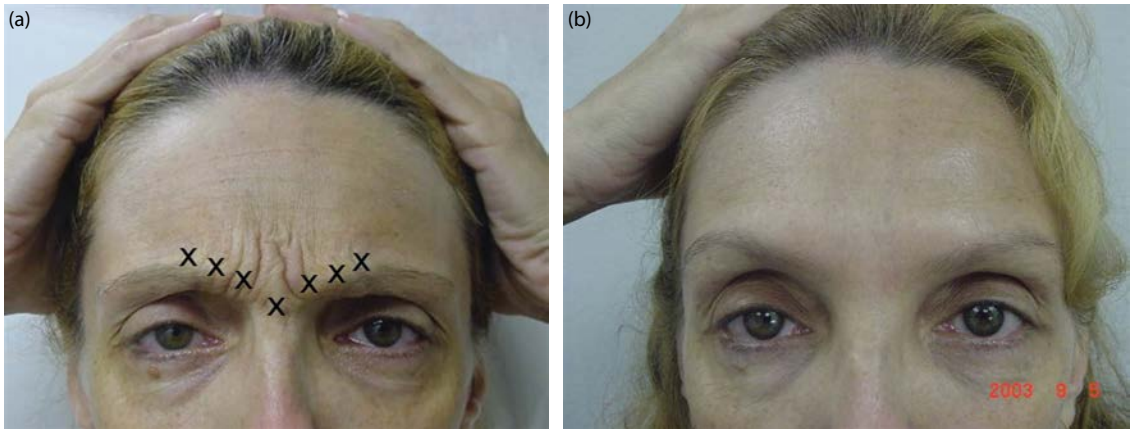

Figure 13.26 (a) Converging arrows or parallel lines pattern of glabellar wrinkling before treatment in a 61-year-old female. Note the absence of procerus contraction and horizontal line across the nasal radix. (b) Same patient 2 weeks after treatment with OnaBTX-A.

Figure 13.27 Arching of the eyebrows while frowning (a) before and (b) after OnaBTX-A treatment in a 52-year-old woman with a converging arrows pattern of glabellar wrinkling. (c) Same patient at rest. Note the nicely arched eyebrows.

lines are treated with OnaBTX-A because of the dynamic relationship between the brow depressors (corrugator supercilii, depressor supercilii, orbicularis oculi, and procerus) and their brow elevator (frontalis), (Figure 13.28).[60,62] Accentuated high arching eyebrows may be attractive in most women, but usually not in men. To avoid a high arching brow in men, an additional 2–6 U of OnaBTX-A can be injected intradermally or intramuscularly into the frontalis 2.5–4.0 cm above the supraorbital ridge at the midpupillary line. This maneuver should straighten a high arching eyebrow without provoking a low-lying brow ptosis, (see section on "horizontal forehead lines").

Usually, one can expect the effect of an OnaBTX-A treatment of glabellar frown lines to last at least 3–4 months. Patients who are treated for the very first time with OnaBTX-A may experience some asymmetry and therefore should return for an evaluation and possible touch-up injections within 2–3 weeks after a treatment. Frequently, the effects of OnaBTX-A may last longer with each subsequent treatment session. Therefore, after the first 2–3 years of regularly scheduled treatment sessions every 3–4 months, some patients may prefer to return for their next retreatment at 5- or 6-month intervals (see Appendix 3).

Figure 13.28 This 37-year-old patient had both the glabella and the forehead frown lines treated during the same session. (a) Frowning before OnaBTX-A treatment. (b) Same patient frowning 2 weeks after treatment. Note the increase in interbrow distance after treatment and elevation of the medial brow.

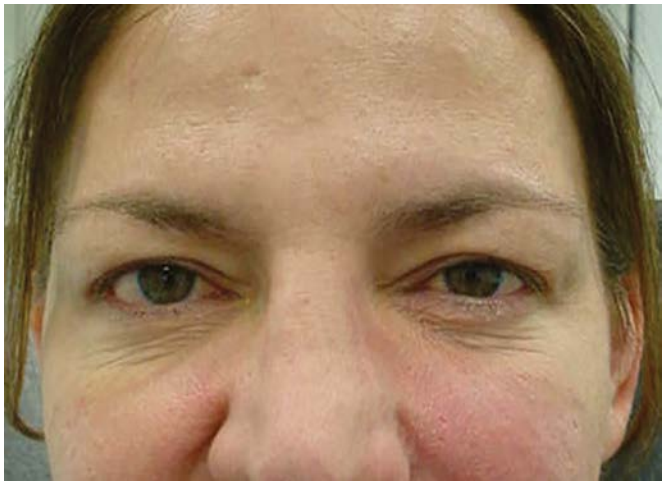

Figure 13.29 Eyelid ptosis in a 49-year-old patient. Note a drop of 1–2 mm of the left upper eyelid that occurred approximately 10 days after an OnaBTX-A treatment.

Complications (Adverse Sequelae) When Treating the Central Brow (Glabella) (See Appendix 6)

Ptosis of the upper eyelid is one of the most significant and frequently occurring complications seen when injecting OnaBTX-A in and around the glabella (Figure 13.29).[8,54,64] It is felt by many that blepharoptosis is caused by the migration of injected OnaBTX-A through the orbital septum, weakening the levator palpebrae superioris (Figures 13.10 and 13.30). This can occur more frequently in older patients in whom the barrier function of the orbital septum is attenuated, or when large volumes of highly diluted OnaBTX-A are injected quickly, deeply, low down and close to the bony supraorbital margin at the midpupillary line. Occasionally at this location, some actual muscle fibers of the levator palpebrae superioris can extend anteriorly into the levator aponeurosis, allowing for easy access of the OnaBTX-A that has diffused through the barrier of the orbital septum to weaken some of the muscle fibers of the levator palpebrae superioris, and produce ptosis of the upper eyelid (Figure 13.10). Unexpected blepharoptosis in a younger patient is usually the result of forceful injections of OnaBTX-A placed too deeply in the area of the midbrow, particularly with high volumes of highly diluted OnaBTX-A. Another reason for inadvertent blepharoptosis is when OnaBTX-A is routinely injected at a fixed distance of 2 cm from the upper border of the *eyebrows* instead of 2 cm from the bony superciliary arch or ridge. In most men and some women, their eyebrows are situated low on the brow and directly over the bony orbital rim (see brow positions below). Injecting OnaBTX-A just above the eyebrows in these individuals puts their levator aponeurosis at risk of contact with the BoNT as the aponeurosis exits the superior margin of the bony orbit (Figure 13.10). OnaBTX-A then can easily weaken any exposed levator muscle fibers contiguous with the aponeurosis, reducing the levator action of the upper eyelid and causing blepharoptosis.

Ramey and Woodward demonstrated by their cadaveric study using injectable blue methylene dye that deep and forceful injections of OnaBTX-A in the vicinity of the supraorbital foramen potentially could allow the toxin to penetrate into the superior aspect of the bony orbit, presumably through the foramen, and affect the levator palpebrae superioris.[65] After injecting 1% methylene blue deep into the corrugator supercilii just above the supraorbital foramen, they found, by an anterior dissection approach, the anterior orbital septum and anterior surface of the levator aponeurosis stained blue. They also found by a posterior dissection approach the intraorbital surface of the periosteum and the periorbita stained with the blue dye. There also was blue dye staining the superior surface of the levator palpebrae superioris and adjacent tissues, including the superior ophthalmic vein and some of its tributaries. From this study, they hypothesized two mechanisms of blepharoptosis. First, BoNT may reach the levator palpebrae superioris as it traverses the pre-periosteal plane anteriorly after a forceful injection. Second, BoNT may track along tributaries of the superior ophthalmic vein, which travels along the levator palpebrae superioris for part of its course. Consequently, blepharoptosis may be avoided by carefully positioning the injection needle far away from the supraorbital foramen and using a gentle, slow injection technique with highly concentrated, low volume BoNT. Deep injections, particularly those overlying the bulk of the supraorbital nerve or near branches of the superior ophthalmic vein, should be avoided to prevent perineural or perivascular infiltration around the levator palpebrae superioris.[65,66]

To avoid injecting OnaBTX-A too close to the bony orbital rim, one should inject superficially and at a point at least 3–4 cm superior to the bony orbital rim or 2–3 cm superior to the superciliary ridge or arch. Any injection less than 3 cm away from the bony orbital rim, regardless of where the eyebrow sits over the superciliary ridge, will allow OnaBTX-A to reach the levator aponeurosis directly or indirectly and weaken its proximal muscle fibers and cause blepharoptosis.

In female patients, the eyebrows commonly sit approximately 5 cm above the upper eyelid crease. On the other hand, men's eyebrows usually grow directly over or below the superciliary ridge. There are some women, however, whose eyebrows rest just as low as men's, that is, at or below the superciliary ridge. Instead of using the eyebrows as a point of reference from where to inject, the upper orbital bony margin or rim should be the reference point. Therefore, injections should be placed no lower than 3–4 cm above the upper margin of the bony orbit.

Blepharoptosis, when it occurs, is seen as a 1–2 mm or more drop in the upper eyelid, obscuring the upper border of the iris (Figure 13.30).[64] Ptosis can appear as early as 48 hours and up to 7–10 days after an OnaBTX-A injection and usually can last 2–4 weeks or even longer. The margin to reflex distance (MRD) is a way to measure and diagnose upper lid blepharoptosis. MRD is defined as the distance from the mid-pupil corneal light reflex to the lower cutaneous margin of the upper eyelid with the eyes in forward primary gaze. A normal MRD should equal approximately 4 mm in vertical height. Blepharoptosis is present when an MRD is measured less than 2 mm. Moreover, an asymmetrical comparative height of more than 1-2 mm between both eyes indicates a certain degree of unilateral compensatory brow elevation[67] (Figure 13.31b).

An antidote for blepharoptosis is apraclonidine 0.5% eye drops (Iopidine®, Alcon Laboratories, Inc., Fort Worth, TX). The ocular instillation of apraclonidine, an alpha-2-adrenergic agonist with mild alpha-1 activity, causes Müller's muscle (a nonstriated, smooth, sympathomimetic levator muscle of the upper eyelid) to contract, temporarily raising the upper eyelid approximately 1–2 mm (Figures 13.10 and 13.30). One or two drops should be instilled into the affected eye. If ptosis persists after 15–20 minutes, intraocular instillation of an additional one or two drops may be required before the affected eyelid will elevate. This procedure can be repeated three to four times a day. It is advisable to use apraclonidine eye drops only when absolutely necessary because approximately 20% of patients can develop a contact conjunctivitis with frequent use. The mydriatic and vasoconstrictor phenylephrine (Mydfrin 2.5%, Alcon Laboratories, Inc., Fort Worth, TX, or Neo-Synephrine® HCl, 2.5% Ophthalmic Solution, USP, Paragon BioTeck, distributed by Bausch & Lomb [a division of Valeant, Laval, Quebec, Canada] also known by other brand names: AK-Dilate, AK-Nefrin, Isopto Frin, Neofrin) is an alpha-1 agonist that also can be used when apraclonidine is not available.[41] However, there are more potential side effects associated with the use of phenylephrine than with apraclonidine. Specifically, even when only the 2.5% ophthalmic solution is used, phenylephrine can increase intraocular pressure, cause systemic allergic and urticarial reactions,

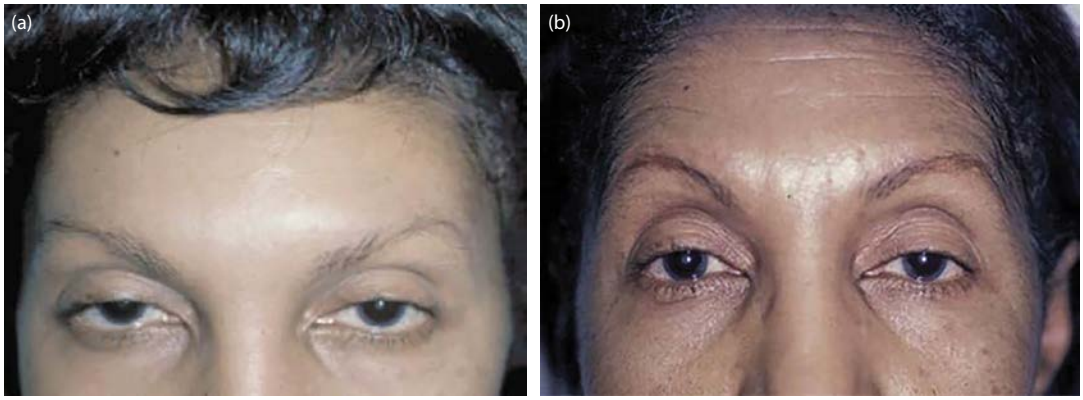

Figure 13.30 (a) Eyelid ptosis in a 67-year-old patient. Note a drop of 1–2 mm of the right upper eyelid that occurred approximately 7 days after OnaBTX-A was used to treat forehead and glabellar wrinkles. Patient is actively blinking. (b) Same patient 30 minutes after the instillation of 2 drops of apraclonidine into the right eye.

local contact and irritant dermatitis and acutely exacerbate narrow angle glaucoma, cardiac arrhythmias, and hypertension. Because it also is a mydriatic, even one drop of phenylephrine will prevent the patient from accommodating as usual and visual acuity can be compromised. Naphazoline (Naphcon-A®, Alcon Laboratories, Inc., Fort Worth, TX) is another ophthalmic decongestant containing adrenergic properties that can be used to stimulate Műller's muscle to contract, temporarily lifting a ptotic upper eyelid.[64] The different brands of naphazoline (e.g., Vasocon-A®, [naphazoline HCl 0.05%, antazoline phosphate 0.5%,], Novartis Ophthalmics, East Hanover, NJ) also contain different antihistaminic additives, and because of their multiple side effects profile, should be used infrequently and with caution, strictly on an as-needed basis when utilizing them just to elevate blepharoptosis. When a patient cannot tolerate any of the topical anti-blepharoptosis medications, then additional injections of OnaBTX-A into the palpebral orbicularis oculi, can be attempted to reduce the remaining strength of the upper eyelid depressor (Figure 13.31a).[64] For the expert, well-seasoned injector, subdermal injections of low-dose, low-volume OnaBTX-A into the pretarsal orbicularis oculi, the antagonist to the upper lid levator (levator palpebrae superioris) can be performed. Similar injections are used to treat various blepharospastic disorders. Depending on the severity of the blepharoptosis, inject 0.5 unit and no more than 1.5 units of OnaBTX-A subdermally into the extreme medial and lateral aspects of the pretarsal orbicularis oculi just above the lid/lash margin, so as to avoid any further exposure of the centrally located muscle fibers of the levator palpebrae superioris with additional onaBTX-A. (Figure 13.31a).[64] An obvious wheal should be produced with these injections.

Blepharoptosis also can be induced secondarily when the lower fibers of the frontalis are weakened, producing a drop in the height of the brow. The weight of the ptotic brow then impinges on the upper eyelid and causes it to drop, narrowing the vertical palpebral aperture or fissure. This secondary blepharoptosis seems to occur more frequently in older patients who possess dermatochalasis of the skin of the eyelids and brow. To compensate for a heavy, lax brow, some individuals, regardless of age, involuntarily use the lower fibers of their frontalis to lift the soft tissue of the brow, which also maintains their upper eyelids in a constantly raised position.[64] When this compensatory brow lifting of the frontalis is weakened by BoNT, a secondary blepharoptosis results.

Careful examination of the upper eyelids for the presence of a separation or weakness of the levator palpebrae superioris can be a preinjection method to identify individuals at risk for true blepharoptosis and to avoid its occurrence after a treatment with any BoNT. The functional strength of the levator palpebrae superioris is determined by measuring the distance of the excursion of the upper eyelid margin from far downward gaze to upward gaze while the frontalis muscle is held still with the injector's hand. A normal excursion is approximately 14 mm or more.[68] When the excursion is less than 14 mm, some degree of blepharoptosis after any BoNT treatment of the glabella mostly likely will occur (Figure 13.31c). Another way to predict the risk for unmasking and intensifying the potential for blepharoptosis is to identify someone with lash ptosis (LP). Individuals with either congenital or acquired blepharoptosis can manifest LP, which is a generalized declination or downward pointing of the eyelash follicles of their upper eyelids. The presence of LP suggests laxity of the terminal fibers of the levator aponeurosis which weave through orbicularis oculi to insert into the subcutaneous tissue and skin of the upper eyelid[69] (Figure 13.31d).

In younger patients with taut skin and no compensatory brow lifting, brow ptosis often can occur medially when there is an overzealous injection of a BoNT in the center of the forehead. Medial brow ptosis is exhibited by the medial head of the eyebrows appearing excessively lower than the lateral tail of the eyebrows. A bulge of skin in the center of the glabella also can accompany this "medial brow dip" of the eyebrows. This occurs because the lower central fibers of the frontalis are overly weakened and there is some activity of the fibers of the medial brow depressors, that is, the procerus, depressor supercilii, and medial orbital orbicularis oculi, pulling down on the center of the forehead and glabella (Figure 13.32).

Lagophthalmos or incomplete eyelid closure is another potential complication that can occur particularly when overzealous injections of a BoNT are given in the periorbital area. Lagophthalmos results when there is a loss of the normal sphincteric function of the orbicularis oculi, and the upper eyelid does not close and approximate firmly against the lower eyelid. Loss of the sphincteric function of the orbicularis oculi either with involuntary blinking or with deliberate forced eyelid closure can occur when BoNT diffuses into the *palpebral* portion of the orbicularis oculi, causing undue eyelid weakness. Lagophthalmos is seen more frequently in patients treated for strabismus when extraocular muscles are injected with higher doses of OnaBTX-A instead of the usual lower doses given for cosmetic purposes in the periocular area. On the other hand, patients who have an attenuated orbital septum because of age or other reasons may be more prone to this adverse sequela. If incomplete eyelid approximation is present for extended periods of time, exposure of the cornea can result in symptomatic dry eyes or exposure keratitis.[70] There is no antidote for lagophthalmos which can persist as long as the effects of the OnaBTX-A are present. So, protecting the patient from developing secondary dry eyes is extremely important because excessive corneal exposure will lead to desiccation of the cornea and superficial punctate keratitis. Immediate consultation with an ophthalmologist at the first sign of lagophthalmos will prevent any additional injury to the eye.

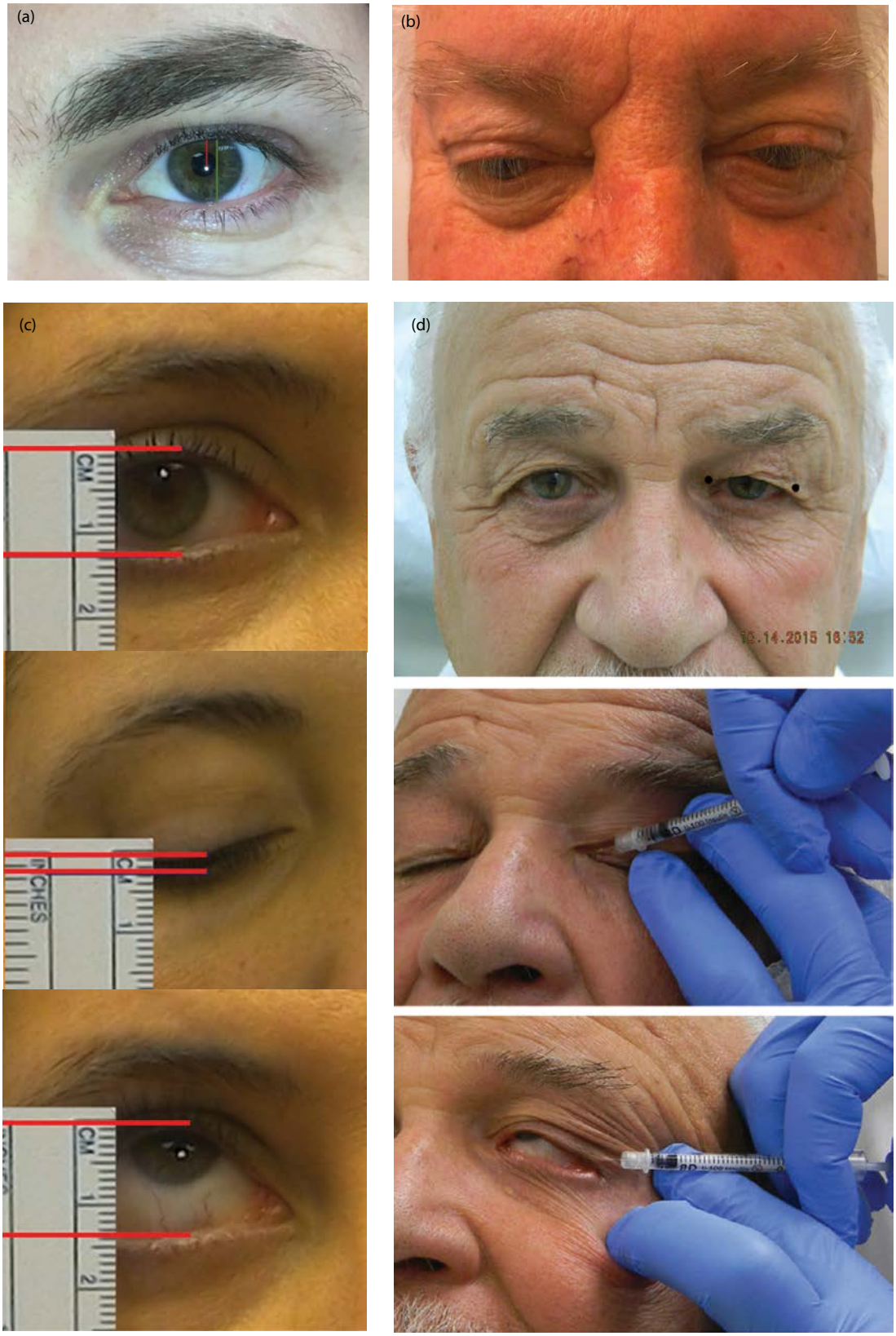

Figure 13.31 (a) The margin to reflex distance (MRD) is a way to measure and diagnose upper lid blepharoptosis. It is defined as the distance from the mid-pupil corneal light reflex to the lower cutaneous margin of the upper eyelid with the eyes in forward primary gaze. A normal MRD, shown here in red, should equal approximately 4 mm in vertical height. The palpebral fissure, shown here in green, is the distance between the upper and lower lid margins and normally measures between 7 and 12 mm. (b) A 69 year old male with lash ptosis and acquired blepharoptosis. Note the generalized declination or downward pointing of the upper eyelashes. (c) The functional strength of the levator palpebrae superioris is determined by measuring the distance of the excursion of the upper eyelid margin from far downward gaze to upward gaze while the frontalis muscle is held still with the injector's hand. A normal excursion is approximately 14 mm or more. When the excursion is less than 14 mm, some degree of blepharoptosis after any BoNT treatment of the glabella mostly likely will occur. (d) To treat mild upper lid blepharoptosis OnaBTX-A is injected into the (far) medial and lateral *pretarsal* orbicularis muscle fibers in the subdermal plane. (See further Reference 64.)

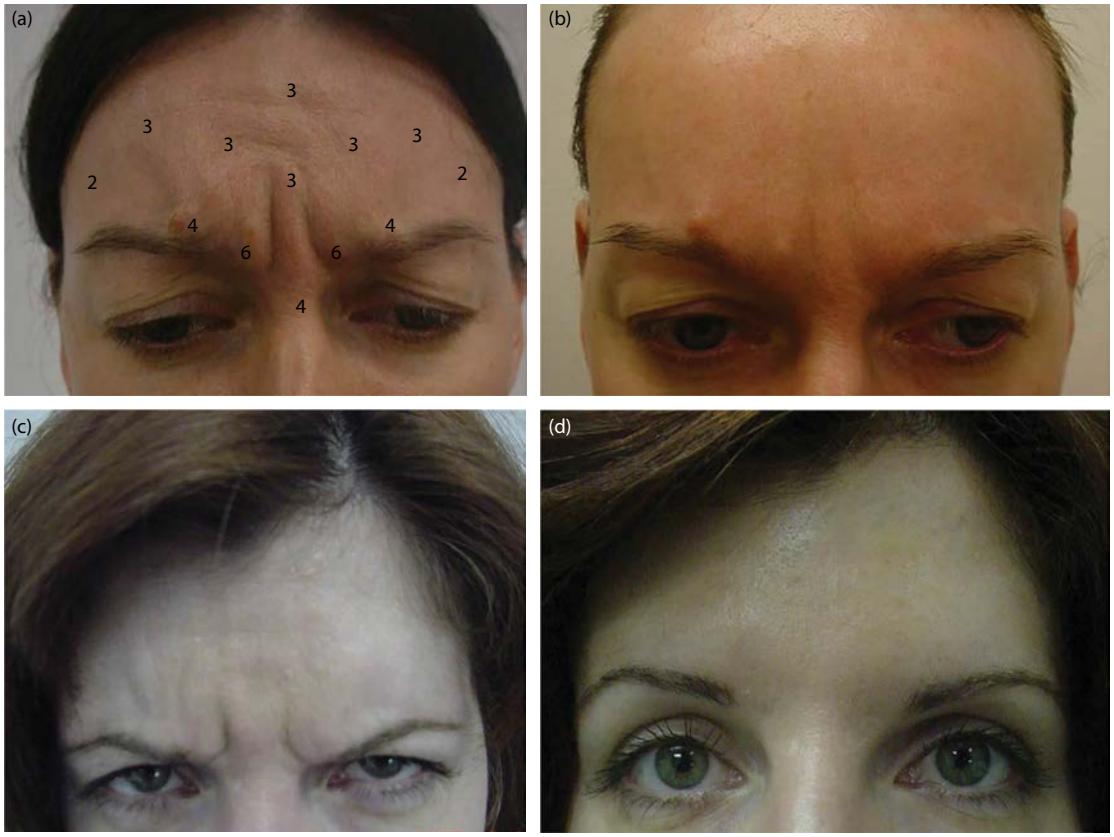

Figure 13.32 The "medial brow dip" of the central glabella and eyebrows of this 40-year-old occurred after OnaBTX-A injections because the lower central frontalis was overly treated. Patient is frowning (a) before and (b) after OnaBTX-A. Note the fullness of the medial brow skin after treatment. (c and d) The "medial brow dip" of the central glabella of this other 45-year-old patient was avoided after OnaBTX-A injections because the central frontalis was not treated.

Asymmetry is a minor adverse sequela that sometimes is unavoidable, particularly when a patient is treated for the first time with a BoNT (Figure 13.33). There are three types of asymmetry that can be corrected with injections of OnaBTX-A: iatrogenic, idiosyncratic, and incidental or acquired. An example of incidental or acquired asymmetry is Bell's or facial (7th cranial) nerve palsy. Additional examples are when one side of the face acquires a weakness because of an event (e.g., cerebral vascular accident), or an accidental, traumatic, or surgical denervation injury. Idiosyncratic asymmetry occurs when a person is born with the inability to control or move a facial muscle to its fullest extent, while its counterpart muscle on the contralateral side of the face is unaffected. This can result, for example, in one eyebrow or one eyelid being higher than the other (Figures 13.34 and 13.35) or in a crooked asymmetric smile (see Chapter 15).

Iatrogenic asymmetry arises when an injection of OnaBTX-A causes one side of the face to become weaker than the other (see Figure 13.34 and 13.39a). There are many reasons for this. The primary reason is because the stronger side is not injected with an equivalent dose of OnaBTX-A as the contralateral side. This could be the result of the OnaBTX-A not diffusing as equally and completely through all the fibers of a muscle or group of muscles. Another reason could be that some of the fibers might have been physically resistant to the OnaBTX-A, because those particular fibers were idiosyncratically thicker or stronger than the rest of the area and may have required a higher dose of OnaBTX-A. Another possibility is that the injections were not given precisely symmetrically or in the thickest and strongest part of the muscle, causing a particular section of muscle to retain most or some of its strength. Iatrogenic asymmetry is probably the easiest type of asymmetry to rectify. Generally, with a few additional units

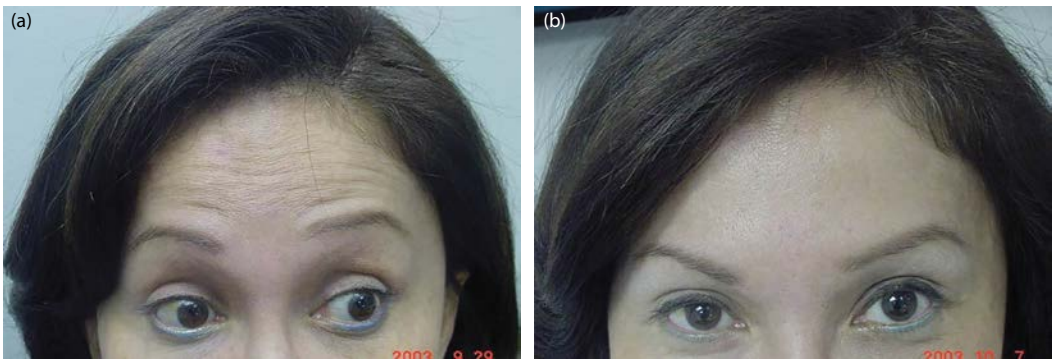

Figure 13.33 (a) Note the left eyebrow is higher than the right before and after treatment with OnaBTX-A. (b) Note the medial brow dip after treatment.

of OnaBTX-A injected into the appropriate area, iatrogenic asymmetry can be expeditiously ameliorated (Figure 13.39b).

Another type of asymmetry is pseudoblepharoptosis. Many individuals regardless of age possess, unbeknownst to them, an idiosyncratic lower lying asymmetric brow on one side. They commonly will also possess a lower lying upper eyelid on the same side and a smaller vertical palpebral aperture causing a narrower eyelid fissure (i.e., a secondary blepharoptosis, see Figure 13.35). With age, compensatory brow lifting will raise the affected lower lying brow and upper eyelid to maintain unobstructed vision (Figure 13.36a). When the frontalis of these patients is treated with injections of OnaBTX-A, the patient's compensatory brow lifting can be unintentionally weakened. This inadvertent diminution of compensatory brow lifting can occur even when only the higher upper fibers of the frontalis are weakened with injections of OnaBTX-A. The lower fibers of the frontalis do not necessarily have to be treated directly with injections of OnaBTX-A to drop the brow a few millimeters. With a drop in brow height comes a concomitant drop in upper eyelid height and a narrowing of the palpebral fissure. Those patients who already have an asymmetrically lower upper eyelid

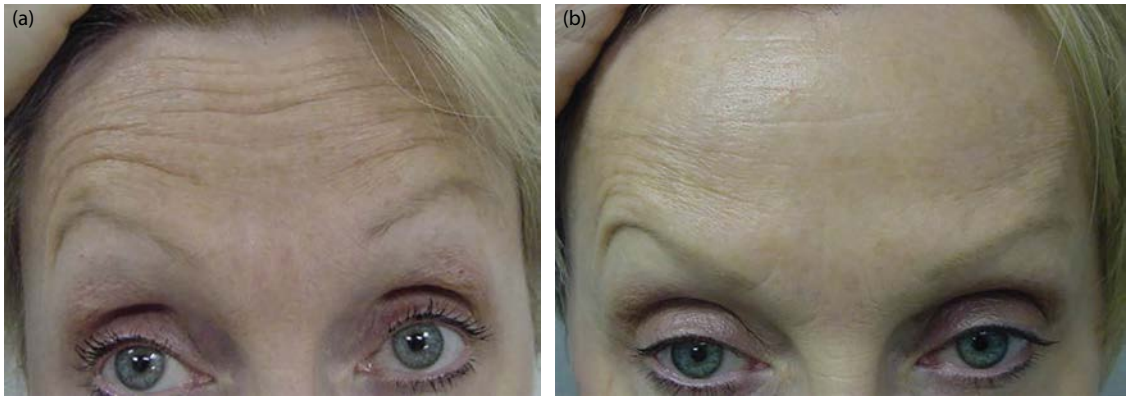

Figure 13.34 Patient is shown (a) before and (b) 2 weeks after OnaBTX-A treatment. Note the slightly higher elevation of the right eyebrow, which is seen as the patient raises her eyebrows before and after treatment. Note also the medial brow dip and right "Mephisto" brow after treatment.

Figure 13.35 (a) This 53-year-old woman at rest did not know that she had a naturally occurring brow ptosis on the right with an accompanying secondary blepharoptosis of the right eyelid. (b) Same patient with an asymmetrical left brow elevation found with forced raising of the eyebrows before a treatment of OnaBTX-A. (c) Same patient at rest and gazing forward, 8 weeks after an OnaBTX-A treatment.

Figure 13.36 A 70-year-old with compensatory brow lifting and an undetected left eyelid ptosis (a) at rest and (b) frowning before OnaBTX-A treatment. (c) Blepharoptosis is seen at rest 1 month after OnaBTX-A. The patient and treating physician assumed the blepharoptosis was caused by OnaBTX-A until the before and after treatment pictures were compared, which then prompted the diagnosis of "pseudoblepharoptosis".

on one side now appear to have developed blepharoptosis from the OnaBTX-A injections (Figure 13.36). In reality, these patients more accurately have pseudoblepharoptosis, which is simply an unmasking of the secondary blepharoptosis they already possessed prior to any BoNT treatment. At times, this can be enhanced because of an age-related attenuation of the strength of the upper lid levator of that eye (Figure 13.37). When the patient first realizes that one upper eyelid is lower than the other, blame on the injector and OnaBTX-A is a foregone conclusion.[71] However, the astute physician will evaluate the patient carefully prior to any treatment and document the asymmetric clinical findings with pretreatment photographs. This will enable the physician to discuss the actual problem with the patient and graphically demonstrate the presence of the compensatory brow lifting before embarking on a perilous course of inevitable treatment failure (Figure 13.38). So, instead of the physician being led to believe that the patient developed blepharoptosis because of a poor injection technique, the physician will be able to identify that the patient always had an idiosyncratic asymmetry and subclinical upper eyelid ptosis that can be unmasked and even exaggerated with injections of OnaBTX-A (Figure 13.39). This manifestation of

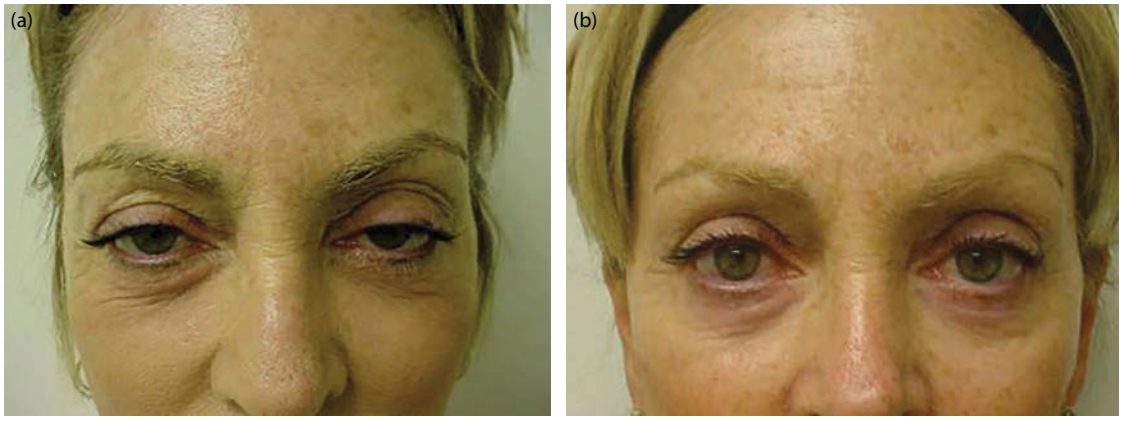

Figure 13.37 (a) A 57-year-old patient with a compensatory left brow lift before treatment with OnaBTX-A injections. (b) Same patient 2 weeks after OnaBTX-A demonstrates a slight pseudoblepharoptosis on the left.

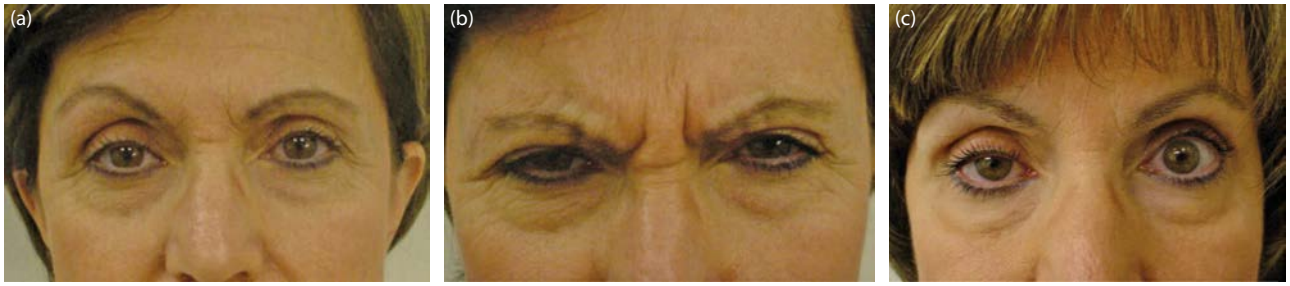

Figure 13.38 (a) Compensatory brow lifting raises the right eyebrow in this 60-year-old patient to correct a ptotic right eyelid. (b) Same patient, brows are fairly symmetrical with frowning, but the right upper lid is still ptotic before injections of OnaBTX-A. (c) Same patient, 1 week after injections of OnaBTX-A. The left brow was lifted with OnaBTX-A and both eyebrows appeared fairly symmetrical. This paradoxically makes the upper eyelid appear ptotic even though the right brow was not treated with OnaBTX-A.

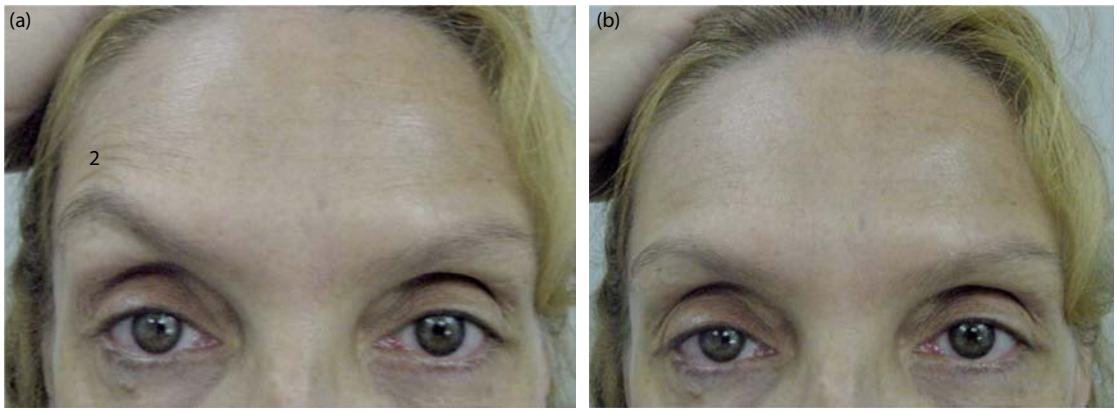

Figure 13.39 An example of iatrogenic asymmetry. (a) A 42-year-old patient is seen at rest with a higher right eyebrow 2 weeks after OnaBTX-A injections of the glabella and forehead and just before an additional 2 U of OnaBTX-A were given. (b) Same patient at rest 3 weeks after the additional 2 U of OnaBTX-A were given and 5 weeks after her initial treatment with OnaBTX-A. Notice the relative symmetry of both eyebrows.

pseudoblepharoptosis frequently occurs in patients over the age of 60 years who are treated for forehead wrinkles and glabellar frown lines with injections of BoNT. Correction of pseudoblepharoptosis is not always completely successful but can be attempted by injecting intradermally the extreme lateral and medial pretarsal orbicularis oculi of the upper eyelid on the affected side with low doses (0.5–1.0 units) of concentrated low volume OnaBTX-A.[64,71]

The best way to avoid additional difficulties with patient rapport and confidence is to keep carefully documented written clinical notes and before and after treatment photographs (see Appendix 4). Discuss the physical findings with the patient and point out existing idiosyncratic asymmetries, anatomical differences, and potential adverse outcomes prior to treatment. Informing the patient of any atypical findings before commencing with a treatment always is regarded by the patient as an accurate diagnosis of a unique situation. Explaining the circumstances and reasons for a particularly poor outcome after treatment always, is considered by the patient as an excuse for an improperly executed procedure.

Other untoward sequelae of more limited significance and duration can occur. These are the same adverse sequelae as those experienced with any type of subcutaneous or intramuscular injection. They include ecchymoses, edema, and erythema at the injection sites (Figure 13.40), headache, and flu-like malaise. Rarely, if ever, do any of these side effects last beyond the day of treatment, except for ecchymoses which can last up to 10 days or more.

For some patients, a dull and transient headache with or without general body malaise occurs after injections of OnaBTX-A that can last beyond 24–72 hours.[72] The occurrence of headache immediately after an OnaBTX-A injection seems paradoxical since OnaBTX-A injections are now FDA approved for treating tension and migraine headaches.[1,73] Headaches seem to occur more frequently in patients after their first and subsequent 2 or 3 treatment sessions. They usually cease to occur with repeat treatments. Studies have documented the incidence of patients who develop headaches after a treatment of OnaBTX-A were similar to those receiving placebo.[45] This seems to indicate that the transient headaches which occur after a treatment of BTX-A are due more likely to the physical act of injection rather than to the actual BoNT-A itself.[45] Other studies have found that patients are more prone to headaches when the volume of the injected BoNT-A is higher than usual. This also seems to support the opinion that headaches after injections of OnaBTX-A are probably due to the trauma of the injection rather than to the actual BoNT product.[74]

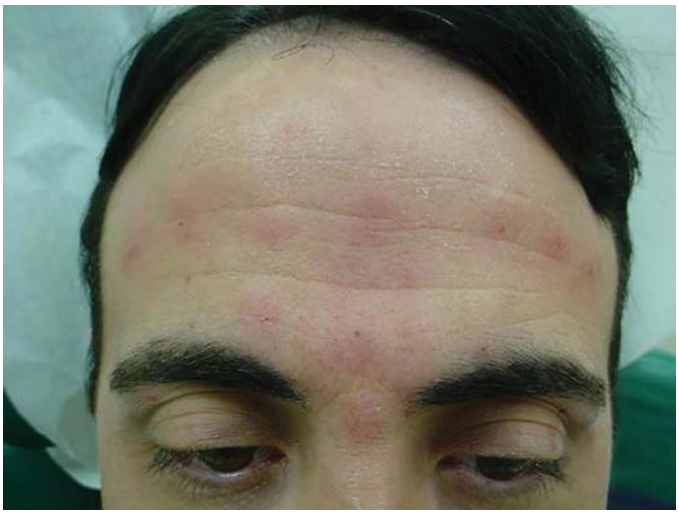

Figure 13.40 Note the erythema and edema in the pattern of the injections 10 minutes after a treatment of OnaBTX-A of the forehead and glabella.

For the first-time recipient of a periorbital treatment of OnaBTX-A, the presence of periorbital edema lasting a few hours to days may occur. This can be attributed to lymph stasis, possibly produced by a nondetectable attenuation of the sphincteric pumping action of the inferior preseptal orbicularis oculi, reducing the efficiency of lymph fluid clearance from the surrounding soft tissue.[64] Moreover, when there is a blatant reduction in lower eyelid tone, eversion of the punctum and reduced blinking can compromise the action and efficacy of the "lacrimal pump," resulting in transient epiphora, until the lower eyelid tone returns (see Figure 13.132).

For some women, habitual squinting and scowling are the result of spending a lot of time outdoors, in front of a computer screen, or suffering from constant and persistent headaches, or being plagued with poor vision and refusing to wear corrective eyeglasses, among many other things. Incessant contraction of the corrugator supercilii and orbicularis oculi, manifested by habitual scowling, causes the medial end of the eyebrows to approach the midline. Sclafani and Jung measured the difference in interbrow distance from maximum elevation to maximum contraction of the brow, and it was slightly greater than 4 mm. The average distance traversed by the medial brow from frowning to repose was 3.26 mm in women and 3.76 mm in men.[75] Many women will pluck and shorten the transverse length of their eyebrows by removing eyebrow hair from the medial end of their brow. This will widen the glabellar interbrow space, so they do not look like they are habitually scowling, when they actually are (Figures 13.39 and 13.41). After injections of OnaBTX-A are given to reduce the number and extent of glabellar frown lines, the corrugators are no longer constantly contracting and adducting the eyebrows toward each other. Consequently, the transverse width of the glabella returns to its normal anatomical position because the corrugators now are more relaxed and less hyperkinetic when they are in repose. However, those women who have plucked the medial portion of their eyebrows now complain after injections of OnaBTX-A that they look practically hyperteloric because their eyebrows appear widely separated. However, it is only because the medial aspects of their eyebrows have been excessively plucked that causes them to appear this way and not the injections of OnaBTX-A. Such an adverse sequela is difficult to predict, but warning patients who pluck their eyebrows of such a potential side effect will prevent further disappointment on the part of the patient and additional frustration on the part of the physician. Also, be aware of the patients without any eyebrow hair who need to color in, the shape of their eyebrows. The shape that is chosen on the day of an OnaBTX-A treatment may not necessarily correspond to the natural anatomical position of that person's brow. Injections of OnaBTX-A may return the area to its natural anatomical position, which paradoxically may appear to be distorting the glabellar area, when in reality it is not. Patients with permanent eyebrow tattooing may present with similar challenges and post-treatment confounding disappointments (Figure 13.42).

Serious reactions, particularly those of immediate hypersensitivity such as anaphylaxis, urticaria, soft tissue edema, and dyspnea have been extremely rare. When they occur, appropriate medical treatment must be instituted immediately (see Appendix 6).[76] However, there has not been a confirmed serious case of spread of toxin effect away from the injection site when OnaBTX-A has been used at the recommended dose to treat glabellar frown lines.[1]

Figures 13.43 through 13.51 are some examples of different patients treated with OnaBTX-A for glabellar frown lines. Note also those who have had their forehead frown lines treated during the same treatment session.

Figure 13.41 Note the widening of the glabellar interbrow space and the shortening of the transverse length of the brow (a) at rest and (b) frowning due to excessive plucking of the eyebrows. Same patient at rest (c) and frowning (d) after a treatment with OnaBTX-A. Note additionally the change in hair color after treatment.

Treatment Implications When Injecting the Glabella

1. Precise amounts of accurately placed injections of minimal volume OnaBTX-A reduce the incidence of brow and eyelid ptosis.
2. Men may need higher doses of OnaBTX-A than women for comparable results.

Figure 13.42 This 58-year-old patient had her eyebrows permanently tattooed prior to any OnaBTX-A treatments. Many years later, after regularly scheduled OnaBTX-A treatments, her eyebrows are now permanently and widely spaced lateral to the medial canthus.

3. Women prefer arched eyebrows; most men prefer straighter, non-arched eyebrows.
4. When injecting the corrugator supercilii with OnaBTX-A, remain medial to the midpupillary line and 3–4 cm above the supraorbital bony margin, and deep within the belly of the muscle.
5. Blepharoptosis can be transiently reversed with alpha-adrenergic agonist eye drops, but brow ptosis cannot be reduced and remits only when the effects of OnaBTX-A diminish.
6. Preexisting asymmetry of the brow and eyelids should be identified and discussed with the patient before treatment, and might be corrected by accurately injecting appropriate doses of OnaBTX-A on both the affected and non-affected sides.
7. Patients with inelastic, redundant skin of the brow who have compensatory brow lifting because of a preexisting subclinical secondary blepharoptosis can easily develop pseudoblepharoptosis when injections of OnaBTX-A decompensate their brow lifting on the affected side.

HORIZONTAL FOREHEAD LINES

Introduction: Problem Assessment and Patient Selection

One of the easiest areas of the face to treat with injections of OnaBTX-A is the forehead.[57] Many individuals contract their frontalis constantly for various and sundry reasons, and, in so doing, the skin buckles, creating parallel furrows and folds transversely across their foreheads. On the other hand, the presence of horizontal forehead lines seems to be directly proportional to one's age or time spent in the sun. Older individuals generally have many forehead lines that become deeper

Figure 13.43 A 56-year-old patient at rest (a) before and (b) 1 month after OnaBTX-A treatment of the glabellar frown lines. Note the different dosages for areas of stronger muscle contraction.

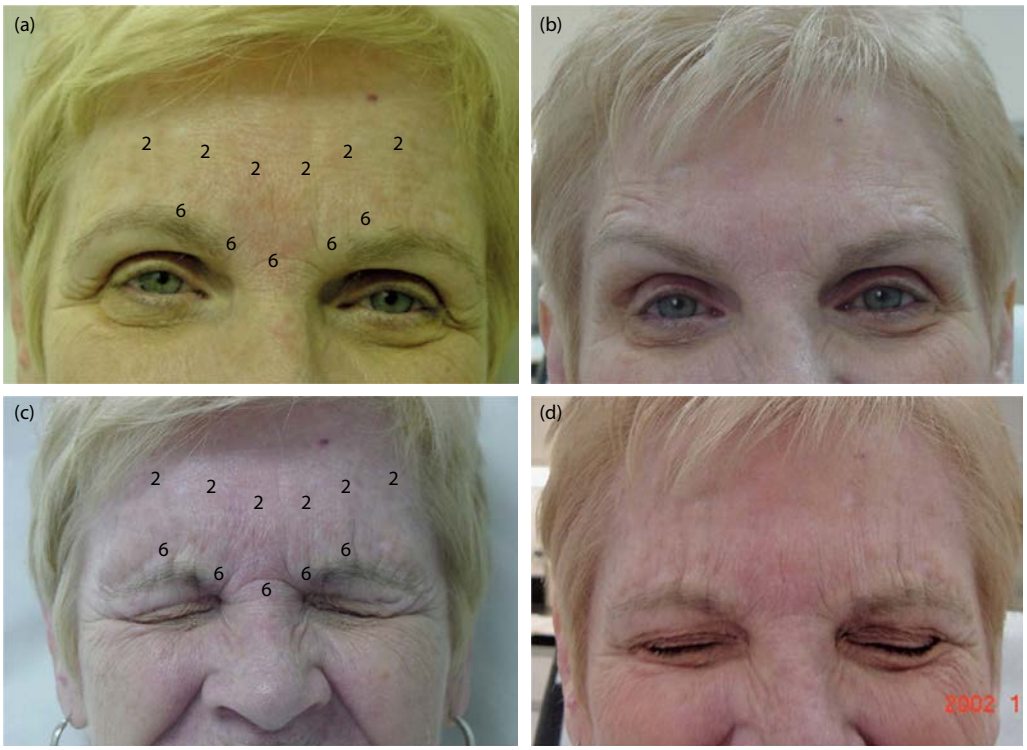

Figure 13.44 A 66-year-old patient at rest (a) before and (b) 4 weeks after OnaBTX-A treatment of the glabellar frown and forehead lines. The same patient is shown frowning (c) before and (d) 4 weeks after OnaBTX-A treatment of the glabellar frown lines.

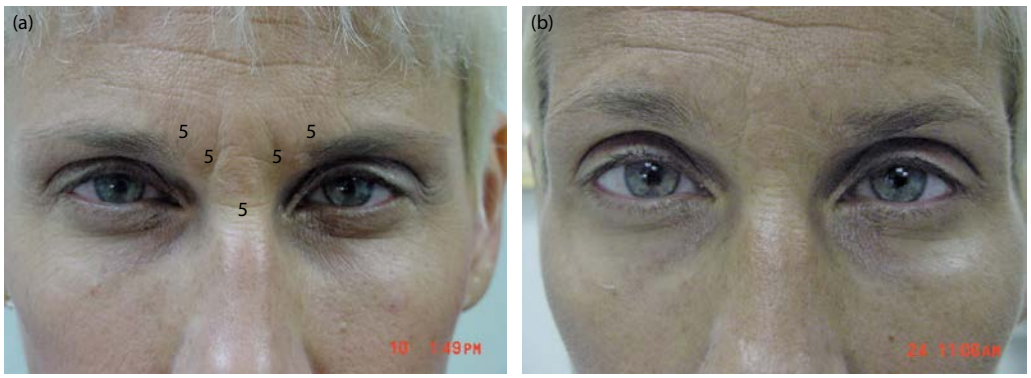

Figure 13.45 A 43-year-old patient at rest (a) before and (b) 2 weeks after an OnaBTX-A treatment of the glabellar frown lines.

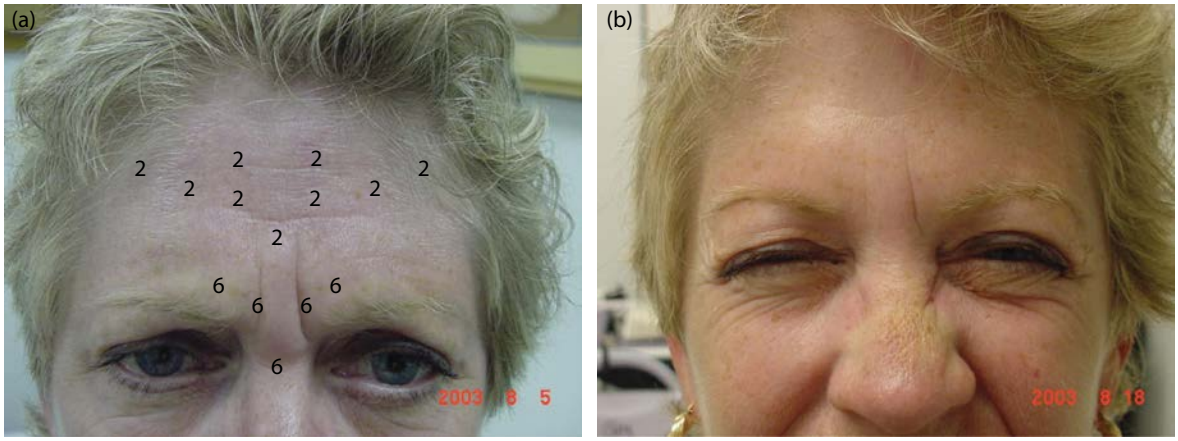

Figure 13.46 A 57-year-old patient (a) before and (b) frowning 2 weeks after an OnaBTX-A treatment of the glabellar frown and forehead lines.

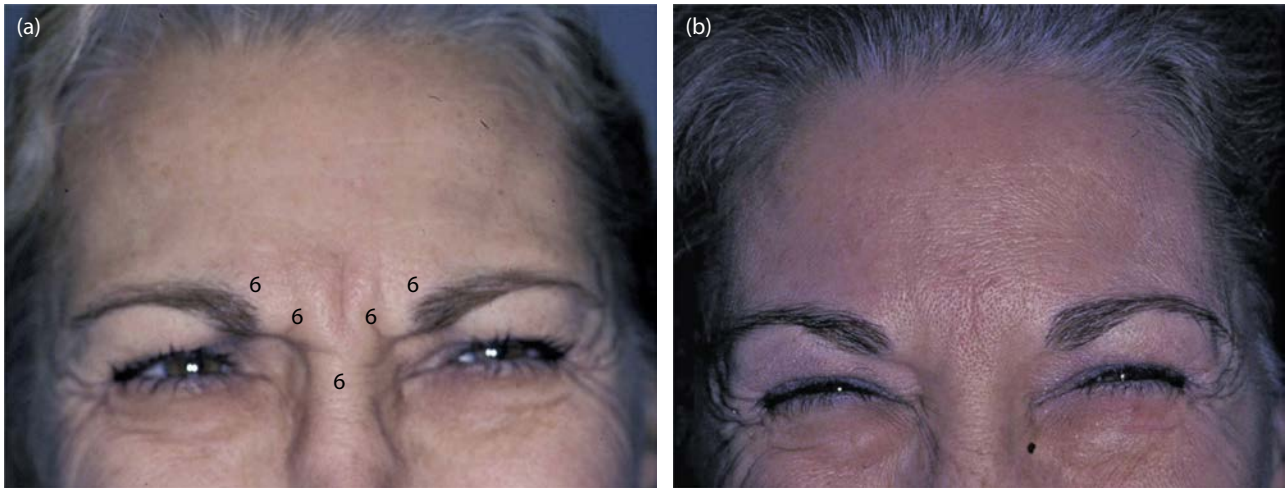

Figure 13.47 A 52-year-old patient (a) before and (b) 2 weeks after an OnaBTX-A treatment of glabellar frown lines.

Figure 13.48 A 43-year-old patient frowning (a) before and (b) 2 weeks after OnaBTX-A treatment of glabellar frown lines.

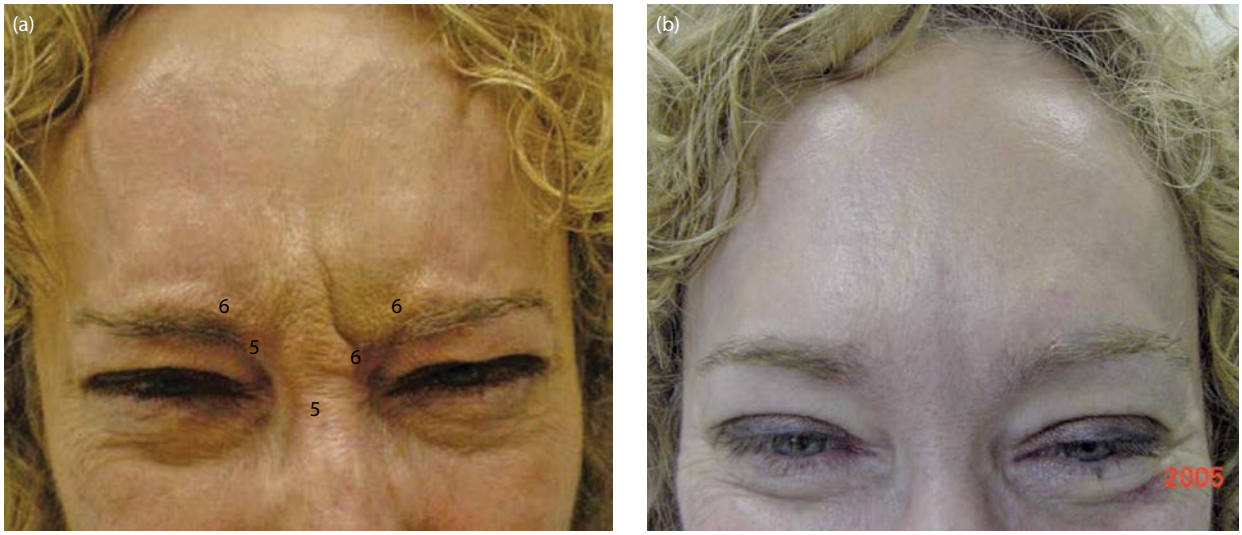

Figure 13.49 A 59-year-old patient frowning (a) before and (b) 2 weeks after an OnaBTX-A treatment of glabellar frown lines.

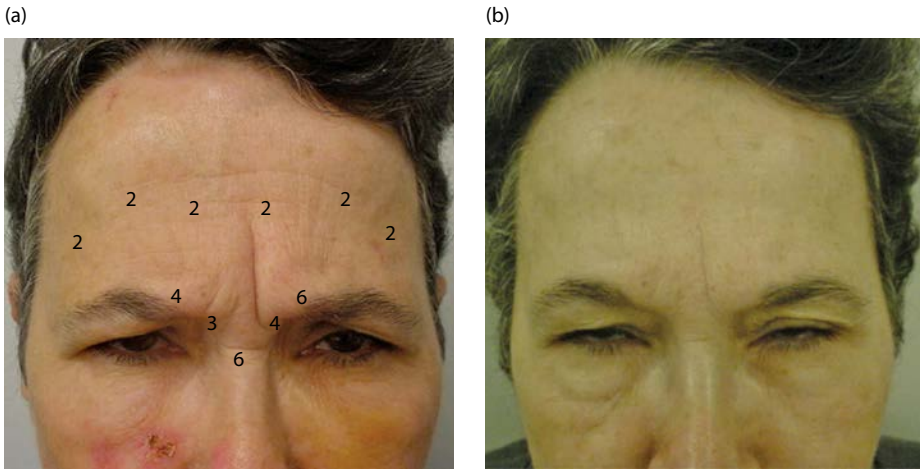

Figure 13.50 A 71-year-old patient frowning (a) before and (b) 2 weeks after an OnaBTX-A treatment of glabellar frown and forehead lines.

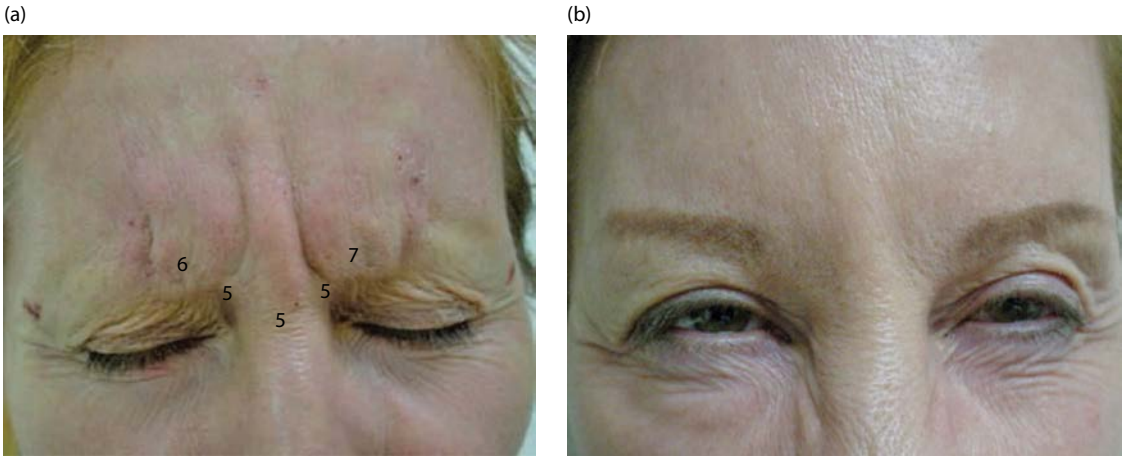

Figure 13.51 A 49-year-old patient frowning (a) before and (b) 2 weeks after an OnaBTX-A treatment of glabellar frown lines.

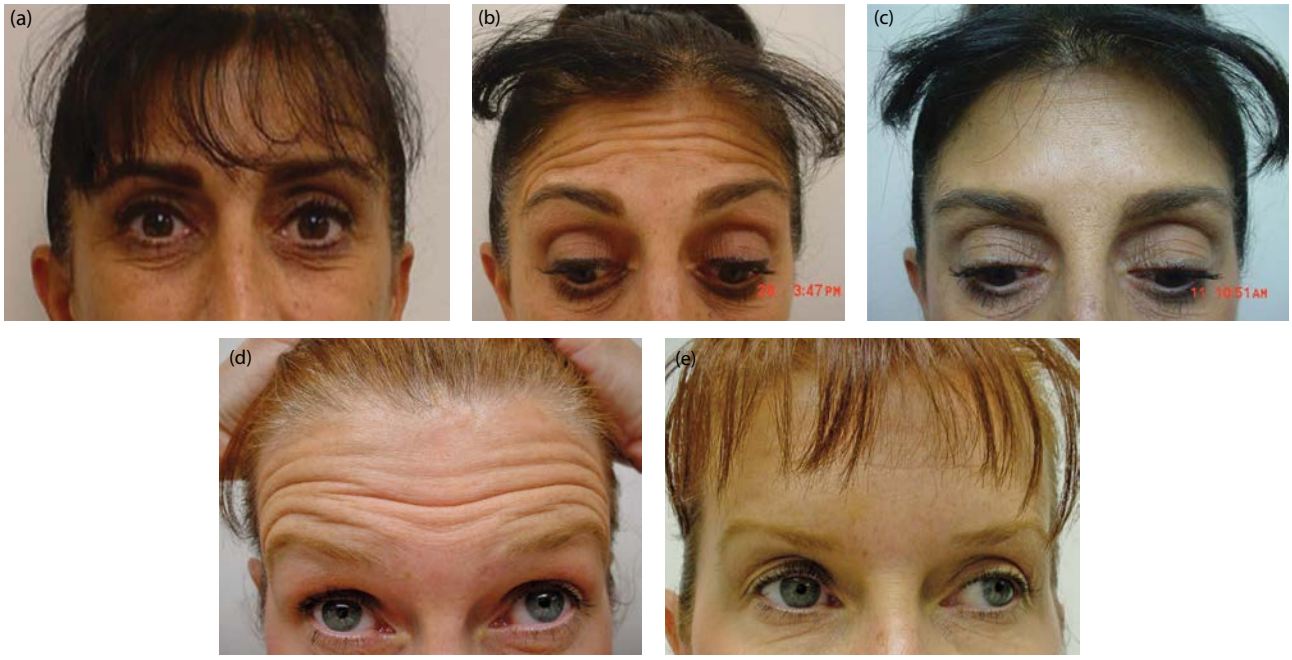

Figure 13.52 (a) Note the fringe of hair concealing the forehead in a 52-year-old with deep forehead lines (b) before and (c) 2 weeks after a treatment with OnaBTX-A. (d) A patient before and (e) 3 weeks after a treatment with OnaBTX-A. The bangs were pulled back to show the forehead rhytides.

with time. As one ages, the skin of the face, along with that of the rest of the body, typically becomes more inelastic and redundant. When this occurs in the upper face, not only do horizontal forehead lines appear, but there also is a characteristic hooding of the brow that frequently develops. Age-related brow hooding first develops commonly over the lateral aspect of the brow, whereby brow skin extends over the lateral aspect of the upper eyelids. This usually occurs in the sixth or seventh decade in those individuals so predisposed (Figure 13.2). For these individuals, a properly functioning frontalis is essential in maintaining a normal unobstructed field of vision. It is the frontalis that will keep the brow from dropping and causing the skin to drape over the upper eyelids, which can interfere with their forward and upward gaze.

Younger women who have horizontal forehead lines commonly attempt to conceal their obtrusiveness by wearing their frontal hair with a fringe or in bangs (Figure 13.52). Generally, the presence of horizontal forehead lines causes one to appear stressed, worried, tired, or old. Abruptly raising the eyebrows by acutely contracting the frontalis also can express an emotion of surprise or even fear; a social cue that one usually may not want to express too readily in certain situations (Figure 13.53). When done properly, injections of OnaBTX-A can diminish forehead wrinkling and replace one's unintended negative expressions with those that are more positive.

All too often it is the female rather than the male patient who is more concerned about the presence of forehead lines. These women are frequently quite determined to eliminate any vestige of the appearance of a forehead wrinkle. A cautious and empathetic cosmetic physician will remind such patients that the absolute absence of forehead wrinkles, especially at full contracture or while expressing an emotion, may not be particularly attractive or appropriate. It portrays an individual as too artificial and mask-like in appearance, and thus should not be one's ultimate goal. Because of the levator function of the frontalis, its antagonistic interaction with the depressor muscles of the glabella and periorbital area, and the potential risk of overtreatment causing brow ptosis, there are many who believe treating the frontalis with OnaBTX-A is not as easy as one might expect.[41]

Functional Anatomy of Horizontal Forehead Lines (See Appendix 2)

The horizontal forehead lines are produced by the contraction of the muscle fibers of the frontalis, the only levator muscle of the upper third of the face (Figure 13.54). The function of the frontalis is to elevate the eyebrows, the skin of the brow and forehead, and to oppose the depressor action of the muscles of the glabella and brow. Its superior aspect also retracts and lowers the scalp as a function of its participation in the occipitofrontalis galea aponeurotic complex.

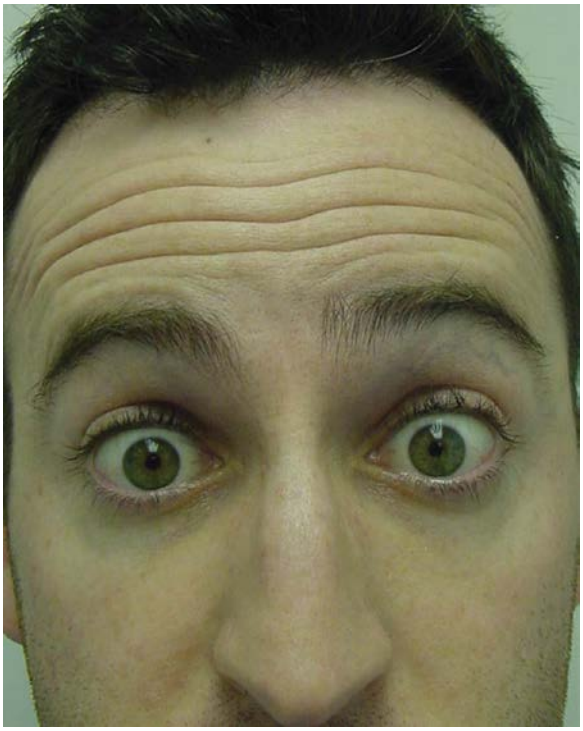

Figure 13.53 Abrupt contraction of the frontalis expresses surprise or even fear.

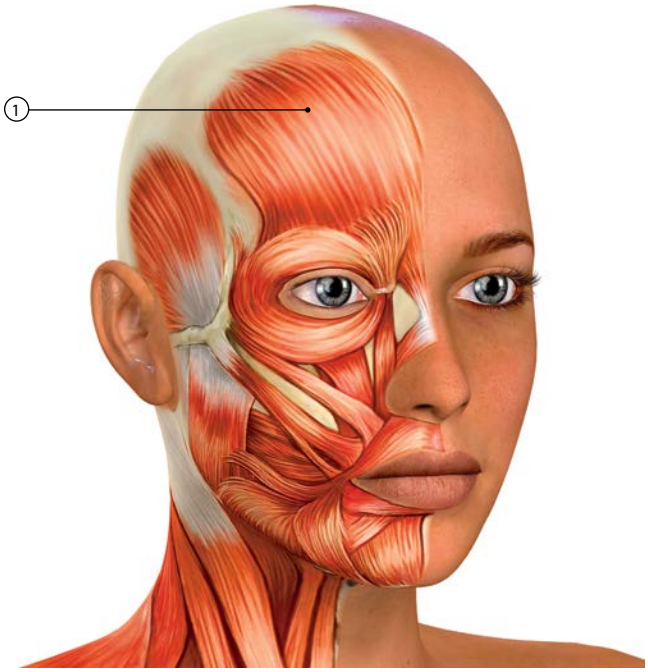

Figure 13.54 Frontalis, the only levator muscle of the forehead.

The frontalis is a pair of quadrilaterally shaped, distinct muscles whose fibers are oriented vertically, contracting in a vertical direction and producing the horizontal wrinkles of the forehead. The frontalis lies beneath a thick layer of sebaceous skin and subcutaneous tissue and has no attachment to bone. The frontalis is indirectly connected to the occipitalis by the epicranial, membranous galea aponeurotica, which attaches to both muscles on either side of the scalp vertex, the occipitalis posteriorly and the frontalis anteriorly. The frontalis originates from the membranous galea aponeurotica superiorly and inserts into the subcutaneous tissue and skin of the brow inferiorly at the level of the superciliary ridge (or arch) of the frontal bone. The fibers of the frontalis also interdigitate with muscle fibers of the brow depressors, that is, the procerus, corrugator supercilii, depressor supercilii, and orbicularis oculi. In some patients, there can be a downward extension of the membranous galea aponeurotica in the midline composed of little or no muscle fibers (Figure 13.54). Injections of OnaBTX-A into this area are ineffective and unnecessary when no muscle fibers are present.[77] However, in some men and even women, there are well-developed muscle fibers in the center of the forehead (Figures 13.52b and 13.55) which can be detected by light palpation over the area while the patient actively raises and lowers the eyebrows. A study of cadavers using punch biopsies to determine the location of frontalis muscle fibers at three different locations along the vertical axis in the forehead midline, revealed a diminishing presence of muscle fibers in the upper forehead.[30] Fibers of the paired frontalis intersected and overlapped in the midline at the level of the eyebrows in 100% of cases. At 2 cm above the eyebrows the two bellies of the frontalis interdigitated only in 40% of cases studied and at 4 cm above the eyebrow line no intersecting frontalis fibers were found in the midline. However, when functional muscle fibers of the frontalis can be detected in the center of the forehead, injections of OnaBTX-A in the midline of the forehead are needed to produce the desired effect (Figures 13.52b and 13.55e,f).

Dilution (See Appendix 3) When Treating Horizontal Forehead Lines

Controlled widespread diffusion can be a desired effect when injecting OnaBTX-A into the forehead. To avoid brow ptosis, the muscle fibers of the frontalis must remain fully functional 1.5–2.5 cm above the eyebrow, which is predicated on the resting position of the eyebrows (i.e., 3–4 cm above the actual bony orbital margin). Then higher dilutions and larger volumes of OnaBTX-A can be injected into the upper forehead. Consequently, injectors will use anywhere from 1 to 4 mL of non-preserved or preserved saline to reconstitute a 100 U vial of OnaBTX-A when treating the forehead.[39,78] The dilution recommended by the manufacturer and approved by the FDA and specified in the OnaBTX-A product's package insert is 2.5 mL of nonpreserved sterile saline or 4 U of OnaBTX-A per 0.1 mL of solution.

Dosing: How to Correct the Problem, (See Appendix 4), (What to Do and What Not to Do) Whenx Treating Horizontal Forehead Lines

Injections of OnaBTX-A into the frontalis for cosmetic purposes were approved by the FDA in October, 2017. The intricate and essential interaction of the frontalis with the brow depressors makes it virtually impossible not to treat the forehead when one is treating glabellar frown lines.

A typical dose for injecting the forehead in women is approximately 8–18 U of OnaBTX-A. However, the FDA approved dose for treating the forehead with Ona-BTX-A is 20 units. This can be injected either subcutaneously or intramuscularly at four to six sites across the forehead with 1–4 U of OnaBTX-A placed into each site at intervals of approximately 1.5–2.5 cm apart on either side of a deep crease (Figure 13.56).[78,79] For men, the typical dose is approximately 16–32 U of OnaBTX-A and occasionally higher.[80–82] These doses can be injected at 4–12 or even more sites either subcutaneously or intramuscularly depending on the height and width of the forehead, with up to 6–8 U of OnaBTX-A placed into each site, depending on the strength of the frontalis (Figures 13.56b and 13.57).[57,81] Some patients, either men or women, can have many rows of fine to moderate forehead wrinkles, whereas others can have one or two rows of deeply set folds and furrows. The number and dosage of the OnaBTX-A injections will depend on many factors, including the number and depth of the wrinkles, the size, shape, and strength of the muscle and the height, width, and shape of the forehead (Figure 13.57).[41,57,81,82] More often than expected, and unbeknownst to the individual, a patient will present with asymmetrical eyebrows prior to their first treatment with OnaBTX-A. Patients must be made aware of their idiosyncratic anatomical differences which must be documented both in the patient's clinical chart and in his or her photographic record. Sometimes the eyebrows can be made symmetrically level with each other with carefully placed injections of OnaBTX-A (Figure 13.58) and sometimes they cannot (Figure 13.59).

The patient usually is injected in an upright sitting or semireclined position. The pattern of injection across the forehead can vary depending on the anatomical dimensions of the forehead and the strength of the frontalis. To determine the overall muscular strength of the frontalis, lightly palpate the forehead at rest and during maximum eyebrow elevation. One can randomly inject 1–4 U of OnaBTX-A subcutaneously or intramuscularly at any point on the forehead that is at least 2–2.5 finger breadths (i.e., 2.5–4.0 cm) above the superior margin of the bony orbit (Figures 13.60 and 13.61).

Otherwise, one can use the on-label recommended technique and total dose of 20 units of OnaBTX-A for treating horizontal forehead lines for both men and women. To identify the recommended injection points one must first locate the superior extent of functionally active frontalis, which is usually approximately 1 cm above the highest horizontal forehead crease. Then locate the lowest row of treatable horizontal wrinkles, by identifying the midway point between the superior margin of active frontalis and the eyebrows. This midway

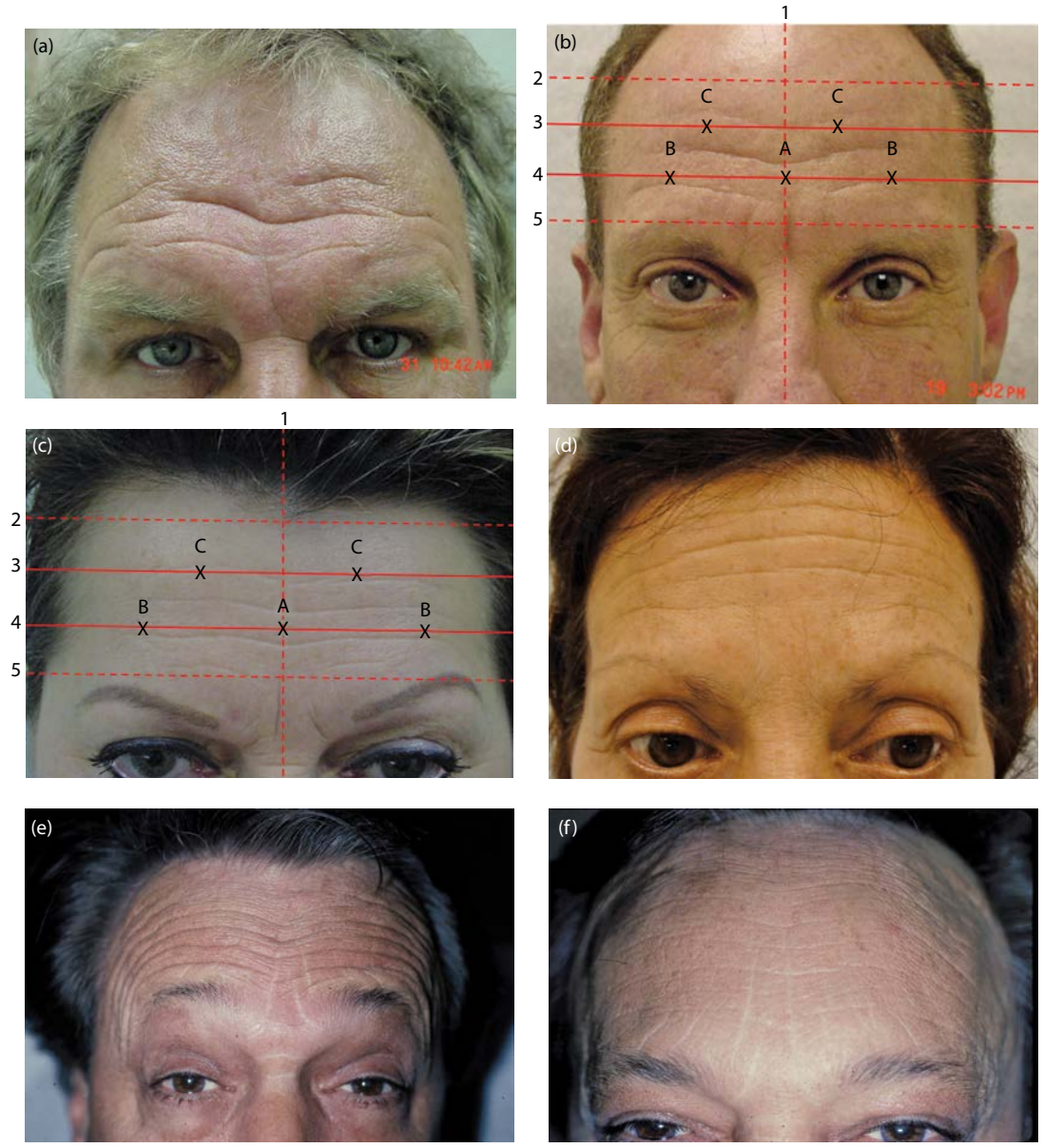

Figure 13.55 (a, b) Men with deep forehead lines; the 58-year-old patient in (b) works outdoors. (c, d) Some women can have a well-developed frontalis in the middle of their forehead. Neither of these women works outdoors. Note the on-label recommended injection points for treatment of the forehead on a patient (b) with a receding hairline and (c) with a fixed hairline: (1) midline; (2) superior margin; (3) upper treatable row; (4) lower treatable row; (5) inferior margin at upper level of eyebrows, and see text for location of injection points. (e, f) This 63-year-old man who spends a lot of time outdoors has a well-developed frontalis, seen here raising his eyebrows (e) before and (f) 2 weeks after an OnaBTX-A treatment. Note the non-tanned skin in the base of the forehead furrows (f) after treatment.

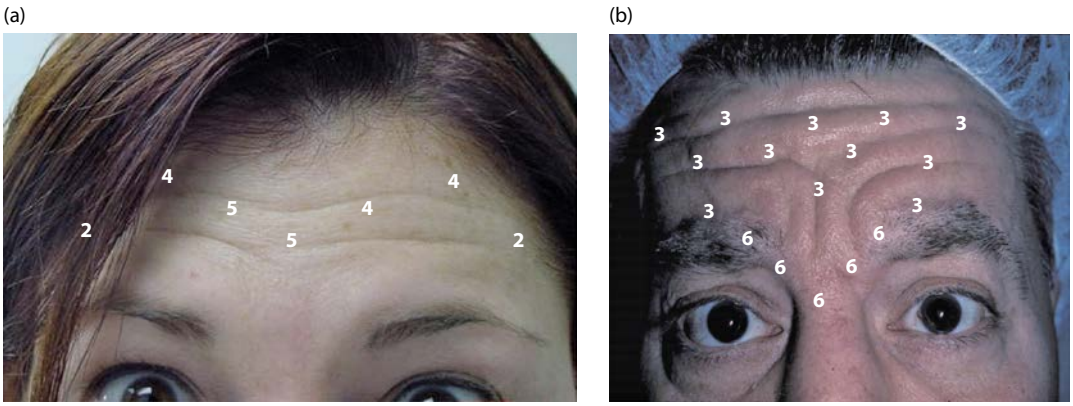

Figure 13.56 (a) Typical injection sites in a woman with an average sized forehead. (b) Typical injection sites in a man with an average sized forehead.