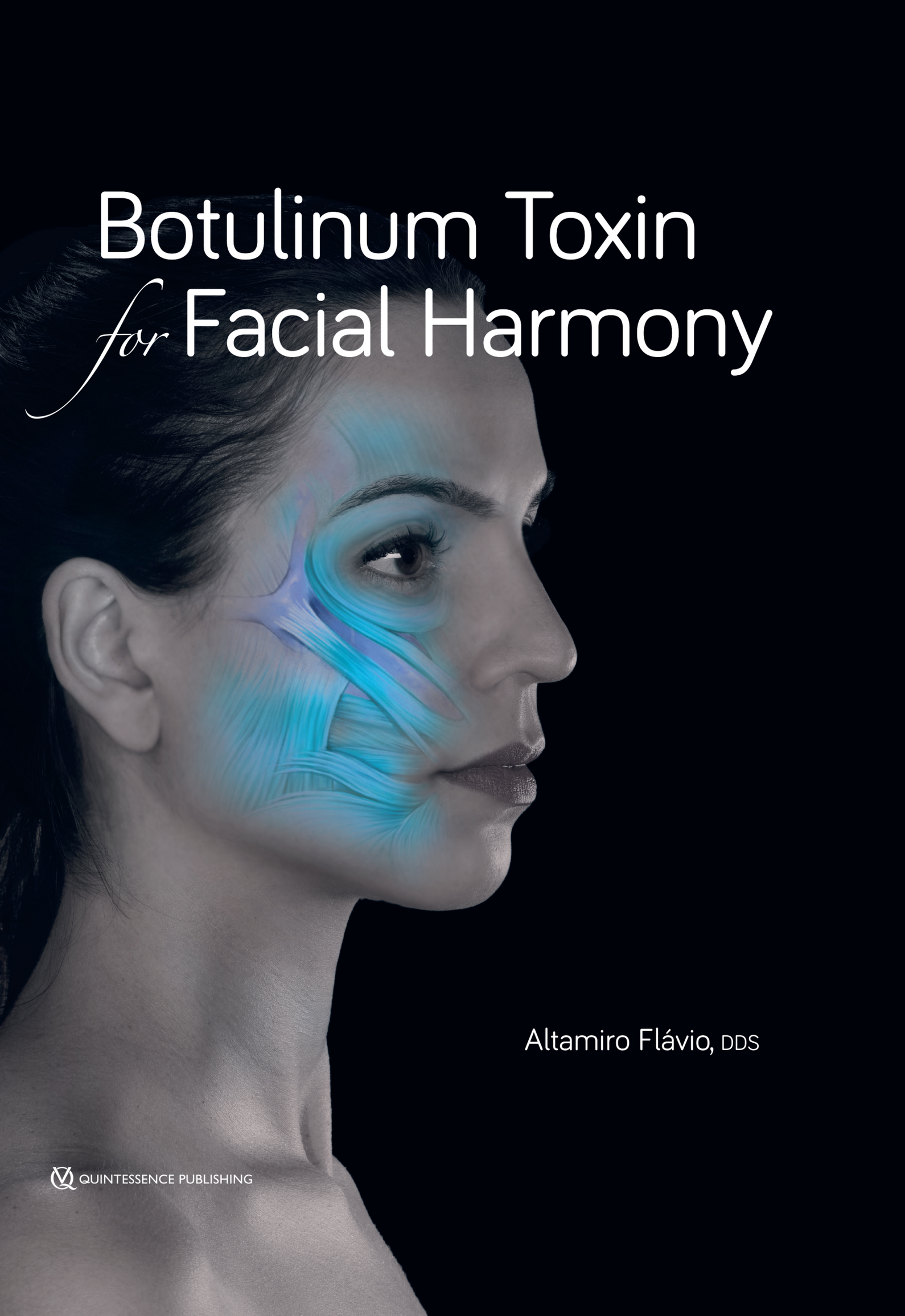
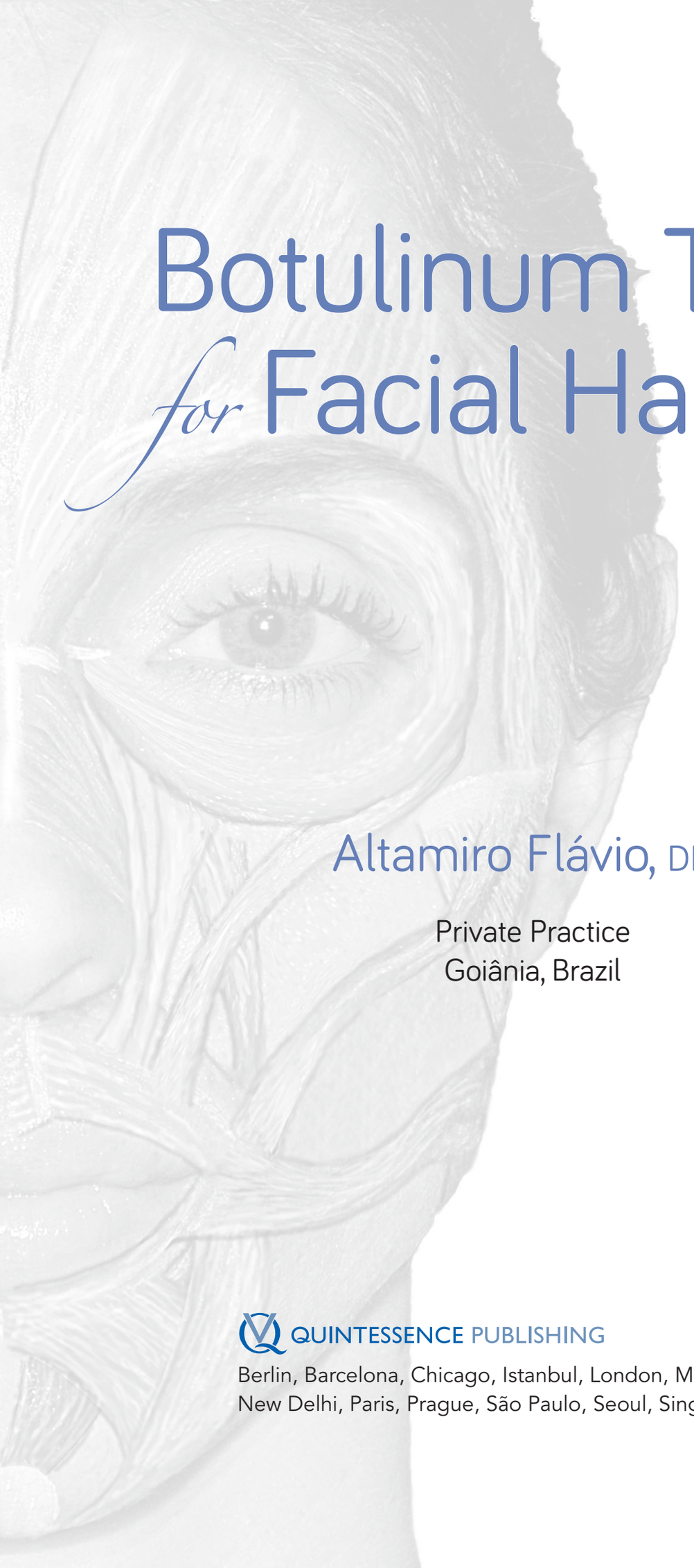
Botulinum Toxin *for* Facial Harmony



Altamiro Flávio, DDS

QUINTESSENCE PUBLISHING

Botulinum Toxin for Facial Harmony



Botulinum Toxin *for* Facial Harmony

Altamiro Flávio, DDS

Private Practice
Goiânia, Brazil

QUINTESSENCE PUBLISHING

Berlin, Barcelona, Chicago, Istanbul, London, Milan, Moscow,
New Delhi, Paris, Prague, São Paulo, Seoul, Singapore, Tokyo, Warsaw

Dedication

This book is dedicated to my parents, who with their example of life and love showed me the path that I now teach my children. I would have loved to be able to show you this book. To my brother, Antônio Eugênio Pacheco, a nature lover and the master of overcoming life's difficulties. To my sister, Marya Olimpia Pacheco, who has found the balance between strength and tenderness and is the most ethical person I have ever met. To my beloved wife, Cláudia Bittar, for her hard work and dedication that keeps our family united. To my beloved children—Gabriel Pacheco, my best friend, and Ana Sofia Pacheco, my turning point for happiness—for all the joy they have given me.

Library of Congress Cataloging-in-Publication Data

Names: Flávio, Altamiro, author.
Title: Botulinum toxin for facial harmony / Altamiro Flávio.
Description: Hanover Park, IL : Quintessence Publishing Co Inc, [2018] |
Includes bibliographical references and index.
Identifiers: LCCN 2018011314 | ISBN 9780867157871 (hardcover)
Subjects: | MESH: Botulinum Toxins, Type A--therapeutic use | Cosmetic
Techniques | Facial Muscles--drug effects | Case Reports
Classification: LCC RL120.B66 | NLM QV 140 | DDC 615.7/78--dc23
LC record available at https://lccn.loc.gov/2018011314

QUINTESSENCE PUBLISHING
USA

Quintessence Publishing Co, Inc
411 N Raddant Road
Batavia, IL 60510
www.quintpub.com

5 4 3 2 1

Editor: Leah Huffman
Design: Sue Zubek
Production: Sue Robinson

Printed in China

contents

foreword

Esthetics should be considered part of dentistry as a whole instead of just a specialty. Regardless of our expertise, a common goal in dentistry will always be to integrate, preserve, or recreate function, biology, structure, and esthetics. Therefore, there is no dentistry without esthetics and no facial esthetics without dentistry.

As the well-known plastic surgeon Ivo Pitanguy once said, "Before performing facial plastic surgeries, we should first take care of the smile." A smile works as a postcard of ourselves, a universal expression unique to human beings. Consequently, esthetics has an essential role as a means to generate self-esteem, confidence, well-being, and joy.

In order to be able to produce esthetic smiles, we first should understand the face itself. All professionals who work with smile rehabilitation should be experts on the face. We have noticed a lack of facial knowledge by dentists as well as a lack of knowledge of smiles by plastic surgeons. This gap should not exist. The integration of these two worlds will transform the way we impact people's lives by modifying their facial expressions.

Patients who need or want more confident smiles deserve a complete orofacial analysis that should be made by a team of professionals with extensive knowledge in areas that include orthognathics, orthodontics, orthopedics, total prosthesis, cephalometry, dentogingival esthetics, airways, occlusion, perioral procedures, dermatology, and plastic surgery procedures. Instead of elaborating esthetically perfect projects, it is essential to obtain harmonious results that will meet the morphopsychologic desires of our patients.

Being an orofacial expert involves more art than math—an art that produces predictable results through the detailed study of facial anatomy and clinical practice of the procedures. This explains why I became a fan of Altamiro, a pioneer and artist of orofacial esthetics. In my point of view, this book will become a reference on this topic due to the great skill of the author in organizing and expressing his ideas, his vast clinical experience, his wonderful results achieved, and his educational method used to gather all of his knowledge. Without a doubt, this masterpiece will help all dentists who wish to go beyond their current scope. For all these reasons, it is a great honor to introduce this book. Best wishes and good luck in this journey.

Christian Coachman, DDS, CDT
Founder of Digital Smile Design

foreword

The challenge of our generation is to look young and youthful for the longest time possible. Botulinum toxin (BTX) is useful in the treatment of many diseases. Dental clinicians are experts on the head and neck area and have a deep comprehension of the anatomy and physiology of the muscles of the face. BTX has been applied in conjunction with hyaluronic acids for the treatment of facial asymmetry, temporomandibular disorders and facial pain, bruxism and clenching, and age-related or other esthetic concerns. The clinical application of BTX can help to control parafunctional habits, improve facial esthetics, and altogether change patients' quality of life.

It is my pleasure to introduce this book written by my mentor on this subject, Dr Altamiro Flávio. The book is divided between the fundamental concepts of BTX application and protocols to use in various clinical situations. This handbook is designed to be a practical introductory and reference guide for students, clinicians, and researchers. The author has gathered the necessary knowledge, clinical fundamentals, scientific evidence, and technical skills and protocols to write the constituent chapters.

I hope you enjoy this book and can achieve success with BTX application in your patients.

Paulo V. Soares, DDS, MS, PhD
School of Dentistry
Federal University of Uberlândia, Brazil

preface

Throughout these 25 years working as a teacher, sometimes I catch myself rereading old educational materials, and I find that the only knowledge we keep is that which we use in our daily practice. This book was based on this concept. All information provided has clinical applicability. When you are 50 years old, it is only natural to start evaluating what is really worthwhile in life. My goal was to write an objective book that could effectively guide professionals who want to provide the different benefits of botulinum toxin to their patients. Even before thinking about treating a patient, we as professionals must concentrate on not causing any injury, so I chose to describe the limits and risks of the most delicate procedures. Science has several theories, some feasible and others not so much. This fact has always confused readers of scientific works. Therefore, I was cautious enough to prove several of the contents in the book through numerous clinical cases, carefully retreated and described in an objective way.

My students often complain that botulinum toxin treatments only last 5 months. When they do this, I ask them to name one type of antibiotic, anti-inflammatory, anesthetic, or antidepressant that has an effect that lasts as long. In fact, the duration time is one of the greatest advantages of the toxin. I see these complaints as an acknowledgment of the toxin's benefits and a subconscious desire for the effect to last longer.

Other students ask themselves why God in his infinite perfection did not allow all human beings to be beautiful. I posit that perhaps this was on purpose so we as humans can develop the skill to love others regardless of their outward appearance. Nonetheless, it is the professional's responsibility to study hard to offer health and esthetics to his or her patients.

I get excited when I see the final results of treatment in my daily practice. This professional accomplishment is a great reward. I rarely have patients who are not secure enough to accept the esthetic procedures. While they understand that aging is a natural part of life, they do not want changes to their face, so these esthetic procedures allow them to maintain their appearance a little longer.

Finally, during the course of reading this book, the reader will find a lot of numbers; these numbers help us to find the correct dimensions and proportions. Because each face has different measurements, we need numbers and proportions to provide specific treatments. It is part of my philosophy to create "one smile for each face."

God bless you all. And please enjoy the reading.

Acknowledgments

I would like to express my gratitude to Dr Paulo Vinícius Soares for the idea and encouragement to write this book. It is an honor to be trusted by this great professional. I am also grateful and have great respect for Bill Hartman, Leah Huffman, Bryn Grisham, Sue Robinson, Sue Zubek, and the entire Quintessence crew involved in giving life to this book. You amaze me with your work. My special thanks to Dr Rubelisa Cândido Gomes de Oliveira for assisting us with the scientific format of this book. Your organization is deeply appreciated. My dear Denise Riley, I am so grateful for the uncountable hours spent on finding the right terms for my books. You are like a sister to me. I wish to thank my secretary, Carina Morais, for her perfectionism and unselfish friendship. I also would like to thank my friends at the Miami Anatomical Research Center—Allan Weinstein, Eduardo Sadao, Heloise Peixoto, Justin Fraioli, Jorge Carrasco, and Maylin Perez Carrasco—for their effort in keeping up with our courses that help educate so many professionals. I wish to acknowledge my first supporter, Dr Francisco Leite Pinto, as well as my friend Dr Newton Fahl Jr, who taught me the meaning of "possessing the knowledge." To my friend Dr Fernando Saad, thanks for your true friendship and for the "true vertical line." Dr Francisco Célio Dantas, thank you so much for all those years as a partner in our mission to educate. Dr Maria Geovânia Ferreira, even after 20 years of partnership your competence still surprises me. Dear anatomists Márcia Viotti and Rogério Zambonato, you amaze all students with your skillful dissections. Congratulations! Thank you, Alberto Van Lima, for spending so many nights working hard to produce such beautiful images all these years. I also would like to express my gratitude to Professor Luis Fernando Naldi for our discussions about esthetic facial references. My grateful thanks to Professor Paula Cardoso and Rafael Decurcio for their noble work at ABO in Goiás. I would like to sincerely thank Rafael Araújo Câmara for his support. Thanks also go to my colleagues from SBOE and SBTI for all the knowledge I have received from you. I greatly respect these two associations. My greatest respect and gratitude goes to all those who have selflessly given their precious bodies to science. To my dear patients who allowed me to use their photos and clinical history to improve the knowledge of so many health professionals through this book, I cannot thank you enough. I would also like to acknowledge the important role of so many teachers I have had throughout my lifetime. I will always carry with me your teachings. Finally, my eternal gratitude to the greatest teacher of all, Jesus, for the daily blessings.


BOTOX®
toxina botulínica A
VIA INTRAMUSCULAR / INTRADÉRMICA
CONTÉM: 100 UNIDADES
ALLERGAN
Lote:
Fab.:
Val.:

CHAPTER

01

Basic Principles of Botulinum Toxin

Box 1-1 Serotypes of BTX

A, B, C1, C2, D, E, F, G, H, and I
A and B have different clinical uses. C, E, and F are used experimentally.

Box 1-2 Characteristics of BTX-A and BTX-B

A	B
Broad range of indications	Shorter duration of effect
Used in different countries	Therapeutic use
Well-described in the literature	Increased pain when injected
Marketed as Botox (onabotulinumtoxinA, Allergan), Dysport (abobotulinumtoxinA, Ipsen), and Xeomin (incobotulinumtoxinA, Merz)	Marketed as Myobloc (rimabotulinumtoxinB, Solstice Neurosciences) and NeuroBloc (no FDA license, Eisai)

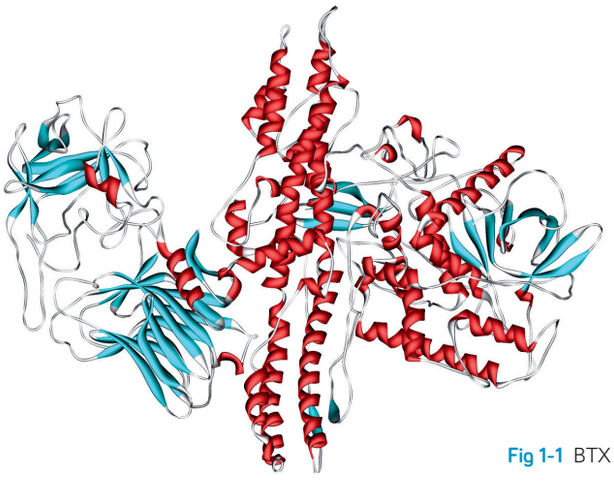


Fig 1-1 BTX neurotoxic protein.

Botulinum toxin (BTX) is a biologic agent manufactured in a laboratory in the form of a crystalline stable substance, freeze-dried in human albumin, and supplied in a sterile, vacuum-dried vial to be reconstituted in a saline solution. It is naturally produced by *Clostridium botulinum*, a gram-positive anaerobic bacterium that produces several distinct serotypes of BTX (Box 1-1).[1–3] In terms of cosmeceutical therapy, type A is the only one that shows a clinically important biologic activity, and hence it is the most often studied and used serotype of BTX.[4] Type B is also commercially available to treat cervical dystonia and for patients resistant to BTX-A,[5–8] but it is generally associated with a higher incidence of pain when injected and a short-lasting effect, although it has a faster onset than type A[9–13] (Box 1-2).

BTX is an organic macromolecule made up of amino acids linked together by peptide bonds (polypeptide chains). Biochemically it consists of a 50-kDa light chain and a 100-kDa heavy chain (Fig 1-1) connected by protease-sensitive disulfide bridges; the bond of these chains results in a

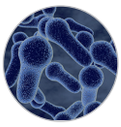
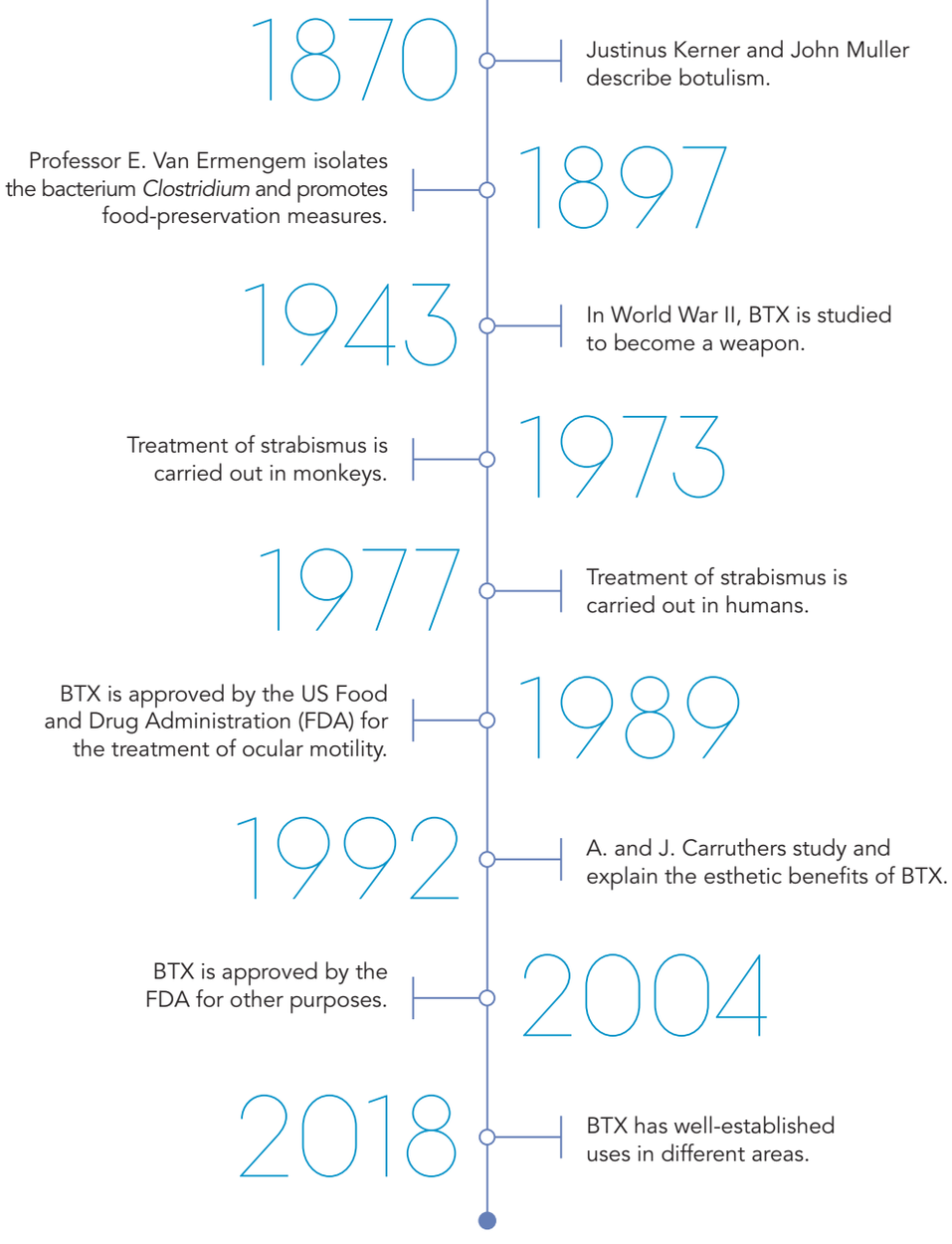


Fig 1-2 Timeline of BTX discovery.



150-kDa protein.[14,15] This toxin is protected by larger nontoxic proteins and by hemagglutinin. The final weight of these multimeric complexes varies from 700 kDa for BTX-B to 900 kDa for BTX-A, reflecting the weight of the surface proteins that form such protection.[1,2,16,17]

Figure 1-2 illustrates a brief history of the discovery and scientific developments surrounding BTX.

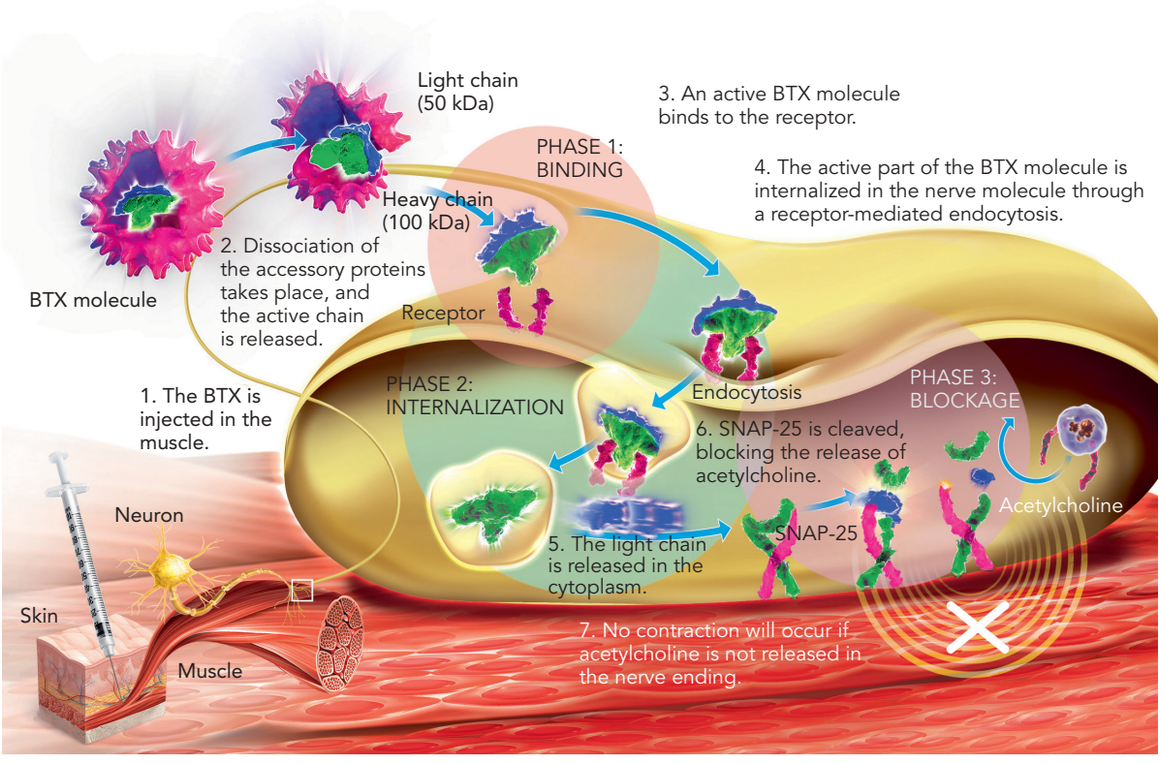


Fig 1-3 Mechanism of action of BTX.

Mechanism of Action of BTX

BTX-A should be injected in the muscle so that it disperses and diffuses to cholinergic nerve endings, where its mechanism of action takes place. BTX essentially breaks down fusion proteins (synaptosomal-associated protein 25 [SNAP-25]) responsible for the release of the neurotransmitter acetylcholine (ACh), thereby inhibiting muscle contraction in the fibers that receive the BTX injection.[16–20] Figure 1-3 shows a detailed illustration of this process, as outlined below.

Once injected, BTX dissociates from the accessory proteins through the action of proteases. Immediately afterward, it is irreversibly bound to high-affinity specific receptors in the neuromuscular junction (NMJ). This is phase 1: binding.

Once the BTX molecule is bound to the receptor at the nerve cell membrane surface, the heavy chain allows the toxin to enter the cell through a membrane invagination, resulting in the formation of a vesicle that will surround the two chains of BTX. This process takes 20 minutes and is called *receptor-mediated endocytosis*. This is phase 2: internalization.

The light chain is then separated from the heavy chain by the dissociation of disulfide bridges through the action of proteases. Under an acidification condition, it is released from the vesicle to the neuronal cytoplasm. Once at the cytosol, the light chain performs its metalloproteinase activity at the intracellular targets that regulate the exocytosis of ACh vesicles. Such targets are part of the SNARE complex (soluble N-ethylmaleimide-sensitive factor attachment receptor) responsible for the binding and coupling of ACh vesicles. This complex is formed by the fusion of three proteins: SNAP-25, VAMP (vesicle-associated membrane protein), and syntaxin 1a.

The light chain of BTX-A, through a zinc-dependent endopeptidase and under an acidic pH, cleaves SNAP-25. (VAMP is cleaved by BTX-B, -D, and -F, and syntaxin 1a is cleaved by BTX-C.) This cleavage prevents the release of the neurotransmitter ACh. This is phase 3: blockage or proteolytic cleavage.

By inhibiting release of ACh from synaptic vesicles, BTX chemically denervates muscles and glands; this process is known as *chemodenervation*. This mechanism is specific to BTX-A and has wide clinical applications, including the modulation of muscle contraction, whose effect is clinically observed for 3 to 4 months. It may also be used to reduce hyperhidrosis for up to 12 months and excessive salivation for up to 6 months.

Box 1-3 Onset and duration of action of BTX

Onset of effects: 6 hours

Onset of clinical results: 24–72 hours

Final stabilization of its clinical action: Up to 14 days

Duration of effect on muscles: 2 weeks to 6 months

Duration of effect on salivation: Up to 6 months

Duration of effect on hyperhidrosis: Up to 12 months

Action of BTX

The physiologic response to BTX injection is observed 6 hours after its administration, and clinical results are seen within 24 to 72 hours after the procedure.[21] While clinical paralysis is observed 24 hours after the injection, the peak of the paralytic effect occurs 14 days later. Depending on individual factors such as doses and postblockage instructions, induced blockage by BTX can last from 2 weeks to 6 months[22] (Box 1-3).

Once BTX is administered, the toxin response is irreversible during the period of time described above. However, eventually the effect is reversed. There are two hypotheses for the reversibility of the BTX effect:

1. Axonal sprouting and muscle reinnervation occur; that is, a new NMJ is formed.
2. Regeneration occurs at the same NMJ altered by the application of BTX. [23]

Subsequently, new SNARE complexes form, thereby preventing the toxin from causing any other effect on the patient.

The duration of BTX-induced blockade, varying from weeks to months, vastly exceeds the recovery time of the action targets of the neurotoxin, which suggests that other intracellular actions are involved in the persistence of its effects. Furthermore, the duration as well as the blocking efficacy is dependent on the doses and formulations of the used serotypes.[22] While the different biochemical cellular events that serve as a basis for this variance are unknown, many factors may contribute:

- Light chain lifetime inside the cytosol
- Turnover (protein renewal) of target SNARE proteins (VAMP, SNAP-25, and syntaxin 1a)
- Secondary biochemical events related to SNARE production and/or peptide release

The metabolic pathway has not been properly documented; however, it may be explained by the presence of proteases that lead to a degradation proteolysis of polypeptide chains present in the molecule.[2]

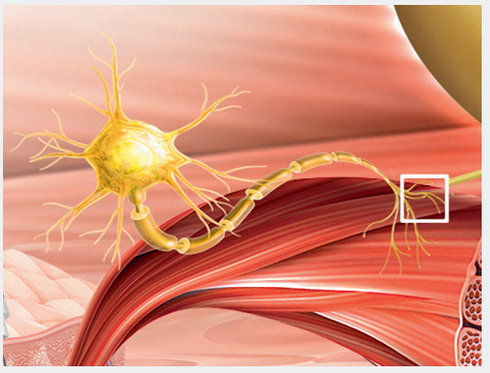
Biosafety

The toxin biosafety is evidenced by its selective action in the peripheral cholinergic nerve ending inhibiting ACh release. It does not pass the brain barrier or inhibit the release of ACh or any other neurotransmitter in this level. The toxin does not bind to nerve fibers of nerve stems or the postsynaptic region.[2]

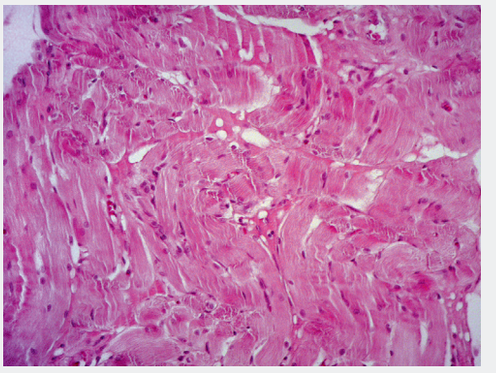
Within the muscle, the amount of BTX administered is reduced to about half within approximately 10 hours. Within the 24 hours postinjection, 60% of the substance is excreted through urine.[2]

The Neuromuscular Histology

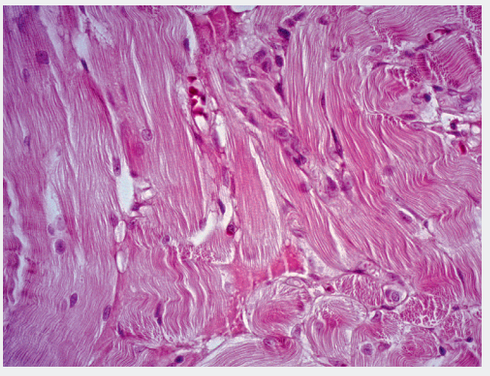
It is important to review the histology of muscle tissues before using BTX (Fig 1-4).



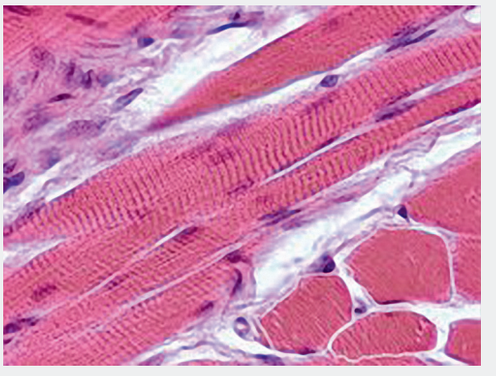
Neuromuscular junction The effects of BTX are especially intense on the hyperkinetic muscles because of the superior number of nicotinic acetylcholine receptors contained therein.



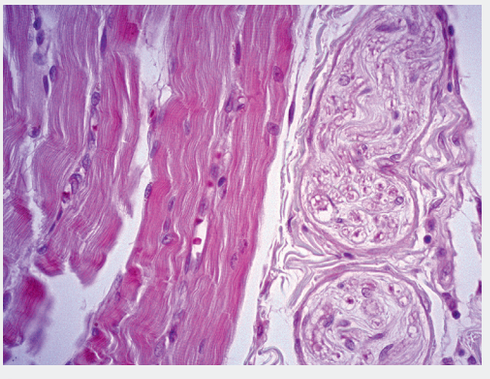
Muscle tissue It is composed of long, multinucleated cells specialized for contractions. Its cytoplasm contains great amounts of contractile protein filaments, primarily actin and myosin. It is a highly vascularized and innervated tissue.



Skeletal muscle Representing most of the muscles in the human body, it is attached to the human skeleton via tendons and is responsible for the performance of various movements, such as walking, running, and holding or manipulating objects.



Cardiac muscle Only found in the heart, it has long, cylindric, and striated cells with ramifications. These ramifications connect one cell to another through a structure permeable to an electric impulse called the *intercalated disc*. This disc makes the contraction of the cardiac muscle uniform.



Smooth muscle Found in internal organs such as the intestine, bladder, and uterus, it is responsible for movement characteristics such as peristalsis, elimination of urine, and labor contractions, respectively. It is also found in blood vessels, where it helps to regulate blood pressure.

Cutaneous or superficial muscles Situated underneath the skin, these muscles have their origin or attachment at the dermis. They are situated in the head, neck, and hand (hypothenar region).
Deep or subaponeurotic muscles These muscles do not present attachments in the deep layer of the dermis and are inserted in bones. They are located underneath fasciae.

Fig 1-4 Histology of the muscle tissues.

Box 1-4 Characteristics of BTX-A

Specificity: The action of this protein specifically occurs in presynaptic neurons of the NMJ.

Temporary irreversibility: The action of BTX-A in the muscle lasts 3 to 4 months. After the third month, a progressive clinical decrease is observed until its total extinction around month 5 or 6.

Immunogenicity: Injections administered less than 3 months apart might cause the "vaccine effect," where the patient no longer responds to the BTX-A injections. A minimum interval of 4 months must be respected.

Diffusion halo: A halo determines the amount of BTX-A diffused around the site injected. The smaller the diffusion halo, the more accurate it is.

Characteristics of BTX-A

Using simple terminology, BTX-A works by reducing the muscle action potential. Its presence in the synaptic cleft decreases the release of the neurotransmitter ACh. Instead of physically sectioning the nerve to weaken a muscle related to it, its tone and strength are chemically reduced, which is a simpler and also temporary process. For this purpose, BTX-A shows some characteristics that make it peculiar, including the following (Box 1-4):

Specificity

BTX-A only affects the muscle tone and contraction power where injected. That is, no other senses are affected by the toxin. Patients will still keep their senses of touch, hearing, smell, sight, and taste. So if the patient presents different symptoms of local muscle hypotonicity after toxin injection, they are not related to BTX-A treatment and may be an adverse event.[24] This specificity provides safety and predictability to professionals using BTX in their patients.

Temporary irreversibility

Once the toxin starts showing its effect, it cannot be reversed until the vesicular activity in the original nerve terminals is restored (reinnervation). If, for instance, when injecting the toxin in the frontal region, an undesired diffusion occurs in the levator palpebrae superioris muscle causing a palpebral ptosis, it is important to understand that this effect is temporarily irreversible. There is no evidence that laser therapy, alpha-adrenergic eye drops, or electric stimulation is able to revert the effect of the toxin.

Immunogenicity

In the manufacturing of BTX in a pharmaceutical laboratory, the stage comprising the purifications is important. Several precipitations in an acid environment are performed to remove ribonucleic acids and other contaminant acids in order to avoid any kind of adverse reactions and to decrease antigenicity.[2]

Immunogenicity refers to the ability of a protein product to elicit antibody formation. As with any therapeutic protein, BTX is regarded as foreign by the host and therefore has the potential to induce an immune response, particularly with repeated administration. This can lead to the development of neutralizing antibodies that may or may not result in secondary treatment failure.[25]

Various factors impact the immunogenicity of botulinum neurotoxins, including product-related factors such as the manufacturing process, the antigenic protein load, and the presence of accessory proteins as well as treatment-related factors such as the overall toxin dose, booster injections, and prior vaccination or exposure.[26]

In clinical practice, it is understood that because the effect of the toxin is temporary, it has to be periodically reinjected to maintain the desired effects. However, it is necessary to wait for a minimum of 4 months between applications. Reinjections in shorter periods might result in the formation of antibodies, which can reduce the duration of BTX's effects or potentially eliminate the effect altogether. Therefore, "touch-ups" should be avoided.[26] Before treatment, the patient should be informed that once the BTX starts to take effect, small asymmetries are likely and are observed even in natural faces. Reinjections to correct asymmetries or readjustments of effects should only be done in cases that really require the procedure. The professional should protect the patient from immunogenicity. Two studies found that patients who developed secondary nonresponse to onabotulinumtoxinA (ONA) received more frequent injections and/or had more booster injections than patients who did not develop resistance.[27,28]

Diffusion halo

Precise location of neurotoxin injection is required to produce the desired clinical results. Temporary disfigurement or functional impairment can occur if the neurotoxin diffuses into adjacent muscle. When injecting BTX-A in the face, it is important to remember that the interface of facial expression muscles is weak due to the lack of fascia. On the other hand, muscles such as the masticatory muscles present a fascia to isolate and individually separate them so that the movements are isolated. While this fascia helps to prevent inflammation from spreading, it also contributes to the muscle-bone attachment. It also protects the muscle from diffusion of toxin.

The origin or attachment of mimetic muscles is located in the dermis, thereby causing skin traction to produce facial expressions. Therefore, the lack of a fascia covering these muscles increases the chance of diffusion when injecting BTX. To achieve a limited action in a specific muscle, it is fundamental to understand and learn how to work with different diffusion profiles of BTX. Choosing a product that allows a higher predictability in terms of results also decreases the possibility of adverse effects. It is also important to consider the dilution to be used and follow the recommendations, because the diffusion depends on the volume to be injected. It is possible to dilute the toxin using different volumes of saline solution; however, using a higher volume of saline solution will increase the chance of diffusion to undesired muscles.

Aoki et al[29] proposed that different diffusion characteristics were attributed to protein complex size and pharmacologic properties, whereby the high molecular weight of ONA limits tissue distribution and explains the reported differences in side effects favoring ONA over abobotulinumtoxinA (ABO). However, more recent studies suggest that this is not the case. These studies compared the diffusion of ONA and ABO by measuring the size of anhidrotic halos following injection of identical volumes into the forehead of patients. Using dose ratios of 1:2.5, 1:3, and 1:4, the authors showed that the area of anhidrosis was larger with ABO in 93% of patients at all dose ratios.[30] Importantly, it has been argued that molecular weight and protein complex size do not affect biologic activity and pharmacologic properties because the BTX-A rapidly dissociates from the complexing proteins (if present) after dilution, drying, and reconstitution of the preparation.[31] A comparison of incobotulinumtoxinA (INCO) with ONA showed no difference in the size of the anhidrotic area produced following injection of the same dose.[32]

These studies also suggest that Dysport (Ipsen) has a greater diffusion halo than Botox (Allergan), and Xeomin (Merz) shows a halo similar to that for Botox.

Frevert[25] evaluated the stability of commercial formulations and found that human serum albumin (HSA) is required to stabilize BTX-A products, with ABO having the lowest content of all. The low amount of HSA in ABO could at least partially explain why not all of the neurotoxin in ABO is bioavailable, depending on the concentration of HSA in the injected volume.[33]

Box 1-5 Dilution of 100U in 1 mL of saline

When diluting a 100U vial of BTX (Botox or Xeomin) with 1 mL of saline in order to inject 10U of toxin in a determined muscle, simple algebra can be used to calculate the volume to be administered:

Given: 1.0 mL = 100U

Problem: X mL = 10U

Solution: X = 0.1 mL

When using a 30U syringe, you can see at the bottom that its maximum capacity is 30U and its maximum volume is 0.3 mL. Again, simple algebra can be used to calculate the number of units that would represent 0.1 mL in this dilution:

Given: 0.3 mL = 30U

Problem: 0.1 mL = XU

Solution: X = 10U

CONCLUSION: When using this dilution to obtain 10U, the professional has to inject 10U.

Box 1-6 Dilution of 100U in 2 mL of saline

To determine the injection volume when diluting a 100U vial of BTX (Botox or Xeomin) in 2 mL of saline in order to inject 10U of toxin in a determined muscle:

Given: 2.0 mL = 100U

Problem: X mL = 10U

Solution: X = 0.2 mL

You can use the same formula to calculate the number of units that would represent 0.2 mL in this dilution:

Given: 0.3 mL = 30U

Problem: 0.2 mL = XU

Solution: X = 20U

CONCLUSION: In this type of dilution, to obtain 10U, the professional has to inject 20U. This requires an injection double the volume of that obtained with a 1-mL dilution.

Dilution Technique for BTX-A

A preservative-free 0.9% sodium chloride (saline) solution is used to reconstitute lyophilized (freeze-dried) BTX, as preservatives might change the solution pH and affect the toxin potency. The injection becomes painful when distilled water is used for dilution. A good technique for Botox is to use 1 mL of saline to dilute the toxin contained in a 100-unit (100U) vial, or 0.01 mL per unit (Box 1-5). However, several professionals use 2 mL to dilute a 100U vial of BTX-A. In this case, one unit of toxin corresponds to 0.02 mL of solution, meaning that it would be necessary to inject double the volume to obtain 1U (Box 1-6). This procedure may lead to the dispersion of toxin to other nontargeted muscles, thereby causing undesired effects.

Lethal dose 50 (LD50) experiments, whereby toxicity is measured in terms of the amount of a given drug required to kill half of a tested population of laboratory mice after an intraperitoneal injection, define the amount of a drug that will constitute the minimum unit of action—that is, the

Fig 1-5 *(a)* BTX vial. *(b)* Sterile, preservative-free 0.9% sodium chloride (saline). *(c)* Luer-Lok syringe (in mL). *(d)* 22-gauge needle. *(e)* Sterile gloves. *(f)* Container to discard the needle.

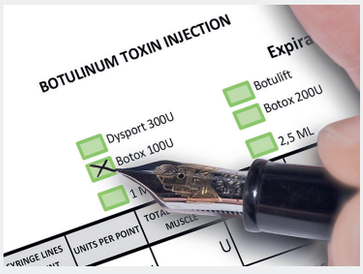
smallest amount of a drug required to promote a minimum effect. Doses of all varieties of BTX are expressed in terms of these units (U), a measure of potency, not milliliters (mL), a measure of volume. A high-volume dilution will result in a less potent solution, meaning that a higher volume of toxin would be necessary to obtain one or more units of BTX. On the other hand, using a small amount of saline solution for dilution will result in a more concentrated and potent solution. With this formulation, the operator would be able to obtain the same number of units with a smaller-volume injection. It is also important to consider that the higher the volume injected, the higher the dispensing of the drug, the level of patient discomfort, and the chances of bruising.

Figure 1-5 shows the armamentarium required for BTX-A dilution, and Fig 1-6 illustrates the procedure. Below are some basic recommendations for this process:

1. Open the box at the recommended site on the side. Do not discard the box.
2. Remove the plastic seal from the vial. Discard it.
3. Do not heat the vial with your hand; instead handle it with the tips of your fingers.
4. Attach a 22-gauge (22G) needle to the Luer-Lok syringe and withdraw the predetermined amount of saline solution required for the dilution.
5. At a 45-degree angle, insert the 22G needle (attached to the syringe) into the rubber stop until the bevel of the needle touches the glass of the vial. Hold the plunger to prevent rapid aspiration of the saline from the syringe, which could cause agitation of the mixture.
6. Do not shake the vial.

1. Refrigerate the vial (2°C to 8°C).

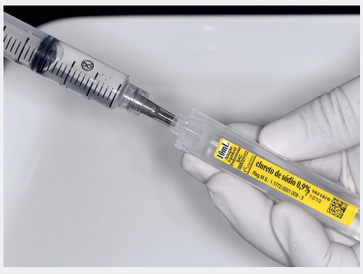
2. Open the box where indicated.



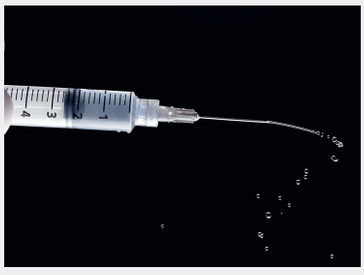
3. Keep the box and record the vial number on the label.

4. Handle the vial with the tip of your fingers to avoid heating.

5. Remove the seal and discard it.



6. Attach the needle to the syringe and withdraw the saline.



7. Withdraw a bigger amount to eliminate the risk of bubbles forming.

8. Introduce the needle (45-degree inclination) until touching the glass.

9. Slowly inject the serum to avoid agitation of the solution.

10. Slowly rotate the vial to humidify its entire internal surface.

11. Insert, remove, and reinsert the needle to weaken the rubber stop.

12. Turn the vial upside down and draw up the toxin.

Fig 1-6 Step-by-step dilution process.

7. Insert, remove, and reinsert a 22G needle approximately 10 times in the same place in the rubber stop to soften the rubber, which will prevent future injection needles from becoming dull. This will reduce patient pain and bruising during the injection.
8. In case all the diluted toxin is not used, put the vial in the preserved box and refrigerate the solution at 2°C to 8°C. Do not freeze it. Write the day of use on the box.
9. BTX (Botox) can be administered within 72 hours of reconstitution when stored at 2°C to 8°C.

Box 1-7 lists other important considerations for the clinical use of BTX.

Box 1-7 Important considerations for working with BTX

- ❑ Botox is available in 50U, 100U, and 200U vials.
- ❑ Vials should be stored between 2°C and 8°C or at or below –5°C.
- ❑ Diluted solutions can be kept at 2°C to 8°C for up to 3 days.
- ❑ The lethal human dose of Botox is 3,000U.
- ❑ The toxin should only be diluted minutes before its application.
- ❑ When diluting, the saline and the BTX should be at a similar temperature.
- ❑ Do not use the needle to perforate the saline vial, as it may be contaminated by bacteria. Open where indicated.
- ❑ The 0.9% saline should be preservative-free so that it will not change the potency of the BTX.
- ❑ The saline solution should be slowly injected to avoid agitation of the solution and degradation of the BTX.
- ❑ The spaces between the marks are greater in a 30U syringe than in a 100U syringe, making it easier to measure precisely.

1. Syringe with 1.1 mL of physiologic saline (with dye).

2. Residual liquid in the syringe and hub.

3. Preparing to draw up the residual liquid in the syringe.

4. Withdrawing the residual liquid.

5. Preparing to withdraw the residual liquid from the hub.

6. Withdrawing the residual liquid from the hub.

7. Liquid withdrawn from the hub.

8. Total residual liquid withdrawn from the syringe and hub = 0.1 mL.

Fig 1-7 Compensating for residual liquid.

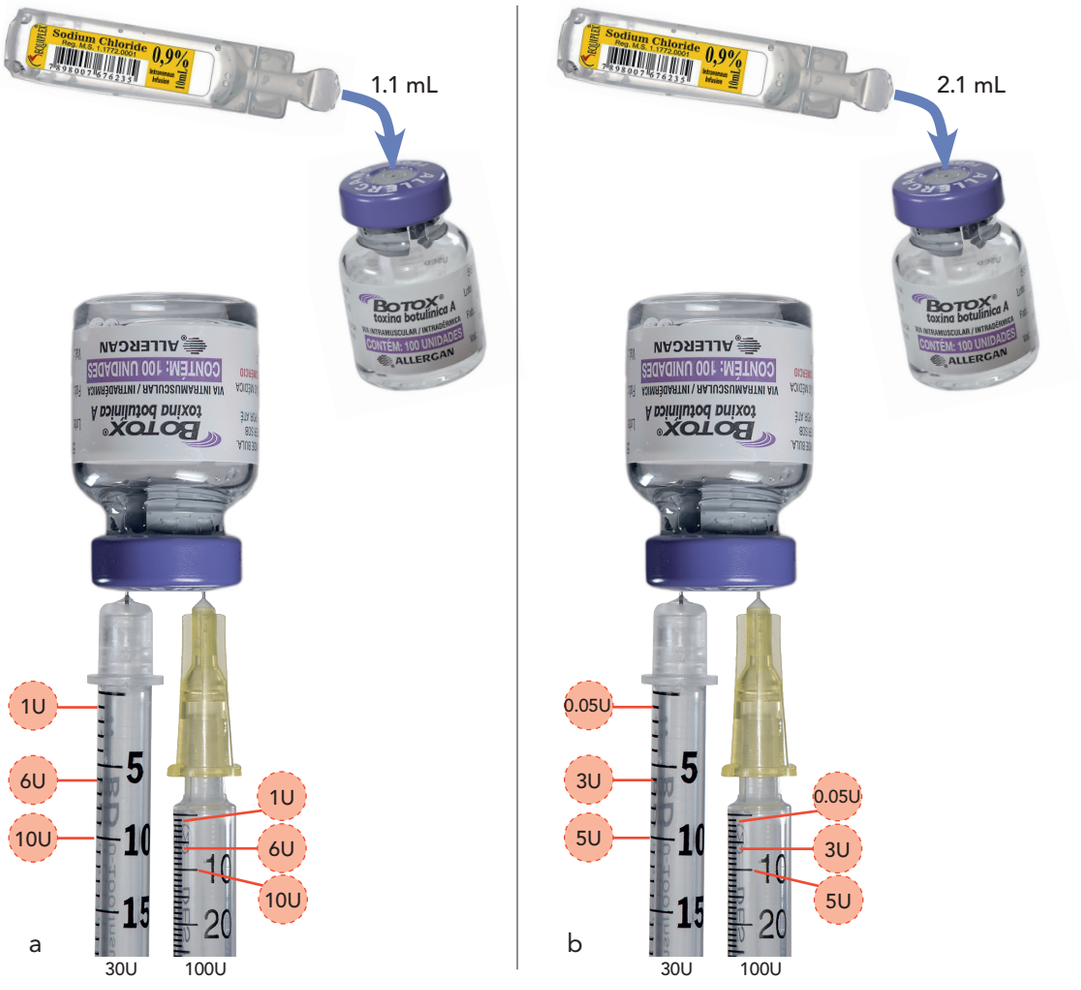


Fig 1-8 *(a)* When diluting 100U of toxin in 1.1 mL of saline, each mark in a 30U or 100U syringe will represent 1U (one toxin unit). *(b)* When diluting 100U of toxin in 2.1 mL of saline, every *two* marks of a 30U or 100U syringe represents 1U (one toxin unit).

Residual liquid

The residual liquid is the amount of saline solution that will not be injected inside the toxin vial because it will be kept inside the syringe and needle used during dilution (Fig 1-7). It is important to compensate for this residual liquid to ensure that no units of BTX are wasted. Therefore, 0.1 mL of sterile physiologic saline may be added to the total volume. That is, if the practitioner plans to dilute the toxin using 1 mL of saline, he or she would draw up 1.1 mL of saline into the syringe, as 0.1 mL will be left in the syringe (see Fig 1-7). If this procedure is not followed, 10% of the dilution in each vial will be wasted, which adds up when you consider a net waste of 1 vial for every 10 vials used. Figure 1-8 illustrates the markings on the syringe when diluting with 1.1 mL and 2.1 mL. It shows that it is easier to use the 30U syringe than the 100U syringe because the space between the marks is greater.

Patient Care

Patient care is an important part of BTX treatment. Figure 1-9 shows the steps involved in a typical appointment.

1. The patient is welcomed to the office.

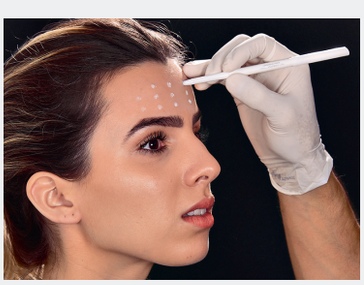
2. The patient is instructed to sit and given the medical history form to fill out.

3. The patient fills out the form.

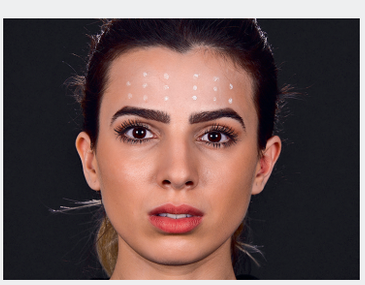
4. The patient is asked to remove all makeup from the face.

5. An assistant helps the patient clean his or her face.

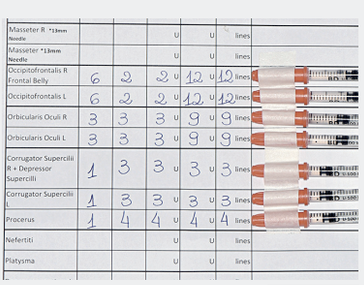
6. An assistant applies topical anesthetic to the face.



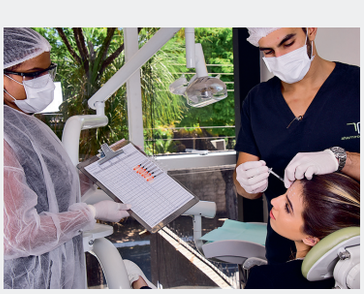
7. A facial analysis is performed, and all injection sites are marked (see protocol for muscle location in chapter 3).



8. A photograph is taken to document the face with the injection sites marked (see protocol photographs in chapter 2).

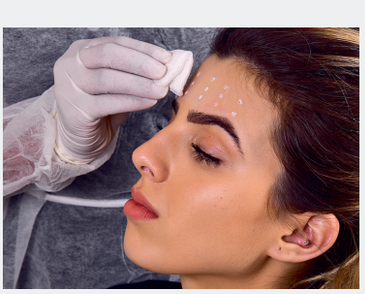


9. The application plan is filled out, and the BTX syringes are prepared and separated (see Fig 1-14b).



10. The BTX is injected.

11. The syringes are discarded in a container specifically for piercing/cutting materials.



12. An assistant performs a light cleansing of the patient's face.

Fig 1-9 Patient care. Postoperative instructions must be given to the patient after treatment.

Box 1-8 **Indications for treatment with BTX-A (Botox, unless otherwise noted)**

INDICATIONS APPROVED BY THE FDA	OFF LABEL (BOTOX)
Strabismus	Temporomandibular disorders
Blepharospasm	Chronic musculoskeletal pain
Hemifacial spasm	Vaginismus
Cervical dystonia (Botox, Dysport, Xeomin, and NeuroBloc)	Wound healing
Cosmetic use	Diabetic neuropathy
Axillary hyperhidrosis	
Chronic migraine	
Neurogenic detrusor overactivity	
Lower urinary tract disorders	
Gastrointestinal tract disorders	
Spasticity	
Spasmodic dysphonia	
Sialorrhea (drooling)	

(Data from Chen.[34])

General Indications for BTX-A

BTX has been a popular medication for over 20 years and has several different therapeutic uses. Increased research on BTX-A has resulted in new indications for its use (Box 1-8). In general, the chemical denervation is a safe technique showing predictable outcomes.

Therapeutic versus cosmeceutical use

- *Therapeutic use:* Focused on the treatment of diseases. There is a pathology present.
- *Cosmeceutical use:* Focused on the preservation or improvement of physical beauty. There is no pathology.

In clinical practice, treatment with BTX-A cannot always be classified as therapeutic or cosmeceutical. Sometimes the same patient will want and/or require both types of therapy, for example, an aging patient with bruxism who may require therapeutic treatment for the bruxism but who also wants cosmeceutical therapy to smooth expression wrinkles.

Therapeutic use

Therapeutic uses for BTX-A in the face include the following:

- Strabismus
- Blepharospasm
- Hemifacial spasm
- Tension headache
- Bruxism
- Sialorrhea
- Temporomandibular disorder
- Cervical dystonia

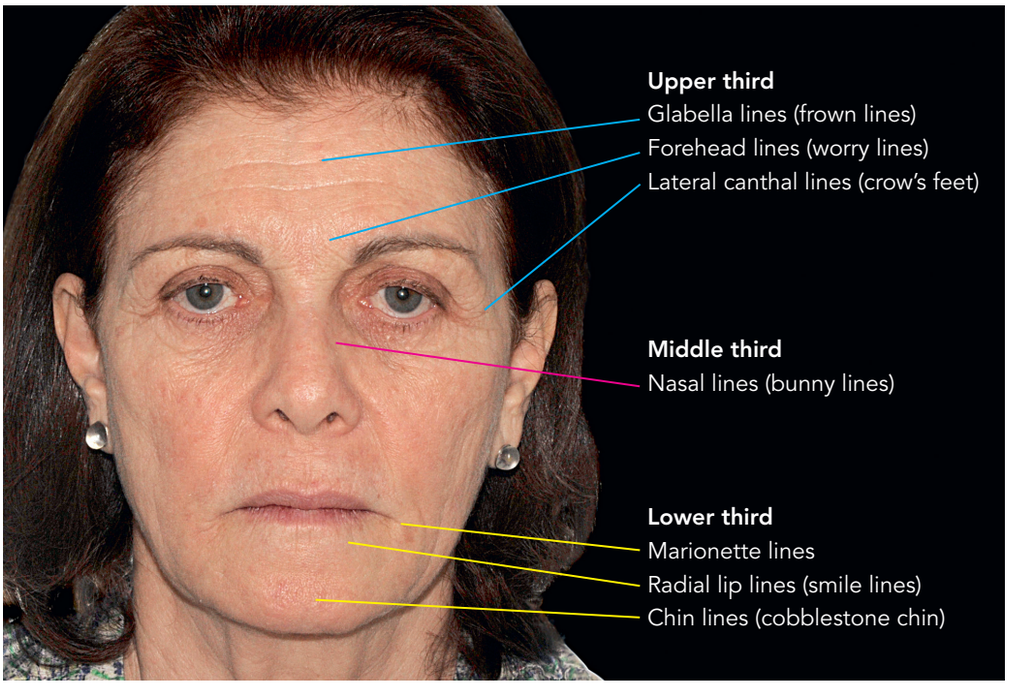


Fig 1-10 Facial wrinkles.

Cosmeceutical use

BTX-A has likely become popular worldwide because of its cosmeceutical use. While most patients understand that its use might improve and/or rejuvenate their physical appearance, its application extends to facial asymmetries resulting from paralysis sequelae or even other facial traumas. In patients living with these conditions, BTX treatment could help restore their self-esteem as well as their social and professional lives.

Cosmeceutical uses for BTX-A in the face include the following:

- Smooth wrinkles related to muscles (occipitofrontal, procerus, corrugator supercilii, nasal, orbicularis oculi, orbicularis oris, mentalis, depressor anguli oris; Fig 1-10)
- Reduce the volume of muscles (nasal, masseter, mentalis, orbicularis oris, platysma)
- Smooth eyelid ptosis
- Improve definition of the jawline
- Lift the eyebrows
- Increase the eye opening
- Reduce the gummy smile
- Elevate the oral commissures

Examples of clinical treatment are illustrated in chapters 2 and 4.

Types of facial wrinkles

Facial wrinkles are caused when muscles attached to the dermis move the skin during facial expressions. When these mimetic muscles contract, the skin is pulled perpendicular to the underlying muscle fibers, leaving it wrinkled. Wrinkles may be classified as dynamic or static (Fig 1-11). When they are formed during facial expression and fade at the end of the muscle dynamics, they

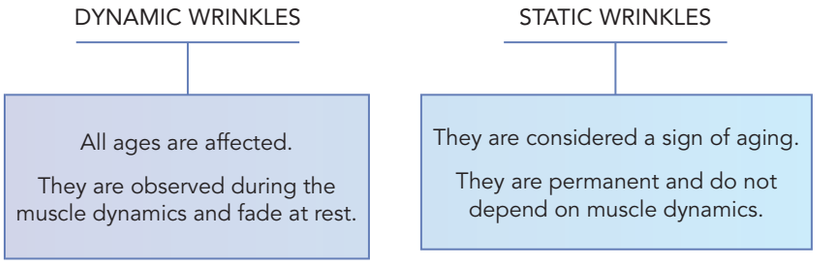


Fig 1-11 Classification of facial wrinkles.

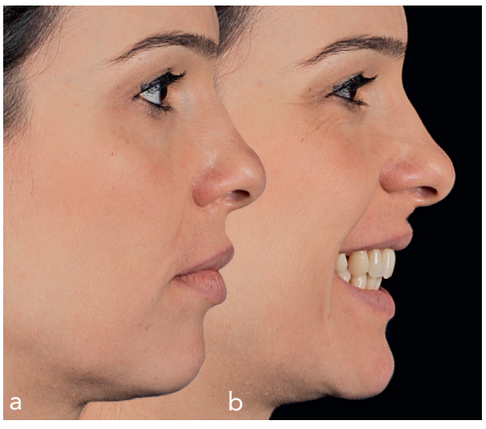


Fig 1-12 *(a and b)* Dynamic wrinkles are formed during mimetics and disappear at the end of the action. At rest, the wrinkles fade away. The lack of wrinkles suggests that this patient is young.

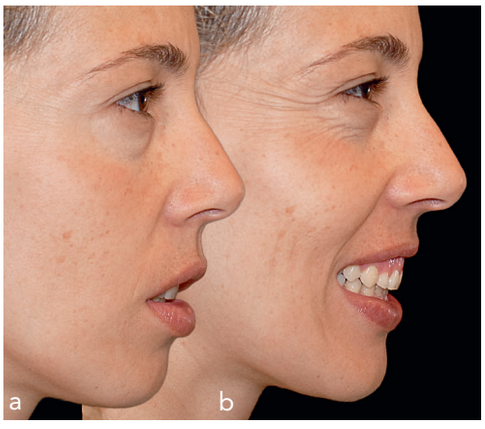


Fig 1-13 *(a and b)* Static wrinkles are formed during facial expressions and do not fade at the end of the muscle action. At rest they are noticeable. The presence of wrinkles suggests that this patient's face is in an aging process.

are classified as *dynamic* (Fig 1-12). However, when they do not fade at rest, they are classified as *static* (Fig 1-13). According to Oriá et al,[35] with aging the skin shows decreased epidermis-dermis thickness, reduced elasticity and secretion of sebum by the sebaceous glands, compromised immunologic response, a decreased number of sweat glands, and reduced vascular tone, with fragility of blood vessels. All of these characteristics associated with repeated skin traction lead to definitive markings (ie, static wrinkles).

It is well known the wrinkles are formed through the action of facial expression muscles. Thus, it is believed that a decrease in muscle action might reduce the number and depth of wrinkles. BTX-A temporarily postpones the wrinkle status from static to dynamic, giving the face a younger aspect. Dynamic wrinkles start to become static around age 30 years, so patients interested in delaying their onset should begin treatment just before then. The procedure must be repeated every 5 months to maintain the results. The main focus of treatment is the upper third of the face (see chapter 2).

The higher the mobility of a skin region, the earlier wrinkles will form. In the upper third, the skin lateral to the eyes tends to show wrinkles because of the sphincter action of the orbicularis oculi. This is an area relatively easily treated with BTX-A. On the other hand, the intense mobility of the muscles in the middle and lower thirds of the face involved with mouth function cause the skin in these areas to show their age more than areas with lower mobility.[36] Due to its complexity, the treatment of the lower third requires more caution and professional expertise.

Box 1-9 shows a checklist of all the facial areas that can be treated with BTX-A.

Box 1-9 BTX treatment checklist

TREATMENT AREAS

- ❑ Glabella lines (frown lines)
- ❑ Forehead lines (worry lines)
- ❑ Lateral canthal lines (crow's feet)
- ❑ Nasal lines (bunny lines)
- ❑ Marionette lines
- ❑ Perioral lines (smile lines)
- ❑ Chin lines (cobblestone chin)
- ❑ Eyelid ptosis
- ❑ Voluminous lip skin
- ❑ Jawline contouring
- ❑ Eyebrow lifting
- ❑ Widening of eye opening
- ❑ Correction of upper gummy smile
- ❑ Correction of lower gummy smile
- ❑ Elevation of lip commissures

Contraindications

BTX is a safe drug. No systemic complications resulting from its use have been reported in the literature. However, as with every pharmacologic product, it should be used with caution and following its indications. Box 1-10 details the contraindications and relative contraindications for BTX.

Box 1-10 Contraindications and relative contraindications for BTX

DO NOT USE in patients:

Who are pregnant or breastfeeding

With any of the following conditions: myasthenia gravis, amyotrophic lateral sclerosis, myopathies, Lambert-Eaton myasthenic syndrome

Taking certain medications (aminoglycosides, calcium blockers)

With infection in the treatment area

With dermatoses in the treatment area (psoriasis, eczema)

Allergic to any of the components of BTX-A or BTX-B (ie, BTX, human albumin, saline, lactose, sodium succinate)

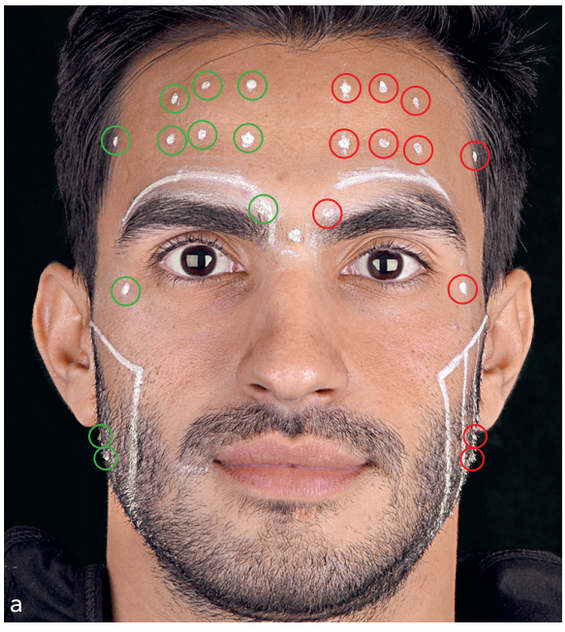
With herpes eruptions in the treatment area

Use with extreme caution in patients:

Whose livelihoods depend on intact facial movements and expressions (eg, actors, singers, musicians, other media personalities)

Who are psychologically unstable or who have questionable motives and unrealistic expectations

(Data from Small,[37] Sposito,[2] Niamtu,[38] and Patel et al.[39])



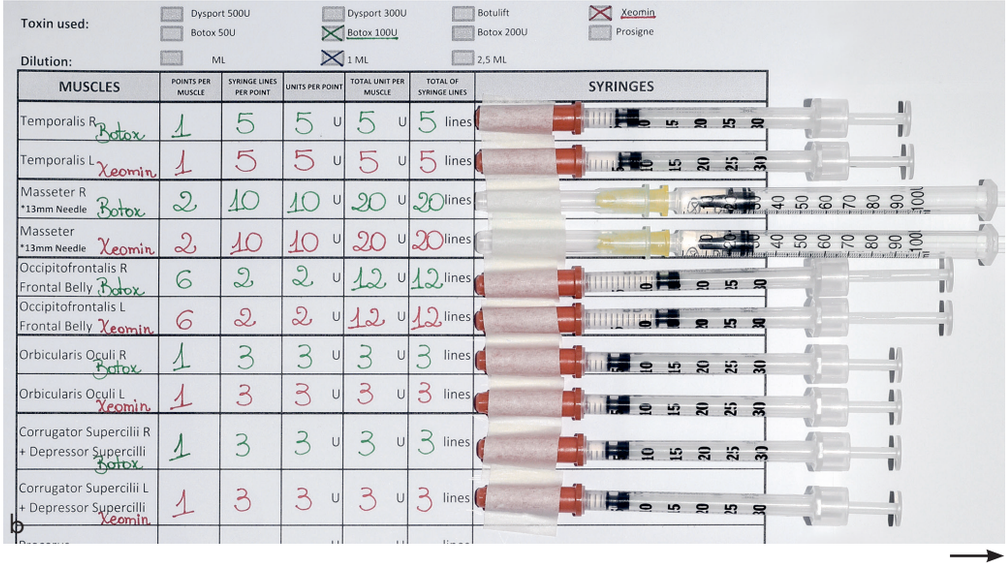


Fig 1-14 Side-by-side comparison of the effects of Botox and Xeomin. *(a)* Injection points for Botox *(green)* and Xeomin *(red)*. *(b)* Chart showing the dosages used at each injection point.

Comparison of Botox and Xeomin

In order to evaluate the clinical effect and duration of two different brands of BTX-A, Botox was injected on the right side of the face and Xeomin on the left side of the face of the patient shown in Fig 1-14. The injections were prepared by the author on the same day as they were administered using the same type of syringes and needles and injected at similar inclinations to similar depths. The green circles in Fig 1-14a represent the injection points for Botox, and the red circles are the injection points for Xeomin. After the injections, several photographs were taken to clinically assess the effects of both toxins, mainly at the occipitofrontalis muscle. During each photographic session, the patient was instructed to lift his eyebrows as much as he could.

This experiment showed that Xeomin had a faster onset than Botox, offering an important advantage for therapeutic use in that the patient will notice quicker relief of symptoms. After the effect was completely installed, the action on the muscles was similar and effective for the same amount of time (ie, 52 days).

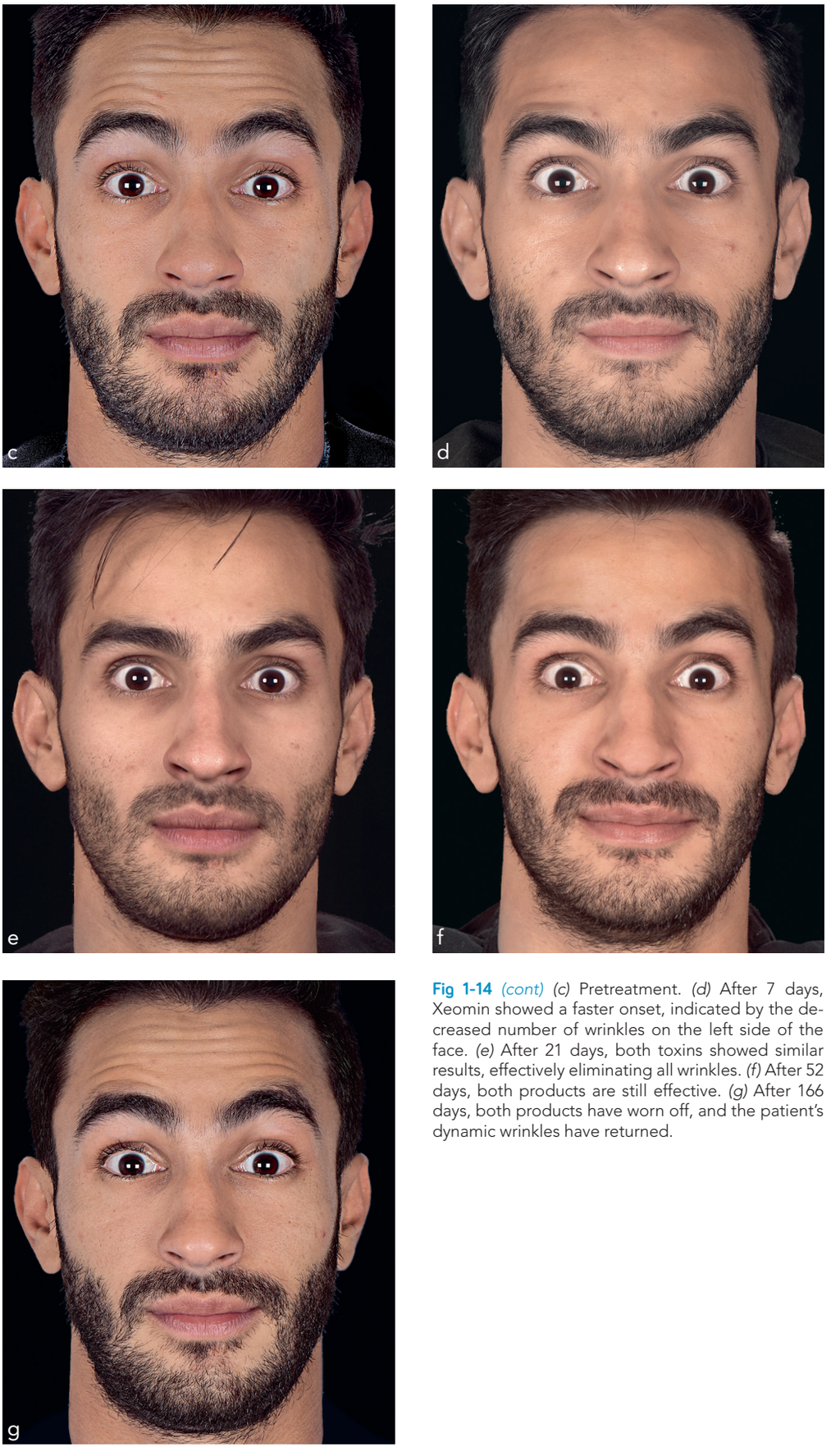
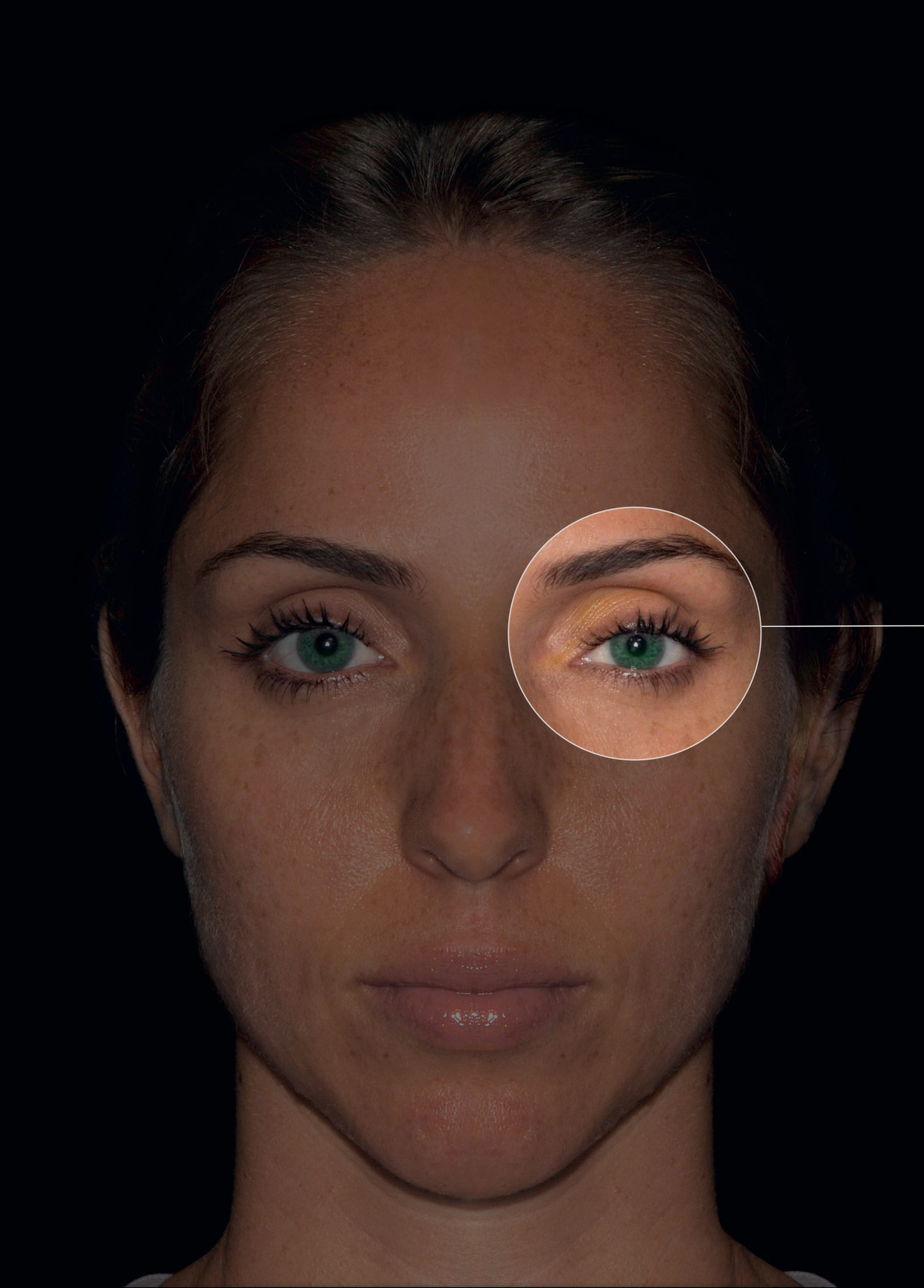


Fig 1-14 *(cont)* *(c)* Pretreatment. *(d)* After 7 days, Xeomin showed a faster onset, indicated by the decreased number of wrinkles on the left side of the face. *(e)* After 21 days, both toxins showed similar results, effectively eliminating all wrinkles. *(f)* After 52 days, both products are still effective. *(g)* After 166 days, both products have worn off, and the patient's dynamic wrinkles have returned.

References

1. Aoki KR. Botulinum toxin: A successful therapeutic protein. Curr Med Chem 2004;11:3085–3092.
2. Sposito MMM. Toxina botulínica tipo A—propriedades farmacológicas e uso clínico. Acta Fisiátr 2004;11(suppl 1):S7–S44.
3. Aoki KR, Guyer B. Botulinum toxin type A and other botulinum toxin serotypes: A comparative review of biochemical and pharmacological actions. Eur J Neurol 2001;8(suppl 5):21–29.
4. Carruthers A, Carruthers J. Botulinum toxin products overview. Skin Therapy Lett 2008;13:1–4.
5. Truong D, Duane DD, Jankovic J, et al. Efficacy and safety of botulinum type A toxin (Dysport) in cervical dystonia: Results of the first US randomized, double-blind, placebo-controlled study. Mov Disord 2005;20:783–791.
6. Factor SA, Molho ES, Evans S, Feustel PJ. Efficacy and safety of repeated doses of botulinum toxin type B in type A resistant and responsive cervical dystonia. Mov Disord 2005;20:1152–1160.
7. Costa J, Espírito-Santo C, Borges A, et al. Botulinum toxin type A therapy for cervical dystonia. Cochrane Database Syst Rev 2005;25:CD003633.
8. Comella CL, Jankovic J, Shannon KM, et al. Comparison of botulinum toxin serotypes A and B for the treatment of cervical dystonia. Neurology 2005;65:1423–1429.
9. Flynn TC, Clark RE 2nd. Botulinum toxin type B (MYOBLOC) versus botulinum toxin type A (BOTOX) frontalis study: Rate of onset and radius of diffusion. Dermatol Surg 2003;29:519–522.
10. Baumann L, Slezinger A, Vujevich J, et al. A double-blinded, randomized, placebo-controlled pilot study of the safety and efficacy of Myobloc (botulinum toxin type B)-purified neurotoxin complex for the treatment of crow's feet: A double-blinded, placebo-controlled trial. Dermatol Surg 2003;29:508–515.
11. Baumann L, Black L. Botulinum toxin type B (Myobloc). Dermatol Surg 2003;29:496–500.
12. Ramirez AL, Reeck J, Maas CS. Botulinum toxin type B (MyoBloc) in the management of hyperkinetic facial lines. Otolaryngol Head Neck Surg 2002;126:459–467.
13. Sadick NS. Prospective open-label study of botulinum toxin type B (Myobloc) at doses of 2,400 and 3,000 U for the treatment of glabellar wrinkles. Dermatol Surg 2003; 29:501–507.
14. Setler PE. Therapeutic use of botulinum toxins: Background and history. Clin J Pain 2002;18(6, suppl):119S–124S.
15. Thakker MM, Rubin PA. Pharmacology and clinical applications of botulinum toxins A and B. Int Ophthalmol Clin 2004;44:147–163.
16. Simpson LL. The action of botulinal toxin. Rev Infect Dis 1979;1:656–662.
17. Gonnering RS. Pharmacology of botulinum toxin. Int Ophthalmol Clin 1993;33:203–226.
18. Neuenschwander MC, Pribitkin EA, Sataloff RT. Botulinum toxin in otolaryngology: A review of its actions and opportunities for use. Ear Nose Throat J 2000;79:788–789,792.
19. Blitzer A, Sulica L. Botulinum toxin: Basic science and clinical uses in otolaryngology. Laryngoscope 2001;111: 218–226.
20. Lam SM. The basic science of botulinum toxin. Facial Plast Surg Clin North Am 2003;11:431–438.
21. Carruthers A, Carruthers J, Cohen J. A prospective, double-blind, randomized, parallel- group, dose-ranging study of botulinum toxin type A in female subjects with horizontal forehead rhytides. Dermatol Surg 2003;29: 461–467.
22. Lew MF, Adornato BT, Duane DD, et al. Botulinum toxin type B: A double-blind, placebo-controlled, safety and efficacy study in cervical dystonia. Neurology 1997;49: 701–707.
23. Hambleton P. Clostridium botulinum toxins: A general review of involvement in disease, structure, mode of action and preparation for clinical use. J Neurol 1992; 239:16–20.
24. Klein AW. Dilution and storage of botulinum toxin. Dermatol Surg 1998;24:1179–1180.
25. Frevert J. Pharmaceutical, biological, and clinical properties of botulinum neurotoxin type A products. Drugs R D 2015;15:1–9.
26. Naumann M, Boo LM, Ackerman AH, Gallagher CJ. Immunogenicity of botulinum toxins. J Neural Transm (Vienna) 2013;120:275–290.
27. Greene P, Fahn S, Diamond B. Development of resistance to botulinum toxin type A in patients with torticollis. Mov Disord 1994;9:213–217.
28. Dressler D, Bigalke H. Botulinum toxin type B de novo therapy of cervical dystonia: Frequency of antibody induced therapy failure. J Neurol 2005;252:904–907.
29. Aoki KR, Ranoux D, Wissel J. Using translational medicine to understand clinical differences between botulinum toxin formulations. Eur J Neurol 2006;13(suppl 4):10–19.
30. Trindade de Almeida AR, Marques E, de Almeida J, Cunha T, Boraso R. Pilot study comparing the diffusion of two formulations of botulinum toxin type A in patients with forehead hyperhidrosis. Dermatol Surg 2007;33 (special issue):S37–S43.
31. Eisele KH, Fink K, Vey M, Taylor HV. Studies on the dissociation of botulinum neurotoxin type A complexes. Toxicon 2011;57:555–565.
32. Sattler G, Callander MJ, Grablowitz D, et al. Noninferiority of incobotulinumtoxinA, free from complexing proteins, compared with another botulinum toxin type A in the treatment of glabellar frown lines. Dermatol Surg 2010;36(suppl 4):2146–2154.
33. Wohlfarth K, Wegner F, Bigalke H, Rummel A. The role of human serum albumin and neurotoxin associated proteins in the formulation of different BoNT/A products. Presented at the TOXINS 2012 conference, Miami Beach, FL, 5–8 December 2012.
34. Chen S. Clinical uses of botulinum neurotoxins: Current indications, limitations and future developments. Toxins (Basel) 2012;4:913–939.
35. Oriá RB, Ferreira FVA, Santana EN, Fernandes MR, Brito GAC. Estudo das alterações relacionadas com a idade na pele humana, utilizando métodos de histo-morfometria e autofluorescência. An Bras Dermatol 2003;78:425–434.
36. Brandt FS, Bellman B. Cosmetic use of botulinum A exotoxin for the aging neck. Dermatol Surg 1998;24: 1232–1234.
37. Small R. Botulinum toxin injection for facial wrinkles. Am Fam Physician 2014;90:168–175.
38. Niamtu J 3rd. Botulinum toxin A: A review of 1,085 oral and maxillofacial patient treatments. J Oral Maxillofac Surg 2003;61:317–324.
39. Patel D, Mehta F, Trivedi R, Thakkar S, Suthar J. Botulinum toxin and gummy smile—A review. IOSR J Dent Med Sci 2013;4:1–5.



CHAPTER

02

Facial Analysis and Photographic Documentation

Fig 2-1 First impression. During the initial patient consultation, the clinician should record all facial aspects with the muscles at rest as well as the problems that might arise during the natural smile and speech.

Dentistry goes beyond treating the oral cavity and smile. A complete facial analysis and use of esthetic references allow the professional to identify changes that can be made to establish facial harmony.

During the first appointment, the patient should fill out a medical history form at the front desk. The clinician should then review this history with the patient considering the following:

- Main complaints
- History of present medical conditions (location, onset, evolution, previous treatments, and possible causes)
- Dental history, including all relevant previous treatments not related to the main complaint
- Medical history, including all medical conditions and medical interventions
- Personal and social history, including oral hygiene, parafunctional habits, and diet habits (sugar, acid)

It is important for the clinician to observe the patient at rest, when speaking, and when smiling during this consultation (Fig 2-1). All spontaneous facial expressions should also be observed and recorded. This will allow the clinician to fully evaluate the patient's face and determine any asymmetries or hyperkinetic muscles.

Complete Facial Analysis

The facial analysis should be as thorough as possible. A complete diagnosis will provide the most effective treatment plan. Therefore, all aspects of the face—the positive and the negative—should be considered from multiple perspectives:

- Frontal view at rest and smiling
- Profile view at rest and smiling
- Photographs of frontal view at rest and smiling
- Photographs of profile view at rest and smiling
- In case of asymmetries during speech, video of the patient speaking

Each facial characteristic and its possible correction should be recorded.

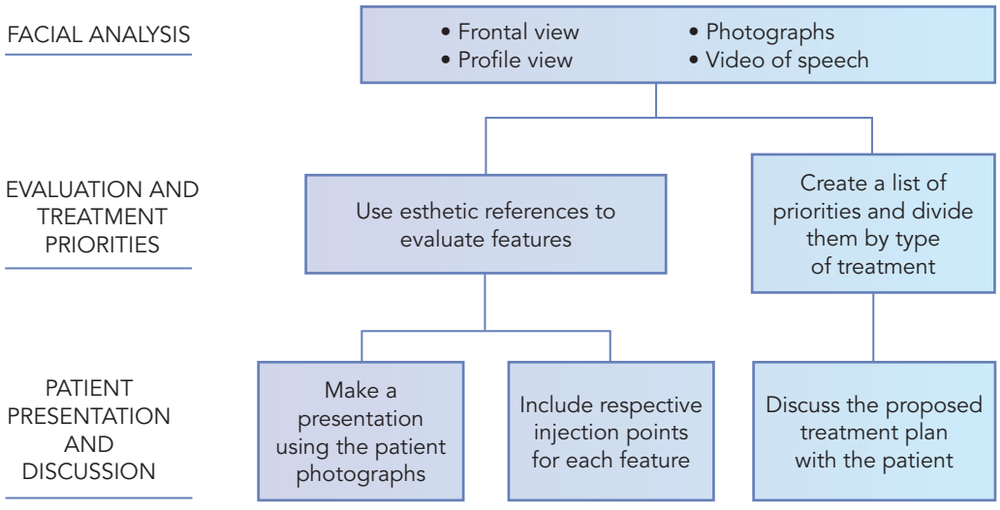


Fig 2-2 Facial analysis and patient presentation.

The clinician should continue the facial analysis with the following steps:

1. Evaluate the findings according to several esthetic references.
2. Create a numbered list of priorities. At the top of the list should be the least esthetic features that require the most attention. This list will help to explain the treatment priorities to the patient.
3. Subdivide the list of characteristics by type of treatment: therapeutic, structural, and aging. Any therapeutic treatment is most important, followed by structural. A frequent mistake is to only consider the aging process of the patient.
4. Make a presentation using the patient photographs and respective injections points.
5. Discuss the treatment plan with the patient. This should be an interactive discussion. Sometimes patients are surprised when looking at their own photographs because they are used to looking at themselves only through a mirror, which provides fewer details than a photograph. This conversation will provide the clinician the opportunity to readjust the plan according to the patient's desires for treatment.

Figure 2-2 summarizes this process.

Photographic Documentation

Photography can be used in dentistry for many different reasons, including assisting the clinician during initial examination of the patient; helping with diagnosis; evaluating treatment over time; storing legal documentation; capturing digital material for publication; educating patients or students; communicating with patients and professional team members, colleagues, and technicians; and finally, marketing. Each of these applications enhances and elevates the status of the practice as well as improves delivery of care to patients.[1]

Regardless of clinical experience, the treatment plan should never be based on a clinician's intuition. Instead, it should be guided by esthetic, facial, and dental analysis.

Evaluation of esthetic references should be performed over the photographs of the patient. Rulers, masks, and projections can be placed over the images and used as tools for facial analysis. This should be done when the patient is not present.

Photographs taken during the first appointment help the operator to perform facial analysis and can be used to help the patient understand the treatment plan and diagnosis. The clinician can also obtain facial data by performing measurements directly on the patient's face. This is faster and more practical than using images for the measurements, which are scale representations. At least one actual measurement on the patient's face should be recorded when the patient is present so that the other measures can be proportionally performed using an image.

Studio infrastructure

It is important to equip the dental office with a photographic studio to ensure that any photograph taken is good quality and captures the necessary information. A proper photographic studio includes the following (Fig 2-3):

- Two medium-sized soft boxes to diffuse a smooth and regular light to the patient's face. They should be slightly longer than the vertical measurement of the patient's face and neck. Avoid smaller light sources because they tend to concentrate the light at the center of the face. Modern digital cameras are able to remotely command the soft box, shooting with no need for cables.
- One hair light to delineate head contour, thereby improving the contrast with the black background. Black backgrounds are neutral and do not compete with the face. Position this light above or below the face so that the device is not displayed.
- Three tripods to support the flash units and hair light devices. They should be positioned higher than a tall standing patient.
- One black background with its own support to standardize the photographs. Avoid a white background, as it will compete with the face because it is brighter than the skin. A matte background is preferred to avoid shadowing.

Preparing the patient

Certain procedures must be performed before photographs are taken to ensure that the photographs capture the necessary information:

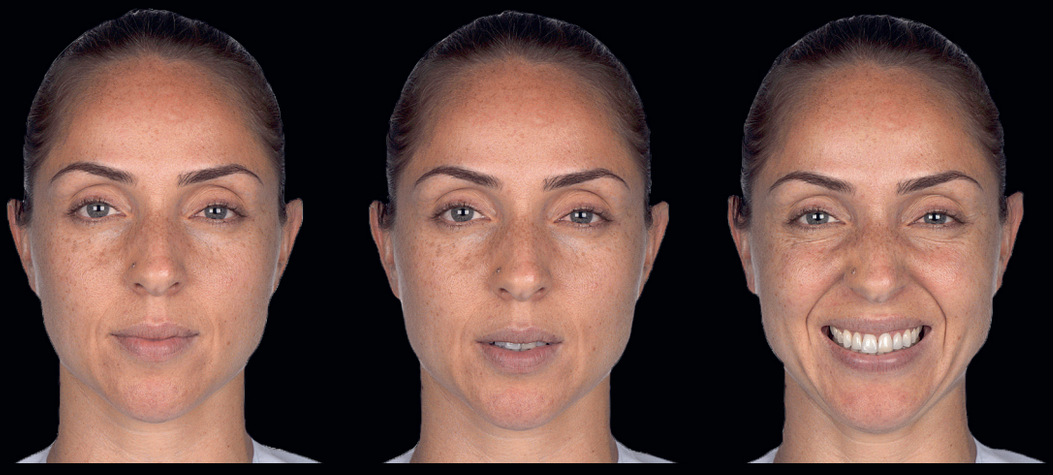
1. Remove all makeup from the face, because it blocks the visualization of the skin. Keep the face dry at all times to avoid reflexes from the flash. → *Provide makeup removers and cotton pads.*
2. Neutralize the hair by tying it up and using headbands. → *Provide the most discreet type of headband.*
3. Ask the patient to remove all jewelry (eg, earrings and necklaces) to eliminate the distraction. → *Focus on the anatomical aspects of the face.*
4. Instruct the patient to look horizontally and not tilt or turn the head. → *Consider the patient's height and indicate on the wall or the flash unit where he or she should look.*

Facial photographs should be taken with the lips closed, with the lips relaxed, and with the patient smiling (Fig 2-4).

Protocol

Frontal and profile facial views should be captured (Figs 2-5 and 2-6). Facial views should also be taken with the patient sitting to diagnose wrinkles, grooves, and volume deficiencies (Figs 2-7 and 2-8).

Fig 2-3 Studio infrastructure. A, soft box. B, hair light. C, tripod. D, black background.



Lips closed: Instruct the patient to avoid moving the face so that the facial muscles will not be activated. Also instruct him or her to slightly close the lips.

Lips relaxed: Instruct the patient to keep the same position but relax the lips. Ask the patient to breathe through his or her mouth.

Smile: Ask the patient to smile as spontaneously as possible. The photographer should also smile and say something funny to encourage a natural smile. Ask the patient not to incline the head sideways when smiling.

Fig 2-4 Facial photographs.

Frontal view

Fig 2-5 The photographer should bend the knees so that the camera is parallel to the ground and at the same level as the patient's face. The flashes are positioned almost perpendicular to the face.

Profile view

Fig 2-6 Only one flash is moved laterally, almost perpendicular to the frontal plane of the face.

Sitting view (“shower technique”)

Fig 2-7 The patient should sit on a stool so that his or her face is below the flash. The seat should not have a back support so that the patient can keep the head in a natural position.

Flash positioning

Fig 2-8 Flash positioning is important when taking photographs to diagnose wrinkles, grooves, and volume deficiencies. *(a and c)* Photographs used for diagnosis with the flashes positioned in a conventional way, that is, at the same height as the patient's face. *(b and d)* Photographs taken on the same day but with the flashes positioned above the patient's face, similar to a shower technique. Note that although the photographs show some dark areas, dynamic wrinkles at the orbicularis oculi and nasal muscles are clearly visible.

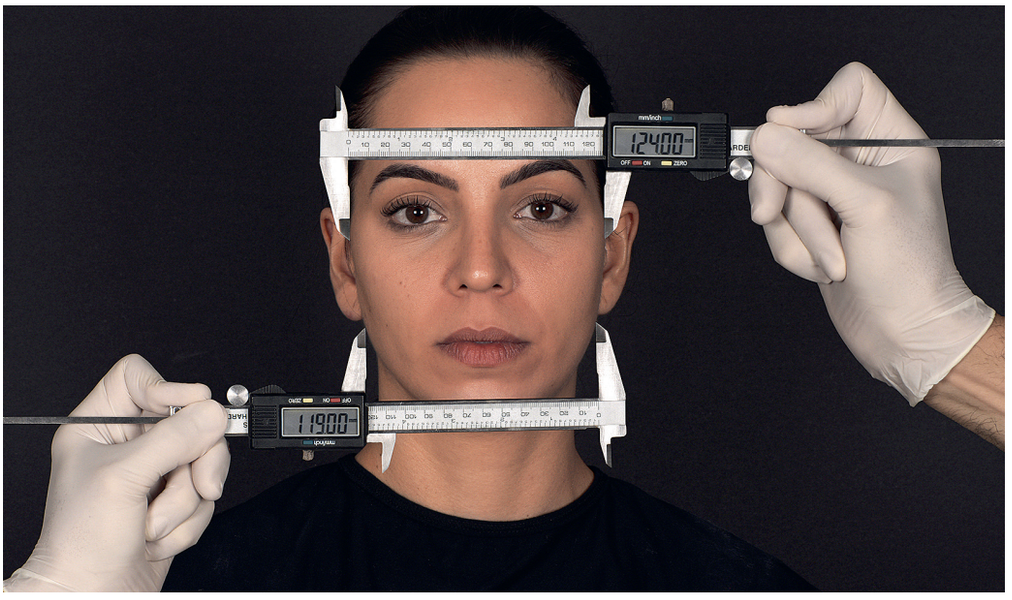


Fig 2-9 Examples of facial measurement. Note the correct measurement of the bizygomatic and bigonial distances. The difference between these two measurements must be at least 4%. A smaller number could mean masseter muscle hypertrophy. A difference of 12% is esthetically very pleasant.

Clinical Examination

Ricketts[2] described *esthetics* as the study of beauty. Dierkes[3] stated that beauty of the face might be defined as a state of harmony and balance of facial proportions, that is, a balanced relationship among skeletal structures, teeth, and soft tissue.

In order to provide more objective guidelines regarding the perception of smile esthetics, numerous studies were performed using digital image manipulation.[4] Characteristics that were better elucidated with this technology include the following:

- The smile arc[5,6]
- The optimal amount of gingival display[7–9]
- The ideal amount of buccal corridors[4,10]
- The prominence of dental and gingival asymmetries[5,11]
- The influence of maxillary anterior diastemata[11–13]
- The impact of midline and long axis deviations[5,7,11]
- The importance of maxillary incisor size, proportion, and symmetry[13–17]

Several anthropometric measurements[18] are extremely important when performing facial and smile analysis, including the bizygomatic distance and the bigonial distance (Fig 2-9):

- *Bizygomatic distance:* From the right to the left zygion, the most lateral points on the right and left sides of the zygomatic arches—that is, the widest part of the face (see Fig 2-11). For females, this distance is 65% to 70% of the face length measured from the middle of the hairline to menton. For males, it is 65% of the face length.
- *Bigonial distance:* From the right to the left gonion, the most external and prominent angle of the right and left side of the jaw—that is, the lowest facial width (see Fig 2-11).

Box 2-1 shows the facial aspects to evaluate during the clinical examination, based on the literature and the author's clinical experience. Each of these is explained in detail in the sections that follow.

Box 2-1 Facial aspects to evaluate during the clinical examination

Face shape: Triangular, square, or oval. Observe if the patient shows a lack of harmony.

Bizygomatic distance: The measurement is made at the widest point.

Temporomandibular joints: Observe for signs of temporomandibular disorders, sounds (clicking and popping), deviations, limitations, and reduction. Palpate the temporomandibular joints as well as masseter and temporal muscles.

Dental exposure: Anterior and posterior, at rest and while smiling.

Dynamic wrinkles: Note when these wrinkles become accentuated. Inject the toxin as a preventive measure.

Static wrinkles: Record all of them. Toxin is injected for correction.

Buccal corridor and commissure asymmetries: Evaluate the face in a static view and during muscle dynamics. See chapter 4 for examples in clinical cases.

Definition of the jawline: Observe if the body and angle of the mandible are outlined. See chapter 4 for examples in clinical cases.

Hyperkinetic muscles: Note the hyperkinetic muscles (see chapter 4).

Nasal tip mobility: Assess during smile and speech, asking the patient to pronounce the letter M several times. See chapter 4 for examples in clinical cases.

Width of jaw and buccal corridor: The patient's eye could be a reference for this evaluation.

Face Shape

The size, shape, and arrangement of the maxillary anterior teeth are the most influential factors for a harmonious appearance, particularly when the face is viewed from the front.[19] These teeth normally dominate during a person's smile.[17,20] Fornaziero and Souza[21] established a correlation between the buccal outline of the maxillary central incisor and the face shape and observed a predominance of triangular maxillary anterior teeth as well as triangular faces. Table 2-1 illustrates the three basic face shapes and their characteristics.

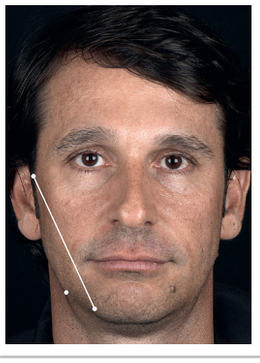
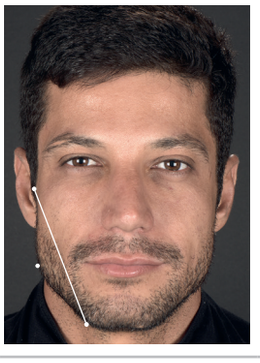
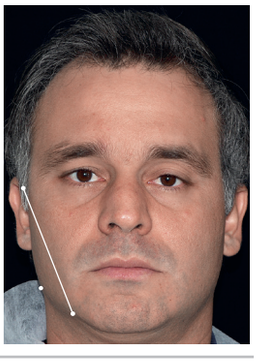
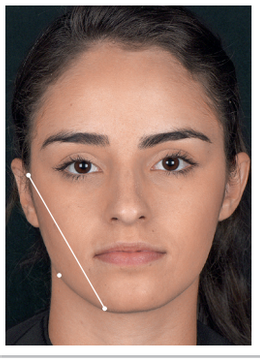
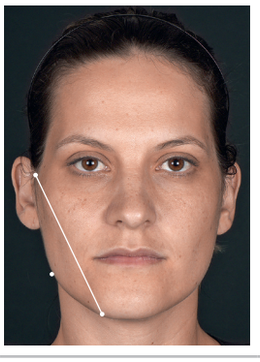
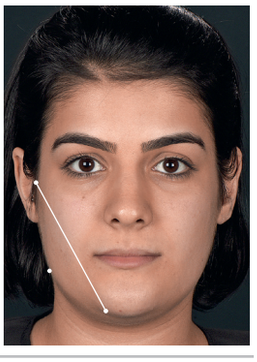
How to determine face shape

Sit in front of the patient and ask him or her to relax all facial muscles. Mark a point at the widest part of the zygomatic bone (bizygomatic distance), another point at the angle of the jaw, and a third point at the lateral aspect of the chin. Draw a line connecting the first and third points (see examples in Table 2-1).

Observing the second point in relation to the neck, the face shape can be determined as follows:

- *Triangular:* The second point is anterior to the junction between the neck and jawline (inside the neck area).
- *Square:* The second point is above the junction between the head and neck (outside the neck area).
- *Oval:* The second point is located exactly at the junction of the head and neck.

Table 2-1 Face shapes and their characteristics

	TRIANGULAR	SQUARE	OVAL
Characteristics	• Shows a bizygomatic distance that is markedly greater than the bigonial distance. • More feminine face shape. • Can be altered in cases of hypertrophic masseters, turning it square. • Generally gives the impression of a delicate, young face.	• Shows a bizygomatic distance that is slightly greater than the bigonial distance. • More masculine face shape. • A bigonial distance greater than the bizygomatic distance might mean masseter hypertrophy. • Generally gives the impression of a strong face.	• Shows a roundness observed between the zygomatic bone and gonial angle. • More childlike face. • Check indication for a bichectomy, which is rare. • Generally gives the impression of a childlike face because of the big cheeks characteristic of children.
Advantage	It adds more value to the patient's mouth because the smaller cheeks avoid competition with the mouth.	It helps to define a better limit of the head/neck, which is an important criterion for beauty.	The face is smoother and more curved.
Disadvantage	Aging and/or overweight patients quickly lose definition of the jawline.	It decreases the dominance of the mouth because the lower third is wide.	A slight malar depression is not observed between the zygomatic bone and the two gonial angles, which in other face shapes accentuates the mouth. Women with this face shape often wear blush to give the impression of this depression.
Male examples			
Female examples			

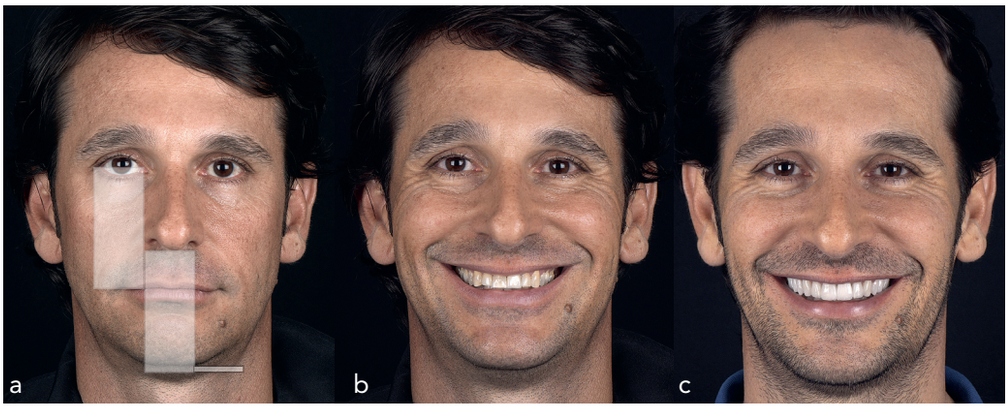


Fig 2-10 *(a)* Patient with decreased OVD. Rectangles of equal length are used to verify if the distance from the lateral palpebral fissure to the buccal commissure is the same as that from the nasolabial angle to the base of the chin. *(b and c)* Smile views before and after treatment. Note that the OVD has been increased with BTX injections and dental restorations.

Observing the line drawn between the points, the face shape can be determined as follows:

- *Triangular:* Between the most superior and most inferior point, the side of the face is almost straight, with no noticeable angle located at the level of the second point.
- *Square:* Between the most superior and most inferior point, the side of the face is angled, with an abrupt change of direction, with a more noticeable angle located at the level of the second point.
- *Oval:* Between the most superior and most inferior point, the side of the face is round, with a curvilinear path and no noticeable angle at the second point.

Decreased occlusal vertical dimension

Facial analysis of the patient pictured in Fig 2-10a revealed a bilateral clicking at the temporomandibular joint (TMJ) and a slight decrease in the occlusal vertical dimension (OVD), assessed using a Willis compass.

Rectangles of equal length are used to verify if the distance from the lateral palpebral fissure to the buccal commissure is the same as that from the nasolabial angle to the base of the chin. This measurement should be taken in the following clinical situations: *(1)* when the lower third of the face is shortened, *(2)* in the presence of parafunctional signals and symptoms, and *(3)* before extensive rehabilitations.

HOW COULD BOTULINUM TOXIN (BTX) HELP?

By decreasing the tonus of the main mandibular elevator muscles to allow the restoration of the OVD. In these cases, the injection should be administered preoperatively to help with the increase of the OVD, intraoperatively if the dental rehabilitation will take more than 4 months, and postoperatively to maintain the effect as long as parafunction is present. In cases of temporomandibular disorder (TMD) associated with parafunctional oral habits, excessive force during maxillary elevation could harm the stomatognathic system. Therefore, reducing the strength of the mandibular elevator muscles might work as an adjuvant therapy to existing treatments.[22,23]

TREATMENT PERFORMED:

1. Ten units (10U) of Botox (Allergan) were injected at two points in each masseter muscle, and 5U were injected at one point in each temporalis muscle.
2. The OVD was increased using direct resin composite restorations on the mandibular posterior teeth.
3. Ceramic veneers were bonded to the maxillary teeth (second premolar to second premolar) to obtain anterior guidance with an overbite (minimum of 2 mm and maximum of 4 mm).
4. Labial and malar augmentation were performed.

Figures 2-10b and 2-10c show the pretreatment and posttreatment smile views.

Fig 2-11 Bizygomatic distance and bigonial distance. The bigonial distance is approximately 12% shorter than the bizygomatic distance.

Bizygomatic Distance

Facial width is defined as the maximum distance between the most external points of the malar prominences (zygomatic width).[24,25] The largest part of the face is the zygomatic width, or bizygomatic distance. The bigonial distance is approximately 30% shorter than the bizygomatic distance.[26] The author observes that beautiful women show a difference of 12% between these two measurements, while a small number is found in men's faces because men have larger masseter muscles. The bizygomatic distance should be visually and numerically greater than the bigonial distance[27,28] (Fig 2-11).

Increased width of lower third of the face

Facial analysis of the patient pictured in Fig 2-12a showed that the bizygomatic distance was not remarkably greater than the bigonial distance. The patient reported left unilateral chewing and parafunctional habits.

Horizontal lines are drawn at the widest point between the zygomatic bones and gonial angles. This measurement should be taken in the presence of signs and symptoms of parafunctional habits.

HOW COULD BTX HELP?

After toxin injection, the volume of the masseter muscle is decreased, leading to a narrowing of the lower third. Injecting a higher dose of toxin in the mandibular elevators on the side the patient prefers to chew will tend to encourage chewing on the other side.

TREATMENT PERFORMED:

1. 10U of Botox were injected at two points in the right masseter muscle, and 5U were injected in the right temporalis muscle. On the left side, injections were given in the same muscles at doses of 50% higher.
2. The central incisors were lengthened with direct resin to improve anterior guidance.
3. The nasolabial fold was filled.
4. Deoxycholic acid was used to reduce fat at the submental region (double chin).

Fig 2-12 *(a)* Patient with increased width of the lower third. Note that the bigonial distance is almost the same as the bizygomatic distance. Also note the asymmetry (wider on left side of the face). *(b)* Measurements after BTX injection. Note the reduction in the bigonial distance and symmetry achieved in the lower third. *(c and d)* Smile views before and after treatment.

Figure 2-12b shows the patient after treatment. The left side of the face, previously a little wider than the right side, became symmetric after the injection (Figs 2-12c and 2-12d). The patient also reported that he began chewing on both sides.

With injections into the masseter muscle, it is important to inform the patient prior to treatment that the lower third of the face will likely be narrower after injection. Even a slight decrease in the definition of the jawline should make the face more esthetically pleasing, but the patient should be prepared for this change.

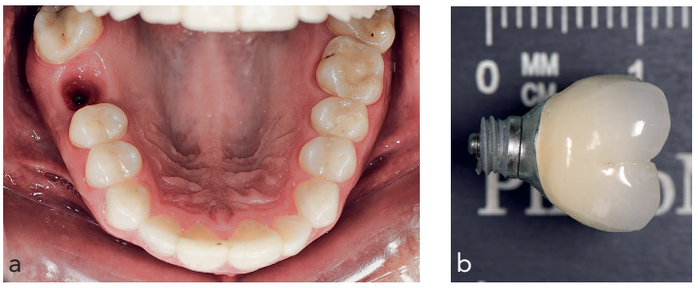


Fig 2-13 *(a and b)* Example of parafunction: Rare fracture of a Brånemark implant caused by clenching. The implant and its crown were functional for 10 years.

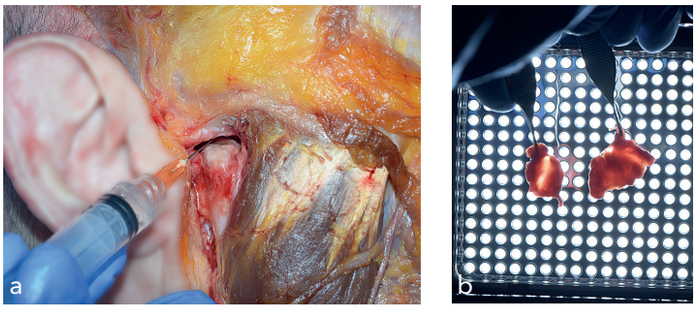


Fig 2-14 *(a)* Cadaver showing TMJ after synovium aspiration. *(b)* The articular disc on the left belonged to a cadaver whose teeth were worn out by attrition. The disc on the right was from a patient with preserved teeth.

Temporomandibular Joints

Any signs or symptoms of TMD should be evaluated and recorded during the clinical examination. These include the following[29,30]:

- Facial pain
- Tension headaches
- Dental loss related to parafunction
- Tooth and/or restoration fracture (Fig 2-13)
- Incisor or canine attrition (Fig 2-14)
- Dental mobility
- Cracks in dental enamel
- Abfraction
- Diastema opening
- A concave occlusal surface in the mandibular second molars
- Articular sounds (clicking)
- Linea alba in the buccal mucosa
- A tongue edge marked by the anatomical shapes of the teeth
- Bone exostosis (torus)
- A decrease in the lip vermilion volume
- Asymmetry and/or hypertrophy of the masseter muscles
- Apical and/or periodontal bone resorptions

HINT:
A good-quality stethoscope should be used to check the TMJ during movement, enabling an early diagnosis.

Kim et al[29] point out that successful TMD treatment starts from correctly differentiating the origin of symptoms. Because myofascial pain and limited mouth opening are the most frequent symptoms of masticatory muscle disorders, directing treatment at the muscular components of TMD could yield therapeutic gains.[31] Therefore, noninvasive conservative treatments such as counseling, a soft diet, behavioral medicine, physiotherapy, oral appliances, pharmacotherapy, and BTX injections are reported to be effective as first-line therapies for extra-articular pathologic conditions.[32]

Intra-articular pathologic conditions such as internal derangement and osteoarthritis could also benefit from the reversible interventions used to treat myofascial pain. Patients with acute pain, however, may require intra-articular injection of lidocaine, hyaluronic acid, or even a corticosteroid.[33] When the symptoms and pain surpass the effectiveness of these techniques, surgical approaches such as arthrocentesis, arthroscopy, and arthroplasty may be performed to treat anatomical pathology.

After the introduction of commercial brands of BTX-A (Botox, Dysport [Ipsen]), its injection therapy on orofacial muscles became a valuable adjunct in managing myofascial components of TMD.[22,30,34,35] Supporting literature dates back three decades, with successes reported in various therapeutic applications since the 1980s.[36] While clinical injection of BTX-A in the masticatory musculature of TMD patients can be considered a useful supportive treatment option for controlling complex TMD and alleviating its associated symptoms, more randomized controlled studies with larger sample sizes and longer follow-up periods are necessary in order to scrutinize and evaluate the full effects of BTX-A injections.

Dental Exposure

At rest

When the lips are at rest and slightly open, part of the clinical crowns of the central incisors should be displayed without any papillae showing. Women generally have shorter upper lips than men (an average of 19.5 mm in young women and 22 to 24 mm in young men), so this central incisor display averages 3.4 and 1.91 mm, respectively.[25] For maxillary lateral incisors, a smaller exposure is ideal, and the mesiobuccal aspect of the crown should be more exposed than the distobuccal. The maxillary canines may not be exposed at all or perhaps just the tip of the crown.

If the papilla between the maxillary central incisors is exposed or if more than the tip of the maxillary canine is exposed while the lips are at rest, the patient may have a gummy smile. The possible treatment could be injection of BTX into the muscles that lift the upper lip. However, before this diagnosis is made, it is fundamental to observe the upper lip during a smile.

Mandibular teeth should not be too exposed when the lips are at rest; this display should be smaller than that of the maxillary teeth. Greater exposure of the mandibular central incisor clinical crowns might mean one of the following:

- The patient is aging, with labial ptosis. This can be treated with fillers at the mentolabial sulcus.
- Dentoalveolar extrusion of the mandibular anterior teeth. This can be corrected with orthodontics.
- Hyperkinetic depressor labii inferioris. This can be treated with BTX injections in these muscles.

Figure 2-15 illustrates an ideal dental exposure at rest and an unesthetic dental exposure at rest.

During a smile

During a smile, the lower edge of the upper lip vermilion should touch the neck of the maxillary central incisors, hiding part of the neck but leaving the central papilla visible. Gingival exposure of up to 3 mm around the maxillary central incisors is considered acceptable.[7] An exposure exceeding 3 mm is considered a gummy smile. One of the possible treatments for gummy smile is the injection of BTX into the muscles responsible for elevating the upper lip. However, it is important to observe the upper lip at rest before any decisions are made.

Ideally, the clinical crowns of the maxillary premolars or at least their papillae should be entirely exposed. Lack of exposure could mean that the depressor anguli oris muscle and/or posterior fibers of the platysma are hyperkinetic.

The clinical crowns of the mandibular teeth should barely be visible during a smile. An exposure of the mandibular teeth greater than that of the maxillary teeth is considered unesthetic because it decreases the dominance esthetically required for the maxillary teeth during a smile. The display of gingiva around mandibular teeth is considered esthetically unpleasant, characterizing a lower gummy smile. The hyperkinetic activity of the depressor labii inferioris might explain this kind of smile.

Figure 2-16 illustrates an ideal dental exposure during a smile and an unesthetic dental exposure during a smile.