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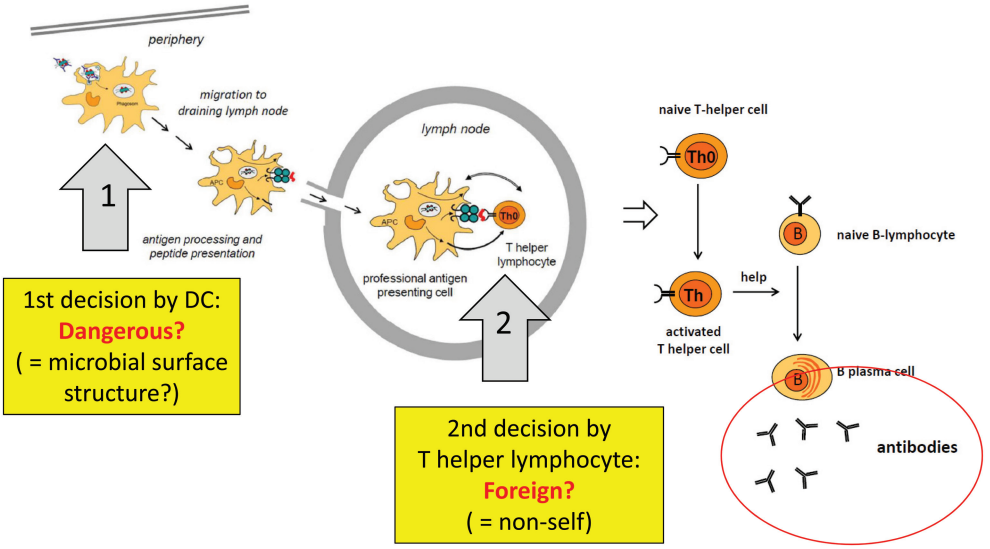

FIGURE 1.3 Scheme of the two-criteria two-step activation model of the human immune system leading to antibody production. (Left) Dendritic cells (DCs) act as sentinels and as first decision maker recognize microbial *danger signals*. DCs become activated and phagocytose the dangerous antigen, process it, and move to the draining lymph node (left). In the lymph node, they present peptides thereof in MHC class II molecules (antigen presentation) to the second decision maker, the naïve antigen-specific T helper lymphocyte (Tho) that recognizes presented *nonself (= foreign) peptides* and becomes activated (middle). T cells finally help B lymphocytes to produce antibodies specific to the dangerous antigen that initiated the whole process (right).

ADJUVANTS ENHANCE THE WEAK IMMUNE REACTION TO BoNT/A BY PROVIDING DANGER SIGNALS

The immunogenicity of a weak immunogen can be increased in a vaccine by adding adjuvants. Adjuvants provide the required danger signals lacking in weak immunogens like pure BoNT/A (Figure 1.5a). Intact killed bacteria or bacterial surface structures like flagellin are excellent adjuvants because they contain microbial surface structures. Adjuvants are mixed with the antigen and injected together at the same site. They activate DCs to phagocytose everything in their close vicinity, including the adjuvant and, most importantly, the weak immunogen, here BoNT/A. Being fully activated by the adjuvant, they digest the "co-phagocytosed" BoNT/A and present peptides thereof on MHC II to T helper lymphocytes, initiating a full adaptive immune response resulting in the production of antibodies to the weak immunogen (Figure 1.5b).

COMPONENTS IN BoNT/A PREPARATIONS THAT CAN ACT AS ADJUVANTS

All BoNT/A pharmaceuticals contain the 150kDa neurotoxin. Clostridia produce the neurotoxin in a large progenitor complex. The pharma protein BoNT/A is purified by different companies with different protocols to yield products with different degrees of purity (Frevert 2015).

Complexing Proteins

Most brands contain bacterial complexing proteins. As of 2020, only two products free of complexing proteins are available: Xeomin® (Merz Pharmaceuticals, Germany), available worldwide; and

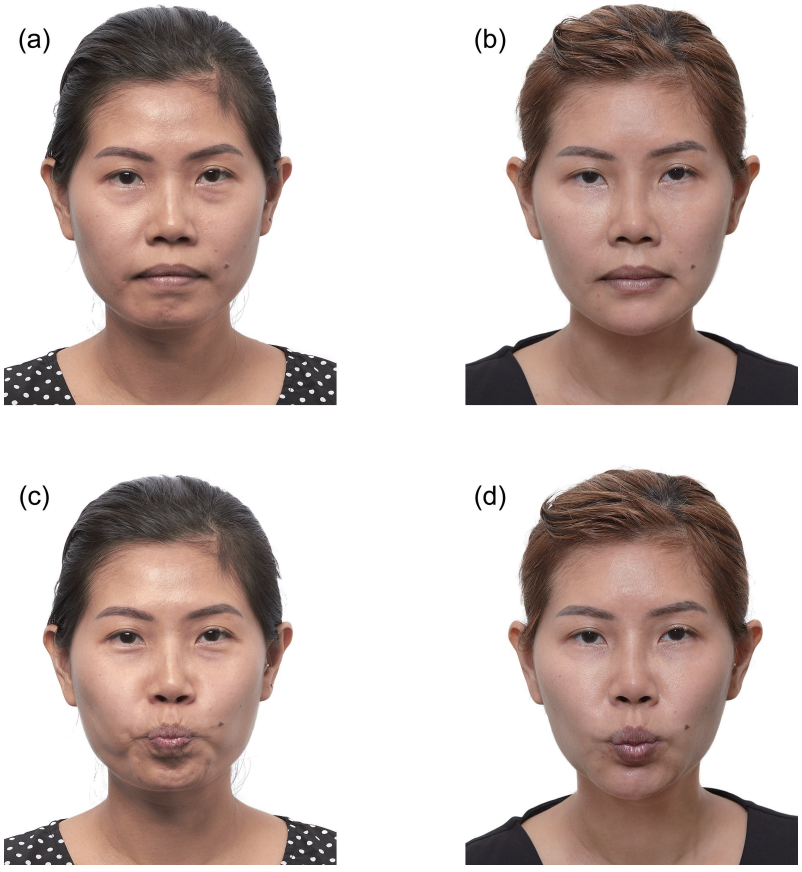

FIGURE 2.4 (a) Some patients' problems need more volume of filler to achieve satisfactory clinical effects. (b,c) The presence of filler underneath the skin and sometimes above muscles can be visible when muscles contract. (d) The use of minimal toxin in some highly mobile areas can reduce the effects of these structures and achieve a more elegant and natural result.

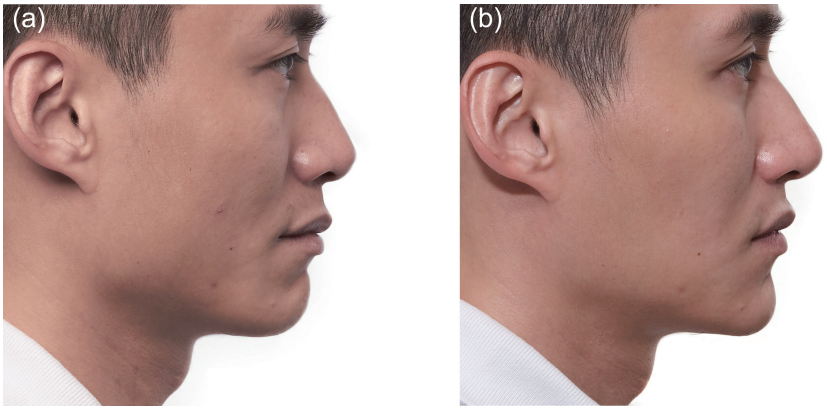

FIGURE 2.5 (a) Imbalance of volume distribution includes both excess and deficiency. A holistic approach to the problematic appearance corrects both deviations. Toxin to the masseter in this patient was combined with cheek filler modification and chin augmentation. (b) These treatments improved the profile proportion and smoothened the facial curve transition.

FIGURE 6.2 Smile movements often involve the muscle of orbicularis oculi and levator muscles including zygomaticus major and minor, risorius, nasalis and dilator naris, etc.

FIGURE 6.3 Spock's deformity occurs when unpaired muscle activities are produced through toxin treatment.

the frontalis muscle results in an imbalance between medial and lateral fibers. The eyebrow tilts under the imbalance, and the lateral end of the eyebrow is elevated. Balance has to be kept not only across the frontalis but also between the elevator and the depressors. Imbalance can occur when the opponents of this antagonism are being treated in preference to one side (Figure 6.4).

Muscles of the glabella complex pull the eyebrow in different directions. Toxin dosing among these muscles should be balanced as well to keep the brow in its original orientation and retain the normal movement direction. Medial depressor muscles counteract both the medial elevating frontalis fibers and the lateral pulling forces. That is why when glabella muscle inhibition is complete, the pivotal structure of the eyebrow moves slightly laterally and upward. The intereyebrow distance can become wider; the arch of the eyebrow can be emphasized and become prominent.

Toxin treatments for structures with multivector opponents need to be calculated with regard to the relative loss and gain and administered with preventive measures to avoid the mismatch.

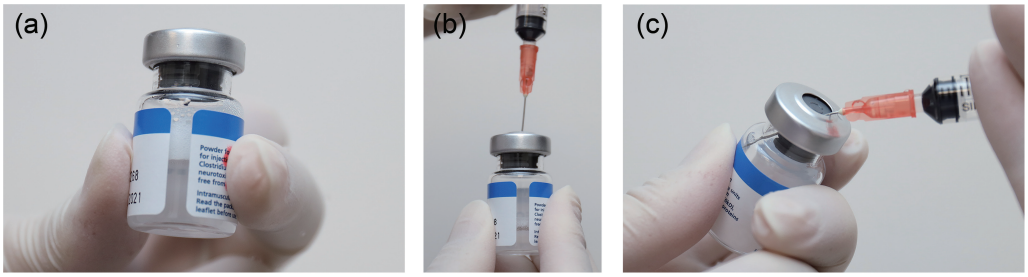

FIGURE 9.3 A thick layer of foam (a) can be visible when the reconstitution proceeds as a rapid flush of saline through a free-hanging needle (b). That is unique and most prominent for incobotulinum toxin. The reconstitution needle should adhere to the vial wall, importing saline with flow following the vial wall (c).

Dilution and Toxin Spread

Toxin spread has long been discussed for the purpose of determining the exact range of blocks for best practice. Fick's law is usually given as the reason for the movement of active toxin molecules, describing the movement driven by a concentration gradient, and concentration level is closely related to the volume of saline added during reconstitution. However, the spread of toxin in tissue is not pure diffusion. As most of the judgment of toxin diffusion is done on the forehead by measuring the diameter of anhidrosis after toxin injection, more discussion on diffusion will be included in Chapter 16.

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FIGURE 10.6 Muscle volume and distribution can vary from patient to patient. Correct evaluation helps decide the proper treatment dose.

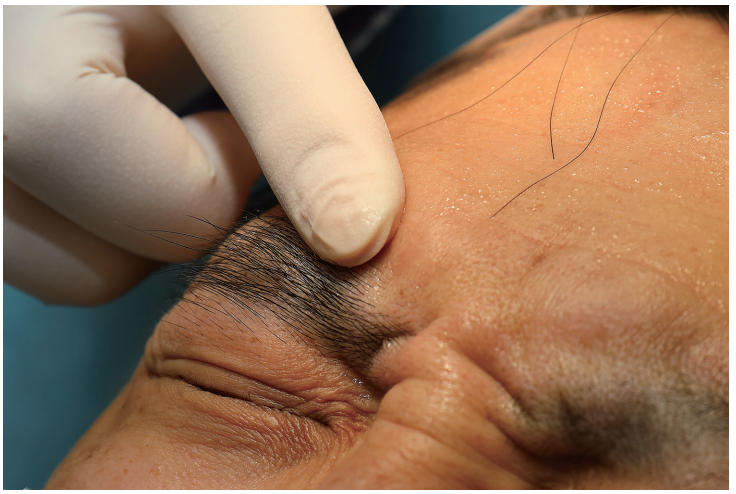

FIGURE 10.7 Facial muscles have more complex interdigitation and connection with other muscles and the skin. The mobility, connection, and restriction of structures can be further recognized through palpable evaluation.

REPEATING TREATMENTS

Aesthetic toxin treatments are popular and have become a recurrent routine for most toxin patients. Quality control is mandatory for practitioners to enable them to offer them as a sustainable business. Even a minor change in point dosage and the arrangement of injecting points could result in changes that weren't anticipated. Any progress or decline can soon be detected by patients, and they perhaps know the difference better than the injector can. Patients will always appreciate the expertise of a professional who can offer precision treatment, resulting in a steady improvement. Since toxin has to be reapplied every 4–6 months, it is embarrassing for the patient to have a face that keeps changing after a period of several months.

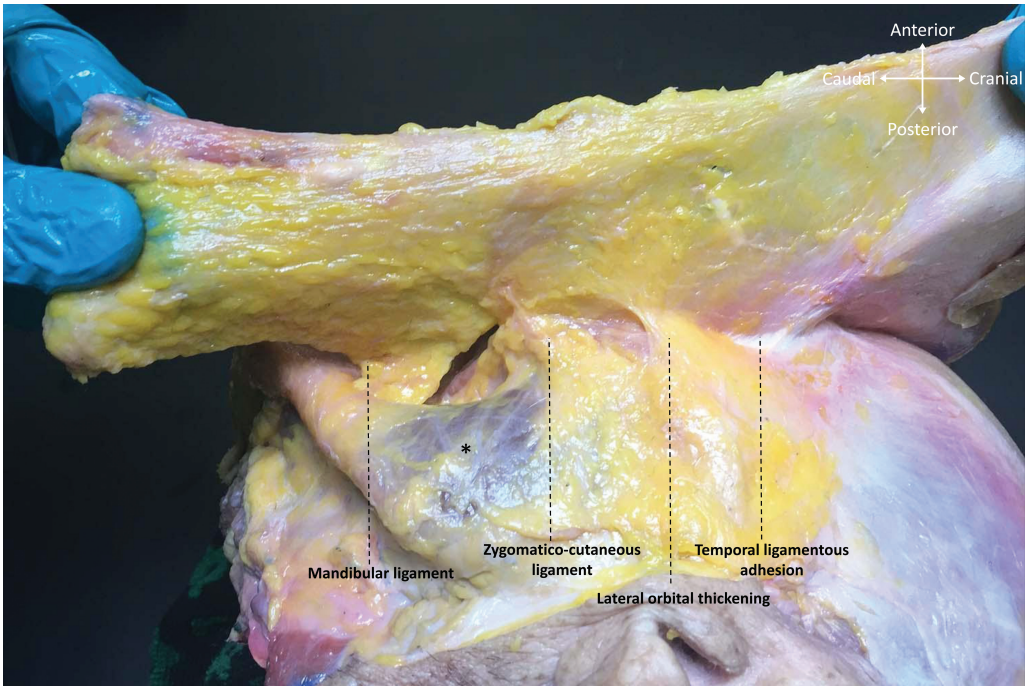

FIGURE 11.5 Cadaveric dissection of the left hemiface showing the continuous layered arrangement of the face. The subcutaneous fat and superficial musculo-aponeurotic system (including superficial temporal fascia, SMAS, and the platysma) are elevated together. Note the facial ligaments. The masseter muscle (*) is covered by the parotideomasseteric fascia.

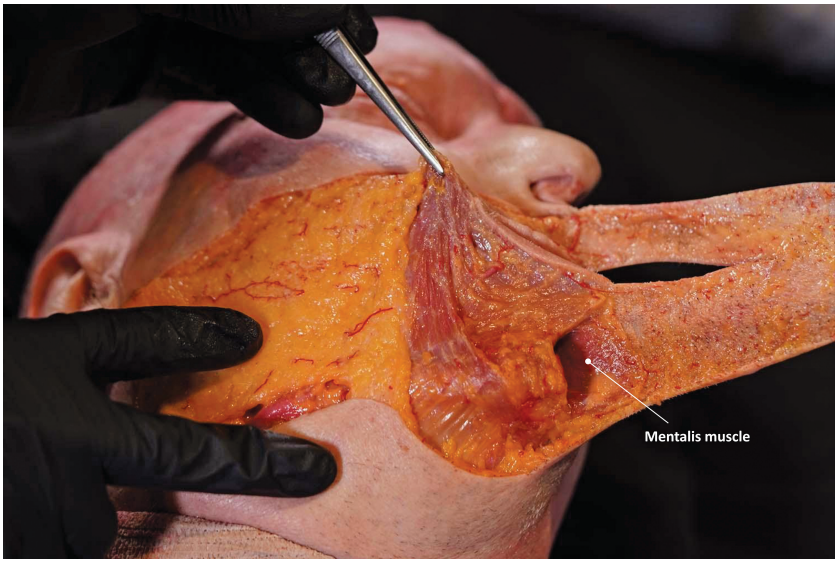

FIGURE 11.6 Cadaveric dissection of the lower face depicting the bony origin of the mentalis muscle, which inserts superficially into the subcutaneous fat and dermis.

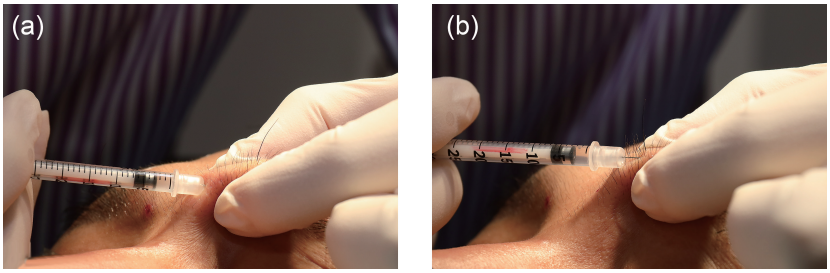

FIGURE 12.1 A corrugator toxin injection is ideally conducted as an intramuscular injection. (a) The injection needle can reach deeper on the medial side as the origin of the corrugator is the deepest part of the muscle, which starts at the orbital rim. (b) The lateral tail of the corrugator can be approached more superficially as it inserts into the supraorbital skin.

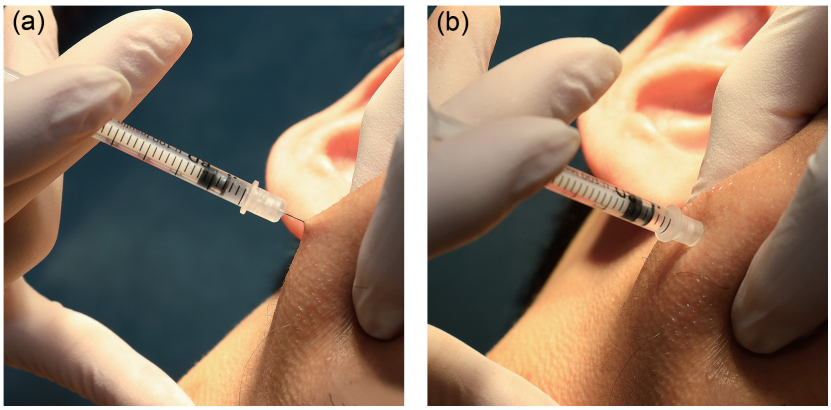

FIGURE 12.2 The masseter muscle is a bulky muscle with multiple compartments. (a) The usual insulin syringes with a fixed short needle can hardly reach the deep compartment; (b) they should be employed only for superficial doses.

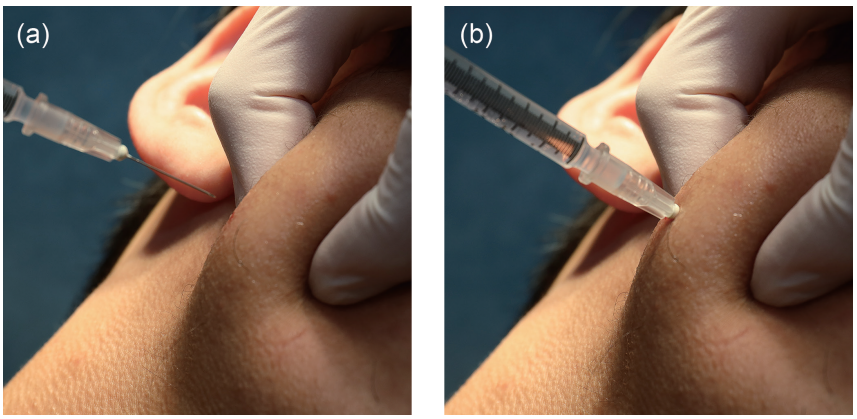

FIGURE 12.3 (a,b) To have a complete effect for the lower masseter, syringes with detachable needles are long enough to reach the deeper compartment of masseter muscles.

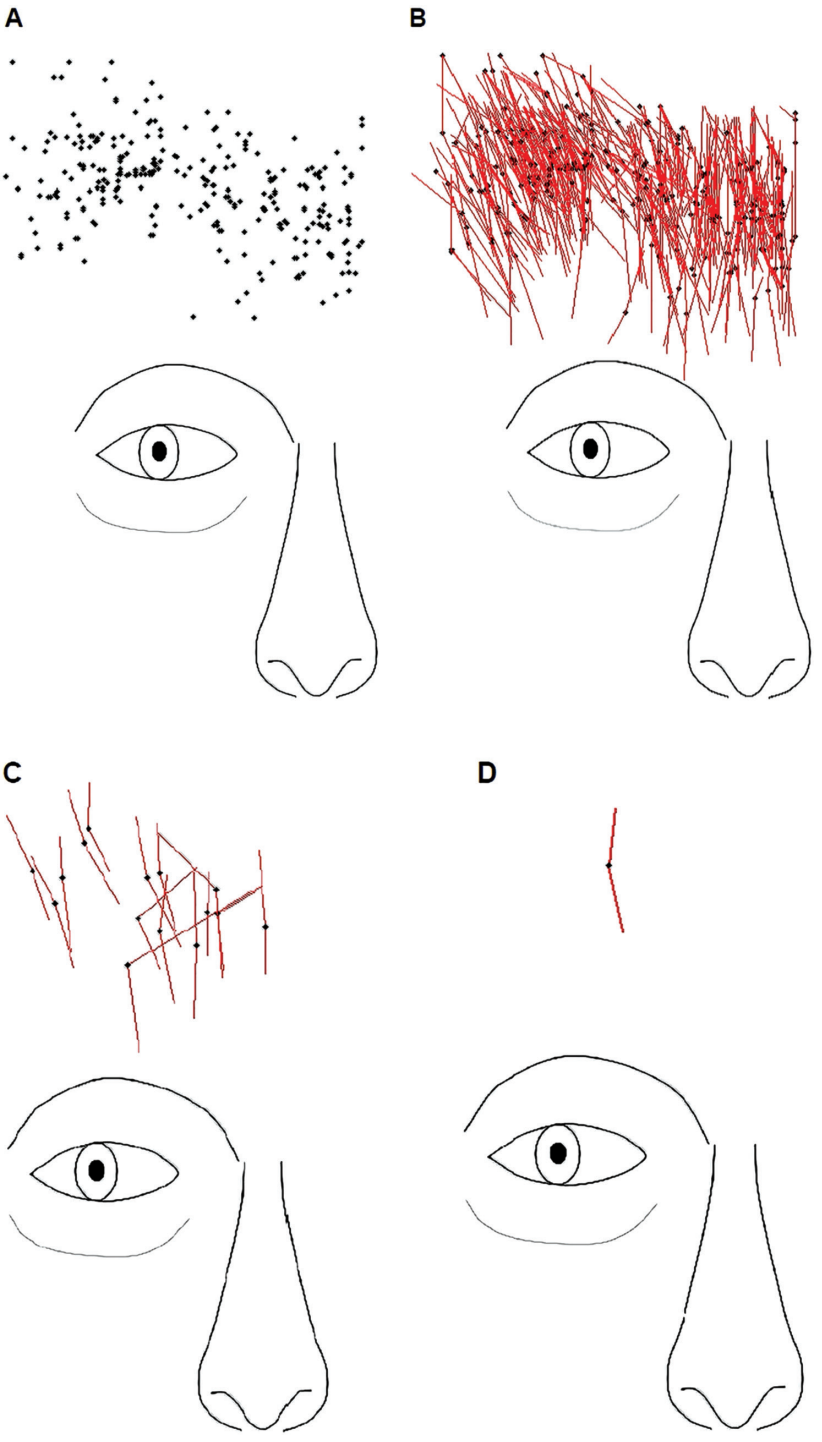

FIGURE 13.2 (A–D) A study of high-density surface electromyography measured the facial muscles about the distribution of motor endplates. MEPs are predominantly localized in the upper forehead and are spread evenly throughout the area, and can be divided into a medial and a lateral cluster. The superior fibers are oriented in a cranial and craniolateral direction; the inferior fibers were in a caudal and caudomedial direction. (From Neubert 2016.)

FIGURE 16.7 (a,b) Using small unit toxins with different depth and concentration of incobotulinum toxin in a patient with relatively thin skin revealed that the result of muscle inhibition is extremely small in diameter but larger and prominent in deep injection (c, left of the patient) (unpublished study). A small area of muscular immobilization is not easily measured as the folding of skin is continuous through the action of surrounding active muscle fibers. The measure of muscle effect by diameter measurement is extremely imprecise. (d) The diameter of the anhidrotic halo is similar in superficial and deep injection in patients with thin skin, but larger when the toxin is more diluted.

To refine toxin treatments that have to cover a wide muscular unit like the frontalis muscle, toxin injection can be administered with more points of injection but be smaller in aliquot size That helps to tailor the wrinkle distribution and structural pattern better. For the traditional forbidden area of caudal forehead, toxin actually could be administrated as well but further refined as in a more elevated tissue layer, in more concentrated reconstitution, and with less toxin units.

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