Periorbital Rejuvenation

A Practical Manual

Ashraf Badawi
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Foreword

The look is the kernel of beauty in most faces. The look centres on the periocular region. Demand for restoration, enhancement and rejuvenation of the periocular region is growing. Indeed, with the use of fillers and botulinum being the new normal for many faces, it is the periocular region which can often seem to be left behind with its hooded lids or hollow sockets or bulging intraorbital fat pads or pendulous infraorbital dewlaps.

It is no surprise therefore that the demand for periocular rejuvenation grows year by year. This is therefore a timely moment for a practical manual addressing periocular rejuvenation from all possible aspects.

Ashraf Badawi, President of the European Society for Cosmetic and Aesthetic Dermatology and Vice President of the European Society for Lasers and Energy Based Devices, is renowned for the clarity of his lectures and scientific talks, for his teaching skills, for his clinical excellence and for his scientific erudition. There is no one more or better skilled than him to present this much needed book.

He starts, as is best, with anatomy, continuing with the ageing process and then exploring the different rejuvenation options for the periocular zone. Each chapter presents the reader with a different therapeutic option which is described in a hands-on practical manner designed to help the reader achieve the best clinical outcome from each procedure described.

This practical manual of periocular rejuvenation is an essential volume for the bookshelves of the aesthetic practitioner whose repertoire of periocular treatments is growing and it will be also invaluable for the beginner in periocular rejuvenation.

Christopher Rowland Payne
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Contents

Anatomy of the Orbit and Periorbital Region

1

Tarek Shaarawy and Amr Aref

Osteology of the Orbit

Dimensions

The orbits (Fig. 1.1) are the bony cavities that contain the globes, extraocular muscles, nerves, fat, and blood vessels. Each bony orbit is pear shaped, tapering posteriorly to the apex and the optic canal. Its volume in the average individual is approximately 25 cm^3, varying from a mean of 17.05 cm^3 to 29.30 cm^3 [1]. Within the orbit, the eye contributes about 7.2 cm^3 based on the average diameter of about 24 mm. A myopic eye is bigger than the standard eye and a hyperopic eye is smaller. The anterior entrance of the orbit forms a rough rectangle measuring approximately 43 mm (36–47 mm) wide by 34 mm (26–42 mm) high [2]. The orbit attains its widest dimensions at about 15 mm behind the bony rim. The human orbit is completely closed behind by the sphenoid bone, except for the superior and inferior orbital fissures. The two lateral orbital walls subtend a 90° angle between them. The four walls of each orbit converge posteriorly toward the orbital apex (Fig. 1.2) where the optic canal and superior orbital fissure pass into the middle cranial fossa. The orbital floor extends to approximately two-thirds the depth of the orbit; the other three sides extend to the apex. The orbital segment of the optic nerve is slightly curved and moves with the eye. This curve allows the eye to move forward with proptosis without damaging the nerve.

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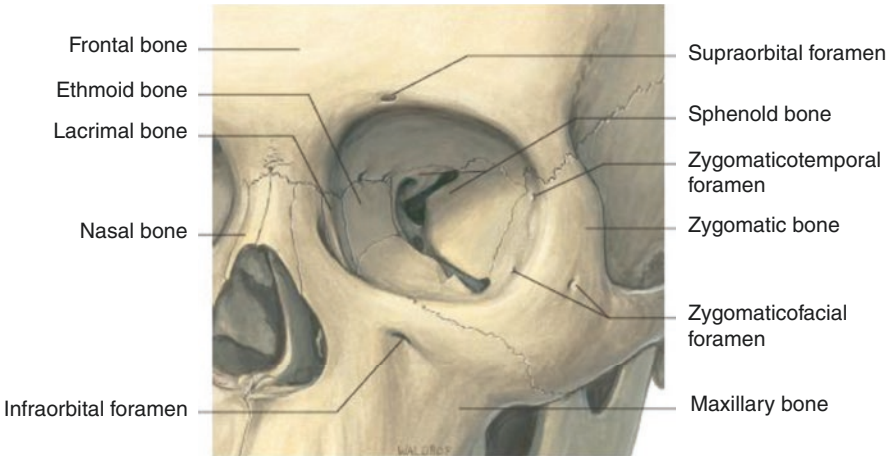

Fig. 1.1 Orbital bones, frontal view

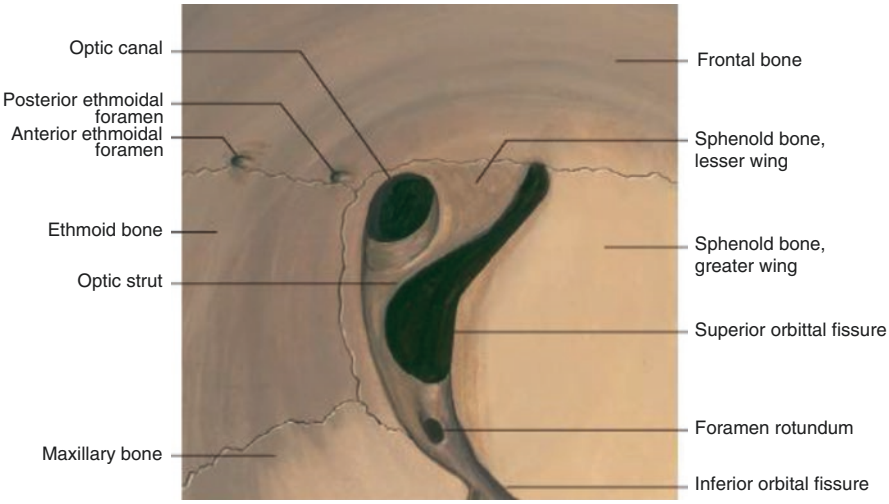

Fig. 1.2 Orbital bones, apex

Orbital Rim

The orbital rim is rounded and thickened, and serves to protect the eye from facial impacts. The superior rim is the most prominent due to expansion of the underlying frontal sinus. It is more protuberant in adult males. The medial third of the superior orbital rim is interrupted by a notch or foramen for passage of the supraorbital neurovascular bundle. One or both sides will have an open notch in 75% of all orbits. In 50% of individuals at least one side may be closed to form

a foramen [3]. The notch is situated about 25–30 mm from the facial midline [4]. The location of this notch is an important guide in avoiding injury to the supraorbital nerve during brow and forehead surgery. The orbital rim is flatter and less prominent between the supraorbital notch and the medial canthal ligament. The supratrochlear and infratrochlear nerves, and the dorsal nasal artery emerge at this site. At the superomedial corner of the orbit lies the cartilaginous trochlea of the superior oblique tendon. Glabellar and forehead anesthesia can happen during surgical access to the medial wall through a frontoethmoidal as incision may interrupt these neural structures. If necessary for orbital access, the trochlea can be disinserted by elevating the periosteum. Medially, the orbital rim extends downward to the posterior lacrimal crest and ends at the inferior entrance to the nasolacrimal canal. The anterior lacrimal crest begins just above the medial canthal ligament, and passes downward into the inferior orbital rim. The medial rim is, therefore, discontinuous at the lacrimal sac fossa. Between the anterior and posterior lacrimal crests is the lacrimal sac fossa formed at the junction of the maxillary and lacrimal bones. The fossa measures about 16 mm in vertical length, 4–9 mm in width, and 2 mm in depth [5]. Just in front of and parallel to the anterior lacrimal crest is a vertical groove in the frontal process of the maxillary bone for a nutrient branch of the infraorbital artery. During dacryocystorhinostomy surgery this groove may be mistaken for the medial edge of anterior lacrimal crest. Brisk bleeding may occur from rupture of this vessel, but it is easily controlled. The inferior orbital rim is formed by the maxillary bone medially and the zygomatic bone laterally. The infraorbital foramen, conducting the infraorbital artery and nerve, is located 4–10 mm below the central portion of the inferior rim. During surgery on the orbital floor, care must be taken not to elevate periosteum anterior to the central rim for more than about 4 mm, since this may injure these neurovascular structures. The orbital rim is thickest laterally. Here it is formed by the frontal process of the zygomatic bone and the zygomatic process of the frontal bone. These two elements meet at the frontozygomatic suture line near the supratemporal corner of the orbit. This suture line is an important landmark for removing the lateral rim during orbital surgery, because the anterior cranial fossa lies 5–15 mm above this horizontal level. This is a weak suture and is frequently the site of separation following facial trauma. About 10 mm below the fronto-zygomatic suture line, about 4–5 mm inside the rim is a small mound, the lateral orbital tubercle of Whitnall. It serves for insertion of the posterior crus of the lateral canthal ligament, Lockwood's inferior suspensory ligament, the lateral horn of the levator aponeurosis, the lateral check ligament and pulley system of the lateral rectus muscle, and the deep layer of the orbital septum. Proper realignment of these structures after lateral orbital surgery or repair of rim fractures is essential for normal cosmetic and functional reconstruction. The entire orbital rim is buttressed by adjacent bones and is frequently involved in complex facial fractures. The surgeon must be alert to the normal anatomic and functional relationships between the orbital bones and the nasal cavity, paranasal sinuses, cranial vault, and the temporomandibular joint.

Topographic Relationships

The orbital septum arises from the orbital rims anteriorly. The paranasal sinuses lie adjacent to the floor, medial wall, and anterior portion of the orbital roof. There are four orbital walls composed of seven bones: ethmoid, frontal, lacrimal, maxillary, palatine, sphenoid, and zygomatic.

Roof of the Orbit

The orbital roof (Fig. 1.3) is triangular in shape. The orbital plate of the frontal bone forms most of the roof, with a small contribution by the lesser wing of the sphenoid bone posteriorly. It measures about 46 mm (range 35–59 mm) from the supraorbital foramen to the optic canal [6]. A concavity for the lacrimal gland lies in the anterior superolateral corner. A small depression in the superomedial corner, about 3–5 mm behind the rim, houses the fibrocartilaginous trochlea for the superior oblique tendon. This structure, along with its associated pulley system, can easily be separated from the adjacent bone along with periorbita if needed during surgery. Its precise repositioning is essential to avoid postoperative motility disturbance. The frontal sinus is located within the frontal bone in the anteromedial portion of the roof. The optic canal is located in the roof at the apex and communicates between the middle cranial fossa and the orbit. It is bounded by the body of the sphenoid bone medially, the lesser wing of the sphenoid superiorly, and the optic strut laterally and inferiorly. The strut arises from the body of the sphenoid and is directed slightly anteriorly, upward, and laterally at an angle of about 36° to the sagittal plane [7].

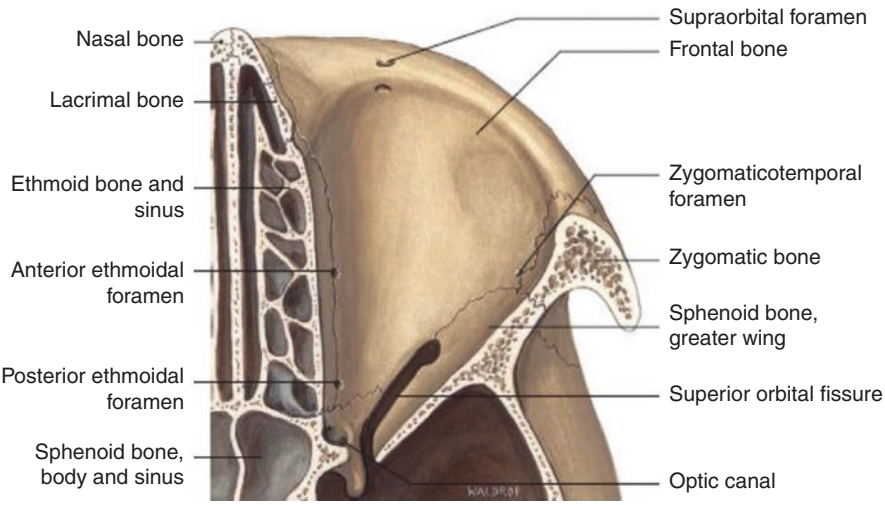

Fig. 1.3 Orbital bones, superior wall, intraorbital view

Lateral Wall of the Orbit

The lateral wall of the orbit (Fig. 1.4) is the thickest, and is composed of the zygomatic bone anteriorly and the greater wing of the sphenoid posteriorly. It is separated from the floor by the inferior orbital fissure, and from the roof, in part, by the superior orbital fissure. The lateral walls of the two orbits form an angle of approximately 90° with each other, and lie at 45° to the mid-sagittal plane. The lengths of the lateral and medial walls, from orbital rim to apex, are about the equal. Because of the oblique orientation of the lateral wall, the lateral rim lies about 10-mm posterior to the medial rim [8]. The length of the lateral wall from the lateral rim at the frontozygomatic suture to the optic canal is about 47 mm (range 39–55 mm). The thinnest part of the lateral wall is at the zygomatico-sphenoid suture, about 8–10 mm behind the orbital rim. Approximately 10 mm behind the zygomatic-sphenoid suture, the sphenoid bone thickens where it divides to form the anterior corner of the middle cranial fossa. In about 40% of individuals there are one or more openings within the fronto-sphenoid suture line, about 30 mm from the orbital rim. This is the cranio-orbital foramen (foramen meningo-orbitale) that transmits an anastomotic branch between the middle meningeal artery and the ophthalmic arterial system. This vessel is easily ruptured during lateral orbital surgery resulting in brisk bleeding. Compression for several minutes is usually sufficient to control it. At the junction of the lateral wall and roof is the superior orbital fissure (SOF). Several small foramina perforate the lateral orbital wall just behind the rim laterally and inferiorly near the anterior end of the inferior fissure. These transmit branches of the lacrimal artery and zygomatic nerve out of the orbit as the zygomaticotemporal and zygomaticofacial neurovascular bundles.

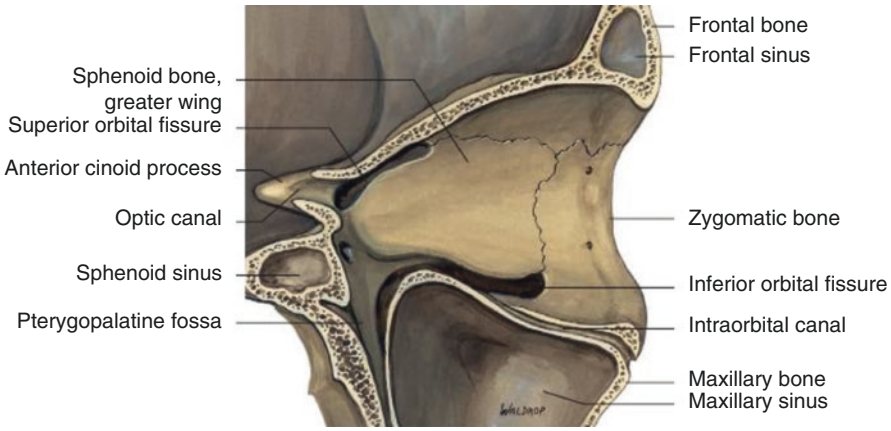

Fig. 1.4 Orbital bones, lateral wall, intraorbital view

Medial Wall of the Orbit

The medial walls (Fig. 1.5) of the orbits are approximately parallel to each other and to the mid-sagittal plane. The separation between the two orbits is approximately 24 mm from the medial wall of one to the medial wall of the other. The medial wall measures an average of 42 mm (range 32–53 mm) in horizontal length from the anterior lacrimal crest to the optic canal [6]. It is composed of the ethmoid, lacrimal, maxillary, and sphenoid bones. Anteriorly, the thick frontal process of the maxillary bone lies at the inferior medial rim. It contains the anterior lacrimal crest and forms the anterior portion of the lacrimal sac fossa. The lacrimal bone is a small, thin, and fragile plate situated just posterior to the maxillary process. It forms the posterior portion of the lacrimal sac fossa. Running vertically along its midpoint is the posterior lacrimal crest. The suture between the maxillary and the lacrimal bones generally lies along the mid-vertical line within the lacrimal sac fossa. Behind the posterior lacrimal crest is the lamina papyracea, which forms most of the lateral wall of the ethmoid labyrinth. It contributes 4–6 cm^2 to the orbital wall surface. It is fragile, measuring only 0.2–0.4 mm in thickness. However, it is made more rigid by the honeycombed bony laminae surrounding the ethmoid air cells, which usually number 3–8. Infections of the ethmoid sinuses may extend through the lamina papyracea to cause orbital cellulitis and proptosis [9]. Superiorly the ethmoid bone joins the orbital roof at the fronto-ethmoid suture line. The anterior and posterior ethmoidal foramina usually lie within the fronto-ethmoid suture line. Posterior to the ethmoid bone is the body of the sphenoid bone that forms the short posterior portion of the medial wall. The sphenoid body lies between the two orbital apices and contains the sphenoid sinus. The optic canal is situated in the superomedial portion of the orbital apex, enclosed by the body of the sphenoid medially, the lesser wing of the sphenoid superiorly, and the optic strut inferolaterally. The lacrimal sac fossa is a depression in the anterior inferomedial orbit [10]. It is bounded by the anterior and posterior lacrimal crests and measures about 4–9 mm in width and 16 mm in height.

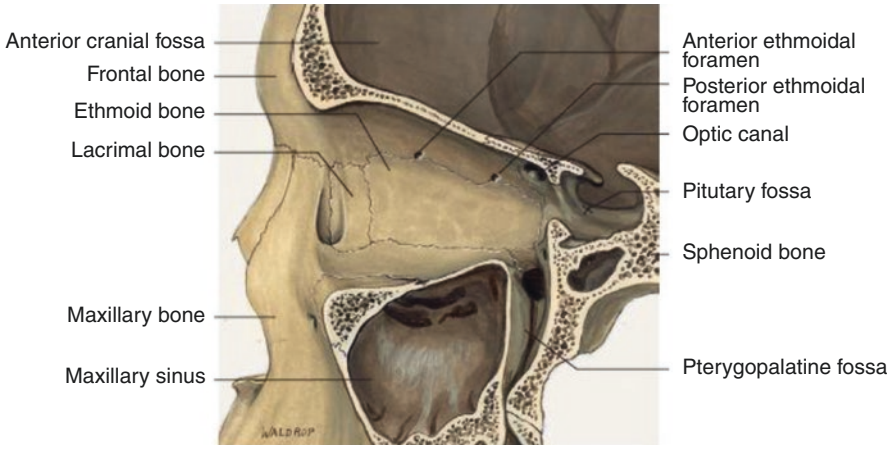

Fig. 1.5 Orbital bones, medial wall, intraorbital view

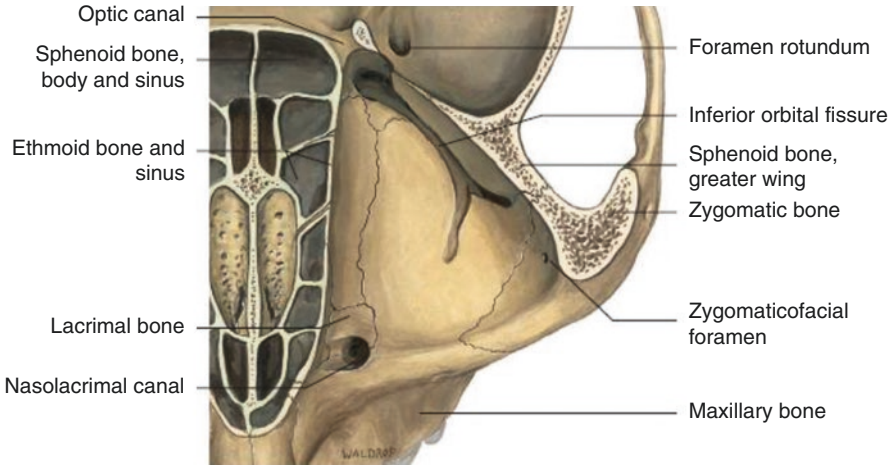

Fig. 1.6 Orbital bones, inferior wall, intraorbital view

The fossa is formed by the frontal process of the maxillary bone anteriorly and by the lacrimal bone posteriorly.

Floor of the Orbit

The orbital floor (Fig. 1.6) is a very thin plate composed of three bones (maxillary, zygomatic, and palatine). Its surface forms a triangular segment extending from the maxillary ethmoid buttress on the medial side, horizontally to the inferior orbital fissure on the lateral side, and from the inferior orbital rim back to the posterior wall of the maxillary sinus. The floor contributes 3–5 cm^2 to the overall orbital wall surface. It is strengthened by the infraorbital canal which runs anteroposteriorly through it near its midline or sometimes closer to its lateral border. The orbital floor shows the greatest degree of deformation with static loading of any of the orbital walls [11]. This explains the high rate of floor fractures associated with blunt trauma. A 3-mm downward displacement of the entire floor results in an increase of about 1.5 cm^3 (5%) to the orbital volume, and about 1.0–1.5 mm of enophthalmos. The major contribution to the floor is from the orbital plate of the maxillary bone, which also forms the roof of the maxillary sinus. Anterolaterally, the zygomatic bone contributes to the orbital rim and a small portion of the floor just in front of the anterior border of the inferior orbital fissure. The palatine bone lies at the extreme posterior end of the floor, near the orbital apex. The floor is bounded medially by the maxilla-ethmoid suture line, and anterolaterally by the zygomaticomaxillary suture. From the inferior orbital rim, the floor dips downward, where it reaches its lowest point. This is about 1.5–2.0 mm below the rim in children and young adults, but reaches 3.0 mm in older adults [12]. From here the floor slopes upward to the orbital apex. In the mid and posterior orbit, the floor ends at the inferior orbital fissure, and the posterior extent of the maxillary sinus. It is important to keep in mind that the orbital floor does not extend all the way to the apex, but rather ends at the

pterygopalatine fossa. The floor is, therefore, the shortest of the orbital walls, extending only about 35–40 mm from the inferior rim to the posterior wall of the maxillary sinus. In the posterior portion of the orbital floor lies the infraorbital sulcus. This fissure runs approximately in the center of the floor from posterior to anterior, and carries the maxillary division of the trigeminal nerve and the associated infraorbital branch of the maxillary artery from the pterygopalatine fossa.

Apertures

The orbital walls are perforated by several important apertures.

Ethmoidal Foramina

The anterior and posterior ethmoidal foramina usually lie within the fronto-ethmoid suture line. These openings transmit branches from the ophthalmic artery and nasociliary nerve passing out of the orbit. The positions of these foramina are clinically important since they relate to important cranial structures such as the cribriform plate, and to the optic foramen. They are key landmarks during surgery along the medial orbital wall. Injury to the ethmoidal arteries can cause excessive orbital bleeding during surgery. Subperiosteal hematoma following trauma frequently results from rupture of one of these arteries, and management requires access to the medial wall with ligation or cautery of the bleeding vessel. These foramina provide a potential route of entry into the orbit for infections and neoplasms from the sinuses [13].

Superior Orbital Fissure

The superior orbital fissure (SOF) lies at the junction of the lateral wall and roof, between the greater and lesser wings of the sphenoid bone near the orbital apex. It is oriented from inferomedial at the apex to superotemporal distally. The anterior most edge of the SOF lies 37 mm (range 34–41 mm) from the lateral orbital rim. In size and shape this fissure shows considerable individual variability [14]. However, its comma-like shape is usually wider inferiorly, but then narrows more superiorly. The fissure measures about 20–25 mm in overall length. The narrow lesser wing of the sphenoid bone separates the medial edge of the superior orbital fissure from the lateral margin of the optic canal. The spinal recti lateralis is a small bony projection situated on the lateral edge of the fissure near its middle portion, at the junction of its wide and narrow portions. This projection serves as the origin for part of the lateral rectus muscle. It is formed primarily by a small groove in the sphenoid wing which lodges the superior ophthalmic vein as it passes through the fissure [7]. The superior orbital fissure transmits most of the vascular and neural structures from the middle cranial fossa into the orbit, with the major exception of the optic nerve and ophthalmic artery, which pass through the optic canal. The central portion of the fissure is anatomically divided by the annulus of Zinn, which serves as the tendinous origin for the rectus muscles. The central opening defined by the annulus, called the oculomotor foramen, transmits structures into the intraconal orbital space.

Most of these structures subserve ocular function and motility. These include the superior and inferior divisions of the oculomotor nerve, the abducens nerve, and the nasociliary nerve. Other structures passing through the superior orbital fissure but outside the annulus are mainly associated with the extraconal orbital space, or are toward extra orbital sites. These include the trochlear nerve, the frontal and lacrimal branches of the trigeminal nerve, and the superior ophthalmic vein above the annulus, and the inferior ophthalmic vein beneath the annulus. In 8–40% of individuals, a linear vertical groove is present lying along the greater wing of the sphenoid bone, between the superior and inferior orbital fissures. Most of the venous drainage from the orbit passes through this fissure by way of the superior ophthalmic vein to the cavernous sinus.

Inferior Orbital Fissure

The inferior orbital fissure is bounded by the sphenoid, maxillary, and palatine bones and lies between the lateral orbital wall and the orbital floor. It transmits the second (maxillary) division of CN V, including the zygomatic nerve, and branches of the inferior ophthalmic vein leading to the pterygoid plexus. The infraorbital nerve, which is a branch of the maxillary nerve, leaves the skull through the foramen rotundum and travels through the pterygopalatine fossa to enter the orbit at the infraorbital groove. This fossa extends laterally to become the infratemporal fossa. The nerve travels anteriorly in the floor of the orbit through the infraorbital canal, emerging on the face of the maxilla 1-cm below the inferior orbital rim. The infraorbital nerve carries sensation from the lower eyelid, cheek, upper lip, upper teeth, and gingiva. Numbness in this distribution often accompanies blowout fractures of the orbital floor and typically improves with time.

Zygomaticofacial and Zygomaticotemporal Canals

The zygomaticofacial canal and zygomaticotemporal canal transmit vessels and branches of the zygomatic nerve through the lateral orbital wall to the cheek and the temporal fossa, respectively.

Nasolacrimal Canal

The nasolacrimal canal is a bony tube extending from the lacrimal sac fossa to the inferior nasal meatus beneath the inferior turbinate in the nose, it runs inferolaterally and slightly posterior in the medial wall of the maxillary bone and it contains the membranous nasolacrimal duct. The canal measures about 5 mm in diameter and is bordered by three bones, the maxilla, the lacrimal, and the inferior turbinate bones. It measures about 12–15 mm in length.

Optic Canal

The optic canal is located in the roof at the apex and communicates between the middle cranial fossa and the orbit. It is bounded by the body of the sphenoid bone medially, the lesser wing of the sphenoid superiorly, and the optic strut laterally and inferiorly. The strut arises from the body of the sphenoid and is directed slightly anteriorly, upward, and laterally at an angle of about 36° to the sagittal plane [7].

The optic canal assumes a vertically oval shape at its orbital end, where it measures about 5–6 mm in horizontal diameter, and 6–8 mm vertically. In its central portion the canal is round in cross-section, and on the cranial end it is oval in the horizontal plane [15]. In about 4% of normal individuals the ophthalmic artery will notch the canal floor, forming a "keyhole" deformity [16]. The canal is 8–12 mm in length and is directed posteromedially at about 35° to the mid-sagittal plane, and upward about 38° to the horizontal. On the cranial side the optic canal measures 5–7 mm horizontally and 4–6 mm vertically. The tendinous annulus of Zinn encloses the orbital opening of the optic canal so that the optic nerve and ophthalmic artery pass into the intraconal space via the oculomotor foramen. Optic canal enlargement accompanies the expansion of the nerve, as seen with optic nerve gliomas. Blunt trauma may cause an optic canal fracture, hematoma at the orbital apex, or shearing of the nerve at the foramen, resulting in optic nerve damage.

Soft Tissues

Periorbita

The periorbita, also called the orbital periosteum or orbital fascia, covers the bones of the orbit. This dense connective tissue membrane serves as an attachment site for muscles, tendons, and ligaments and is a support structure for the blood supply to the orbital bones. The periorbita is attached only loosely to the underlying bone except at the orbital margins, the sutures, and the edges of fissures and foramina. At the orbital margins it is continuous with the periosteal covering of the bones of the face; at the edges of the superior orbital fissure, the optic canal, and the ethmoid canals, the periorbita is continuous with the periosteal layer of the dura mater. At the anterior portion of the optic canal, the periorbita splits such that a portion becomes continuous with the dura of the optic nerve and another portion reflects forward to take part in the formation of the common tendinous ring. At the inferior orbital fissure the periorbita is continuous with the periosteum of the skull. At the lacrimal crests a sheet of periorbita covers the lacrimal sac, and the periorbital is continuous with the tissue lining the nasolacrimal canal. Another portion of the periorbita covers the lacrimal gland.

Intraorbital Optic Nerve

Neural fibers of the optic nerve arise from primitive neuroblasts that become the ganglion cells in the retina, and grow toward the brain. Because the retina differentiates from the wall of the forebrain, the optic nerve is not a true peripheral nerve, but is an evaginated fiber tract of the diencephalon. Nevertheless, these fibers are customarily classified as a special somatic sensory cranial nerve. The fibers are myelinated, but lack a neurolemmal sheath. In the adult, the optic nerve is about 50 mm in length from the optic disc to the chiasm. Each nerve contains proximately 0.7–1.4

million axons, with a mean axon diameter of 0.85 mm. The highest axonal density is in the temporal inferior segment of the nerve, corresponding with the location of the major portion of the papillomacular bundle [17].

Within the orbit the nerve is invested with pia, arachnoid, and dural sheaths. The subarachnoid space is continuous from the middle cranial fossa, along the nerve, and into the posterior sclera. This space is partially interrupted at the orbital apex superiorly and medially where the pia and arachnoid are loosely adherent to the dura and annulus of Zinn. Clinically, this relationship may result in optic nerve compression and papilledema from increased intracranial cerebrospinal fluid pressure. The dura of the optic nerve becomes fused to periosteum within the optic canal superomedially. There are four anatomically important portions of the optic nerve; intraocular, Intraorbital (Fig. 1.7), intracanalicular, and intracranial. The center of the nerve leaves the globe 4 mm medial to, and 0.1 mm below the level of the macula [18]. The intraocular portion of the nerve lies within the limits of the posterior sclera, and measures approximately 1 mm in length. Here, it lies within the lamina cribrosa. The latter is a sieve-like connective tissue region of the posterior sclera through which pass the retinal ganglion cell axons and central retinal vessels. It preserves a pressure gradient between the intraocular and the extraocular spaces. The lamina cribrosa contains approximately 220–240 pores, each averaging 0.004 mm^2 in diameter [19]. As the retinal ganglion cell axons approach the lamina cribrosa they become crowded, forming the elevated papilla at the beginning of the intrascleral portion of the optic nerve. This is visible on funduscopic examination as the intraorbital portion of the optic nerve is approximately 30-mm long. The nerve is longer than the orbit, making an S-shaped curve to allow for movement with the eye.

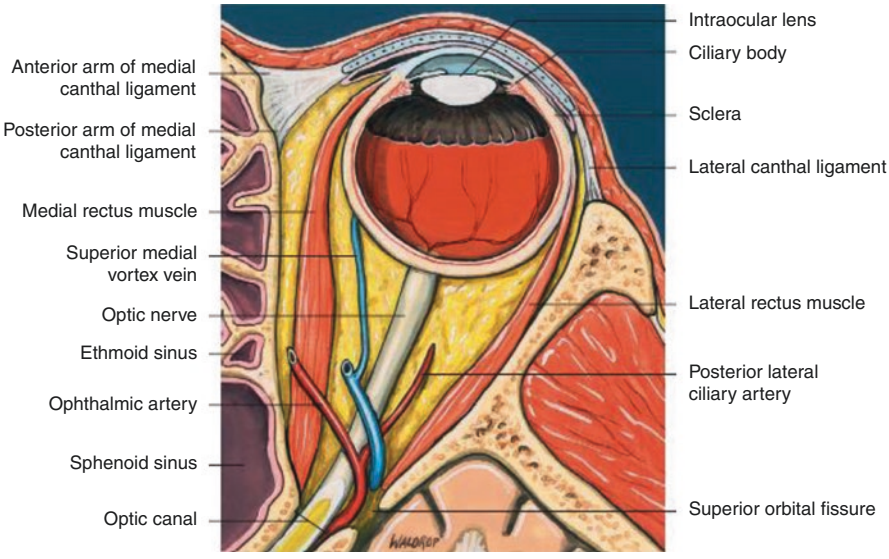

Fig. 1.7 Axial section through the mid-orbit at the level of the optic nerve

Extraocular Muscles and Orbital Fat

The extraocular muscles (Fig. 1.8) are responsible for the movement of the eye and for synchronous movements of the eyelids. All of the extraocular muscles, except the inferior oblique muscle, originate in the orbital apex and travel anteriorly to insert onto the eye or eyelid. The four rectus muscles (superior. medial, lateral, and inferior recti) originate in the annulus of Zinn. The levator muscle arises above the annulus on the lesser wing of the sphenoid. The superior oblique muscle originates slightly medial to the levator muscle and travels anteriorly through the trochlea on the superomedial orbital rim, where it turns posterolaterally toward the eye. The inferior oblique muscle originates in the anterior orbital floor lateral to the lacrimal sac and travels posterolaterally within the lower eyelid retractors to insert inferolateral to the macula. In the anterior portion of the orbit, the rectus muscles are connected by a membrane known as the intermuscular septum. When viewed in the coronal plane, this membrane forms a ring that divides the orbital fat into the intraconal fat (central surgical space) and the extraconal fat (peripheral surgical space). These anatomical designations on a magnetic resonance (MR) or computed tomographic (CT) scan are helpful for describing the location of a mass. A knowledge of these spaces helps direct the surgical dissection to the mass. The orbit is further divided by many fine fibrous septa that unite and support the globe, optic nerve, and extraocular muscles. Accidental or surgical orbital trauma can disrupt this supporting system and contribute to globe displacement and restriction. In many cases of diplopia after fracture, restriction of eye movement is caused by the entrapment of the orbital connective tissue rather than by the muscles themselves. The motor innervation of the extraocular muscles arises from cranial nerves Ill, IV, and VI. The superior rectus and levator muscles are supplied by the superior division of the 3rd

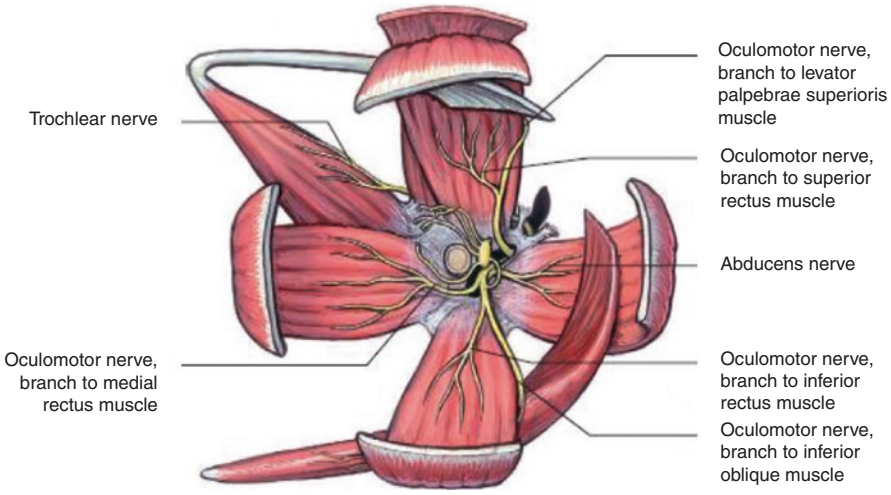

Fig. 1.8 Motor nerves, frontal view with extraocular muscles

nerve (oculomotor nerve). The inferior rectus, medial rectus, and inferior oblique muscles are supplied by the inferior division of the 3rd nerve. The lateral rectus is supplied by VI (abducent nerve). The cranial nerves to the rectus muscles enter the orbit posteriorly through the superior orbital fissure and travel through the intraconal fat to enter the muscles' intraconal surface at the junction of the posterior third and anterior two-thirds. Crania l nerve IV (trochlear nerve) crosses over the levator muscle and innervates the superior oblique on the superior surface at its posterior third. The nerve to the inferior oblique muscle travels anteriorly on the lateral aspect of the inferior rectus to enter the muscle on its posterior surface.

Annulus of Zinn

The annulus of Zinn (Fig. 1.9) is the fibrous ring formed by the common origin of the four rectus muscles. The ring encircles the optic foramen and the central portion of the superior orbital fissure. The superior origin of the lateral rectus muscle separates the superior orbital fissure into two compartments. The portion of the orbital apex enclosed by the annulus is called the oculomotor foramen. This opening transmits CN III (upper and lower divisions), CN VI, and the nasociliary branch of the ophthalmic division of CN V (trigeminal). The superior and lateral aspect of the superior orbital fissure external to the muscle cone transmits CN IV, as well as the frontal and lacrimal branches of the ophthalmic division of CN V. Cranial nerve IV is the only nerve that innervates an extraocular muscle and does not pass directly into the muscle cone when entering the orbit. Cranial nerves III and VI pass directly into the muscle cone through the oculomotor foramen. The superior ophthalmic vein passes through the superior and lateral portion of the superior orbital fissure outside the oculomotor foramen.

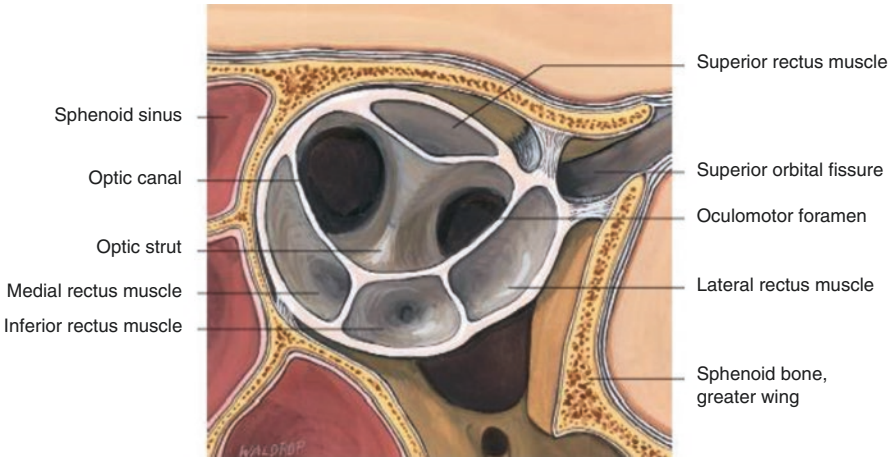

Fig. 1.9 Annulus of Zinn, anterior surface with origins of the extraocular muscles

Vasculature of the Orbit

The ophthalmic artery (Fig. 1.10) arises from the internal carotid artery just medial to the anterior clinoid process. It passes through the optic canal below the nerve and within its dural sheath and enters the orbit lateral to the nerve. It gives origin to the lacrimal artery lateral to the optic nerve and to the supraorbital artery as it crosses the optic nerve to reach the medial wall. It terminates by dividing into the dorsal nasal and supratrochlear arteries. It may give origin to the two medial palpebral arteries before it terminates. The lacrimal artery passes forward on the upper border of the lateral rectus muscle accompanied by the lacrimal nerve. It supplies the lacrimal gland, then pierces the septum, and divides into two lateral palpebral arteries in the lids. The supraorbital artery joins the supraorbital nerve in the roof of the orbit and accompanies it through the supraorbital notch. It passes upwards deep to the brow fat pad and then pierces the frontalis muscle. Its branches contribute to the supply of the forehead, scalp, and upper lid. The dorsal nasal artery pierces the septum above the medial canthal tendon to supply the skin of the root of the nose and the lacrimal sac. It gives origin to the medial palpebral arteries if these have not arisen separately from the ophthalmic artery. The two medial palpebral arteries enter the lids above and below the medial canthal tendon. The superior ophthalmic vein provides the main venous drainage of the orbit. This vein originates in the superonasal quadrant of the orbit and extends posteriorly through the superior orbital fissure into the cavernous sinus.

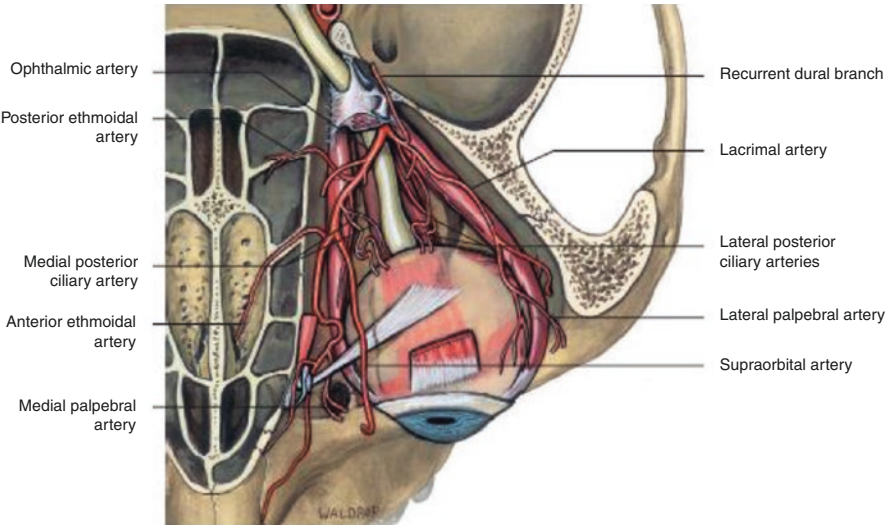

Fig. 1.10 Arterial supply to the ocular adnexa and globe

Nerves

Sensory innervation to the periorbital area is provided by the ophthalmic and maxillary divisions of CN V. The ophthalmic division (Fig. 1.11) of CN V travels anteriorly from the ganglion in the lateral wall of the cavernous sinus, where it divides into three main branches: frontal, lacrimal, and nasociliary. The frontal and lacrimal nerves enter the orbit through the superior orbital fissure above the annulus of Zinn and travel anteriorly in the extraconal fat to innervate the medial canthus (supratrochlear branch), upper eyelid (lacrimal and supratrochlear branches), and forehead (supraorbital branch). The nasociliary branch enters the orbit through the superior orbital fissure within the annulus of Zinn, entering the intraconal space and traveling anteriorly to innervate the eye via the ciliary branches. The short ciliary nerves penetrate the sclera after passing through the ciliary ganglion without synapse. The long ciliary nerves pass by the ciliary ganglion and enter the sclera, where they extend anteriorly to supply the iris, cornea, and ciliary muscle. The muscles of facial expression, including the orbicularis oculi, procerus, corrugator superciliaris, and frontalis muscles, receive their motor supply by way of branches of CN VII (the facial nerve) that penetrate the undersurface of each muscle. Parasympathetic Innervations enters the eye as the short posterior ciliary nerves after synapsing within the ciliary ganglion, parasympathetic innervation to the lacrimal gland originates in the lacrimal nucleus of the pons and eventually joins the lacrimal nerve to enter the lacrimal gland. The nerve fibers follow the arterial supply to the pupil, eyelids, and orbit and travel anteriorly in association with the long ciliary nerves. Interruption of this innervation results in the familiar signs of Horner syndrome:

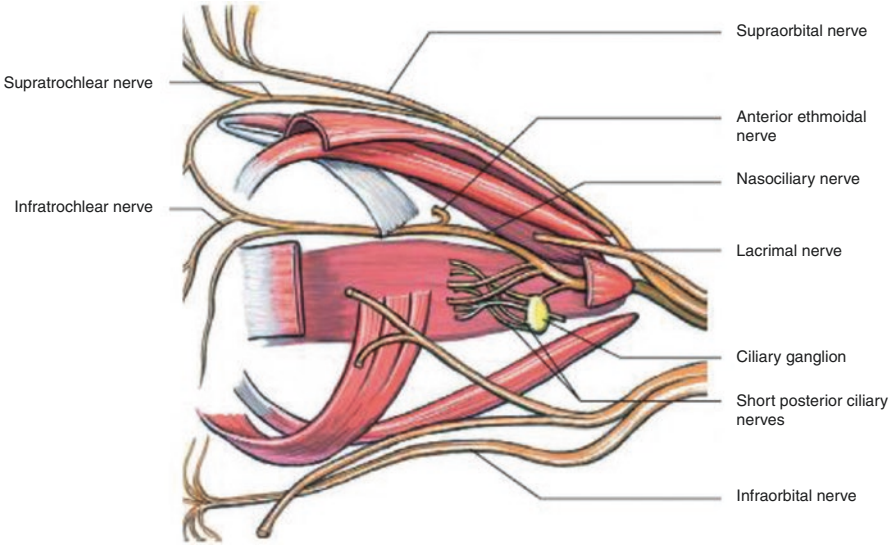

Fig. 1.11 Sensory nerves, lateral view with extraocular muscles

ptosis of the upper eyelid, elevation of the lower eyelid, miosis, anhidrosis, and vasodilation.

The motor innervation (Fig. 1.8) of the extraocular muscles arises from cranial nerves (N) lll. IV. and VI. The superior rectus and levator muscles are supplied by the superior division of nerve lll (oculomotor nerve). The inferior rectus, medial rectus, and inferior oblique muscles are supplied by the inferior division of N lll. The lateral rectus is supplied by N VI (Abducent nerve). The cranial nerves to the rectus muscles enter the orbit posteriorly through the superior orbital fissure and travel through the intraconal fat to enter the muscles' intraconal surface at the junction of the posterior third and anterior two-thirds. Crania l nerve IV (trochlear nerve) crosses over the levator muscle and innervates the superior oblique on the superior surface at its posterior third. The nerve to the inferior oblique muscle travels anteriorly on the lateral aspect of the inferior rectus to enter the muscle on its posterior surface.

Lacrimal Apparatus

The lacrimal gland (Fig. 1.12) is wrapped around the posterior border of the lateral horn of the levator aponeurosis. The superior, orbital part of the gland lies in the lacrimal gland fossa. Anteriorly, it is in contact with the septum and posteriorly, with orbital fat. Inferiorly, the lateral rectus muscle lies laterally and the levator lies medially. Its secretory ducts pass down into the inferior, palpebral part of the gland which is one-third the size of the orbital part. The anterior border of the palpebral

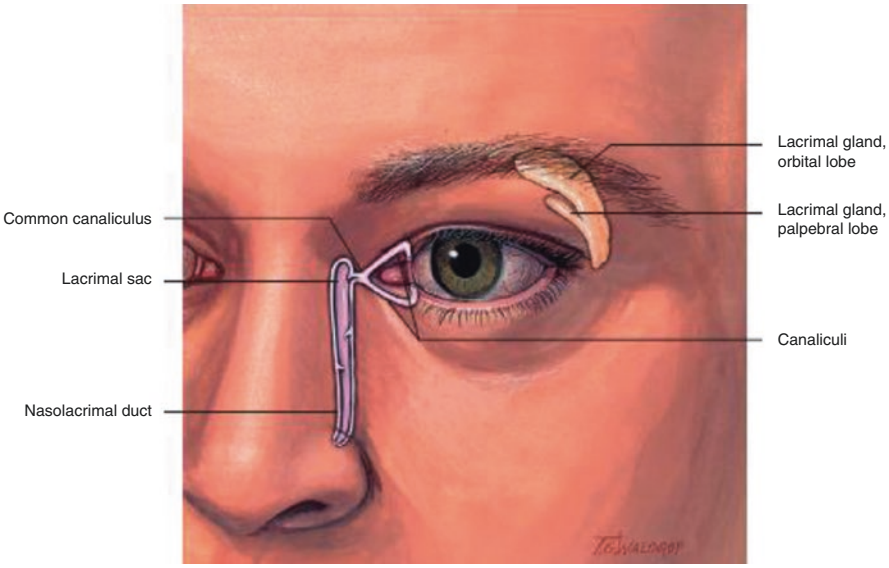

Fig. 1.12 The lacrimal secretory and drainage systems

part can be seen laterally in the upper fornix and its secretory ducts emerge there. With age, the orbital lobe of the lacrimal gland may prolapse inferiorly out of the fossa and present as a mass in the lateral upper eyelid.

The lacrimal canaliculi, surrounded by the orbicularis muscle immediately medial to the puncta, pass medially and posteriorly between the limbs of the medial canthal tendon to pierce the fascia overlying the lacrimal sac. They usually join to form a common canaliculus before entering the sac. The sac lies in the lacrimal sac fossa which is bounded anteriorly and posteriorly by the anterior and posterior lacrimal crests. Periosteum at the posterior lacrimal crest splits to enclose the sac and reunites at the anterior lacrimal crest. The lateral leaf is the stronger and it is reinforced further by the posterior limb of the medial canthal tendon. The anterior part of the tendon crosses the upper part of the sac and the septum covers the lower part. The inferior oblique muscle arises just behind and lateral to the orifice of the nasolacrimal canal. Anterior to the medial canthal tendon, about 8-mm medial to the medial canthus, is the angular vein.

Periorbital Structures

Nose and Paranasal Sinuses

The bones forming the medial, inferior, and superior orbital walls are close to the nasal cavity and are pneumatized by the paranasal sinuses, which arise from and drain into the nasal cavity. The sinuses may serve to decrease the weight of the skull, or they may function as resonators for the voice. The sinuses may also support the nasal passages in trapping irritants and in warming and humidifying the air. Pathophysiologic processes in these spaces that secondarily affect the orbit include sinonasal carcinomas, inverted papillomas, zygomycoses, Wegener granulomatosis, and mucoceles as well as sinusitis, which may cause orbital cellulitis or abscess. The nasal cavity is divided into two nasal fossae by the nasal septum. The lateral wall of the nose has three bony projections: the superior, middle, and inferior conchae (turbinates). The conchae are covered by nasal mucosa, and they overhang the corresponding meatuses. The frontal sinus and the anterior and middle ethmoid air cells drain into the middle meatus. The nasolacrimal duct opens into the inferior meatus. The nasal cavity is lined by a pseudostratified, ciliated columnar epithelium with copious goblet cells. The mucous membrane overlying the lateral alar cartilage is hair bearing and therefore less suitable for use as a composite graft in eyelid reconstruction than the mucoperichondrium over the nasal septum, which is devoid of hair. The frontal sinuses develop from evaginations of the frontal recess and cannot be seen radiographically until the sixth year of life. Pneumatization of the frontal bone continues through childhood and is complete by early adulthood. The sinuses can develop asymmetrically and vary greatly in size and shape. The frontal sinuses are almost always separated by the midline intersinus septum. Each sinus drains through separate frontonasal ducts and empties into the anterior portion of the middle meatus. The ethmoid air cells are thin-walled cavities that lie between

the medial orbital wall and the lateral wall of the nose. They are present at birth and expand as the child grows. Ethmoid air cells can extend into the frontal, lacrimal, and maxillary bones and may extend into the orbital roof (supraorbital ethmoids). The numerous small, thin-walled air cells of the ethmoid sinus are divided into anterior, middle, and posterior. The anterior and middle air cells drain into the middle meatus; the posterior air cells, into the superior meatus. Orbital cellulitis develops most frequently from the spread of ethmoidal sinusitis through the lamina papyracea into the orbit. The sphenoid sinus evaginates from the posterior nasal roof to pneumatize the sphenoid bone. It is rudimentary at birth and reaches full size after puberty. This sinus is divided into two cavities by a bony septum. Occasionally, pneumatization extends into the pterygoid and occipital bones. The sinus drains into the sphenoethmoidal recess of each nasal fossa. The optic canal is located immediately superolateral to the sinus wall. Visual loss and visual field abnormalities can be direct sequelae of pathologic processes involving the sphenoid sinus. The maxillary sinuses are the largest of the paranasal sinuses. Together, the roofs of each maxillary sinus form the floor of the orbits. The maxillary sinuses extend posteriorly in the maxillary bone to the inferior orbital fissure. The infraorbital nerve and artery travel along the roof of the sinus from posterior to anterior. The bony nasolacrimal canal lies within the medial wall. The sinus drains into the middle meatus of the nose by way of the maxillary ostium. Orbital blowout fractures commonly disrupt the floor of the orbit medial to the infraorbital canal. The infraorbital nerve is often damaged, causing hypoesthesia of the cheek.

Eyelid Anatomy

The eyelids form a soft-tissue protection to the globe and the anterior entrance to the orbit. The orbital septum separates the bony orbit from the eyelid and represents the anterior most orbital structure. All structures anterior to the orbital septum are technically in the eyelid. The eyelid provides important components of the precorneal tear film, and help its distribution on the surface of the eye. Together with the lacrimal drainage apparatus, the eyelids collect and propel tears to the medial canthus, where they pass to the nose. The face and scalp are arranged in concentric tissue layers, which more or less, follow a single basic pattern [20]. This pattern consists of five basic layers: skin, subcutaneous tissue, superficial musculoaponeurotic layer, loose areolar tissue, and the deep fascia and periosteum.

The Adult Eyebrow

The eyebrows mobility is part of the system of facial expression, they are situated over the bony superior orbital rims, at the junction between the upper eyelid and the forehead. They extend from just above the trochlear fossa medially, nearly to the frontozygomatic suture line laterally. The flattened and generally hairless glabellar region separates the two eyebrows in the midline. The eyebrow consists of thickened

skin overlying the supraorbital torus, from which it is separated by a prominent fat pad. The eyebrow is capable of a wide range of movement, averaging 1-cm downward and 2.5-cm or greater upward [21]. Excursion is more extensive in the medial portion of the brow. These complex movements are provided by the interdigitation of five striated muscles that insert partially along the brow namely; the frontalis, procerus, depressor supercilii, corrugator supercilii, and orbicularis oculi muscles. All are innervated by the seventh cranial, or facial, nerve. The frontalis muscle fibers are oriented vertically on the forehead and form the anterior belly of the occipitofrontalis musculofascial complex that forms the epicranius. The latter includes two flat muscle masses, the frontalis muscle anteriorly and the occipitalis muscle posteriorly.

Frontalis Muscle

The frontalis muscle is usually considered to be part of the epicranius, or occipitofrontalis muscle that includes the occipitalis muscle posteriorly and the frontalis muscle anteriorly, with the galea aponeurotica joining the two portions. The frontalis muscle has no bony attachments. Rather, its proximal fibers originate from the galea aponeurotica at about the level of the coronal suture line and extend toward the supraorbital rim. On the lateral side, frontalis muscle fibers extend slightly more than on the medial border [22]. The muscle belly is surrounded by layers of the galea, anteriorly by the thin superficial layer and posteriorly by the thicker deep layer. The frontalis muscle is paired with a distinct midline separation. Its medial fibers blend with those of the procerus muscle. More laterally, under the brow, frontalis fibers interdigitate with the corrugator and orbital portion of the orbicularis muscles. The frontalis muscle does not extend laterally beyond the junction of the middle and lateral thirds of the brow, so that the lateral brow lacks an elevator. Because of this the lateral brow is under the depressor influence of the lateral orbicularis muscle [23]. The frontalis muscle is separated from the periosteum by a fat pocket in the deep fascia of the forehead. This has been referred to as the sub-brow fat pad or the superior retro-orbicularis oculi fat pocket (ROOF) [24]. The frontalis muscle elevates the brow, and together with the occipitalis belly, tightens the scalp and provides mobility of the skin along the temples. Brow elevation may be transmitted through other tissues to serve as an accessory retractor of the eyelid. This function is the basis for the frontalis suspension operations used to repair poor-function upper eyelid ptosis. Because of this contribution to eyelid elevation it is essential to mechanically immobilize the frontalis muscle during preoperative evaluation of levator muscle function in ptosis patients.

Eye Lid

The interpalpebral fissure measures 10–11 mm in vertical height, but with advancing years the upper eyelid assumes a more ptotic position, resulting in a fissure of only about 8–10 mm. The horizontal length of the fissure is 30–31 mm, and is achieved by the age of about 15 years [25]. The upper and lower eyelids meet medially and laterally at an angle of approximately 60°. Laterally, this canthal angle rests against the

globe, but medially it is displaced away from the globe about 5–6 mm. Within this medial space, called the lacus lacrimalis, are a fleshy mound, the caruncle, and a fold of conjunctiva lateral to it called the plica semilunaris. The interpalpebral fissure is usually inclined slightly upward at its lateral end, such that the lateral canthal angle is about 2–3 mm higher than the medial canthal angle. In the primary position of gaze, the upper eyelid margin usually lies at the superior corneal limbus in children and 1.5–2.0 mm below it in the adult. To be kept in mind during ptosis repair or eyelid reconstructions is that the lower eyelid margin rests at the inferior corneal limbus and the upper eyelid marginal contour reaches its highest point just nasal to the pupil. The margin of each eyelid is about 2-mm thick. Posteriorly, the marginal tarsal surface is covered with conjunctival epithelium, interrupted by the Meibomian gland orifices. Anteriorly, the margin is covered with cutaneous epidermis from which emerge the eyelashes. Separating these two regions is a faint linear zone, sometimes forming a slight sulcus. This is the gray line, which is the marginal projection of the pars ciliaris of Riolan's muscle. Eyelid skin is the thinnest of the body and is unique in having no subcutaneous fat layer. The upper eyelid crease is a horizontal indentation caused by attachments of superficial levator aponeurotic fibers into orbicularis intermuscular septa and subcutaneous tissue. It lies about 8–11 mm above the eyelid margin centrally. Medially, the crease is generally lower, about 4–5 mm from the lid margin. Laterally, it lies about 5–6 mm above the margin. This crease should be reformed during ptosis or blepharoplasty surgery to maintain normal cosmetic appearance, and to prevent downward displacement of preaponeurotic fat or overhang of eyelid skin.

Protractors

The orbicularis oculi (Fig. 1.13) is a complex periocular striated muscle sheet that lies just below the skin and is an integral component of the superficial musculoaponeurotic system (SMAS). The SMAS is that part of the superficial fascia of the head and neck which covers the midface. A fibroadipose layer separates the orbicularis muscle from the overlying dermis [20]. The orbicularis muscle consists of striated

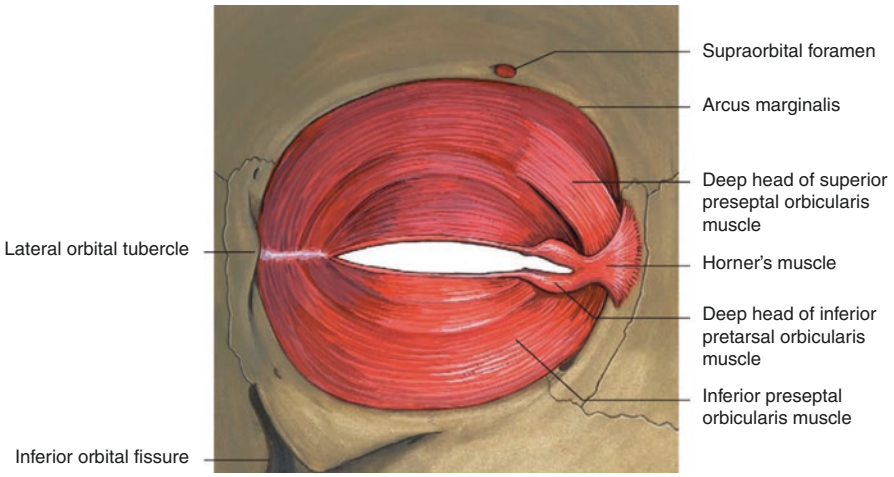

Fig. 1.13 Orbicularis oculi muscle

fibers that run parallel to the eyelid margins. The orbicularis muscle is divided anatomically into four segments, three contiguous and one separate. The contiguous parts are the orbital, preseptal, and pretarsal portions of the orbicularis, and the separate part is the muscle of Riolan. The orbital portion of the orbicularis muscle overlies the bony orbital rims. It arises from insertions on the frontal process of the maxillary bone in front of the anterior lacrimal crest, from the orbital process of the frontal bone, and from the common medial canthal ligament. A medial slip of this muscle passes superficial to the depressor supercilii and the origin of the corrugator supercilii, and inserts onto the dermis at the medial brow [26]. The major bundle of fibers passes around the orbital rim to form a continuous ellipse without interruption at the lateral palpebral commissure. These fibers insert medially just below their points of origin. They are innervated by the temporal and zygomatic branches of the facial nerve, and serve as a sphincter of the eyelids. The palpebral portion of the orbicularis muscle overlies the mobile eyelid from the orbital rims to the eyelid margins. The muscle fibers sweep circumferentially around each eyelid as a half ellipse, fixed medially and laterally at the canthal ligaments. Although this portion forms a single anatomic unit in each eyelid, it is customarily further divided topographically into two parts, the preseptal and the pretarsal orbicularis. The preseptal part is positioned over the orbital septum in both upper and lower eyelids, and its fibers originate perpendicularly along the upper and lower borders of the medial canthal ligament. The inferior preseptal muscle arises as a single head from the entire length of the common ligament. Posterior muscle fibers may be seen to attach to dense collagen fibers that insert onto the upper portion of the lacrimal sac [27]. The preseptal muscle arises by two heads in the upper lid. The anterior or superficial head is the more prominent, arising as a broadsheet from the upper surface of the common canthal ligament. The posterior head arises from the superior limb, and to a lesser extent from the posterior limb of the canthal ligament. The superior limb of the medial canthal ligament (Fig. 1.14) is fused to the fundus of the lacrimal sac by

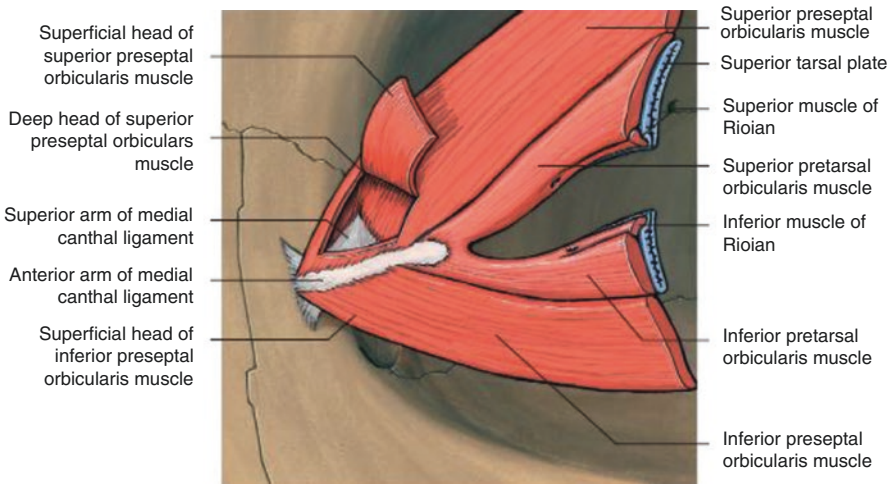

Fig. 1.14 The medial canthus

a layer of fibrovascular fascia so that on contraction, this deep head of the preseptal muscle pulls the sac laterally, thus contributing to the lacrimal pump mechanism. Fibers of the upper and lower preseptal muscles arc around the eyelids and interdigitate laterally along the lateral horizontal raphe. From its orientation, the preseptal orbicularis muscle appears to function largely in counteracting opposing tone in the retractors of the eyelids by distally displacing the levator aponeurosis and capsulopalpebral fascia. Secondarily, it likely contributes to the lacrimal pump mechanism at the level of the lacrimal sac. The pretarsal muscles, firmly attached to the tarsal plates, insert medially by a superficial head and a deep head. The superficial head from each lid blends with a fibrous component to form the anterior part of the medial canthal tendon. The deep head from each lid is also known as the pars lacrimalis, or Horner's muscle. Its fibers begin at the medial ends of the tarsal plates and insert into the posterior lacrimal crest a few millimeters behind the lacrimal sac. Contraction of the deep head pulls the lid medially and posteriorly. At the lateral canthus the pretarsal muscles join and insert by a common tendon into Whitnall's tubercle. The preseptal muscles join laterally to form a lateral raphe, which is connected to the underlying tendon. Deep to the muscle insertions a Y-shaped fibrous thickening in the orbital septum joins the lateral ends of the tarsal plates to Whitnall's tubercle. These muscular and fibrous structures together form the lateral canthal tendon. The medial canthal tendon also has a fibrous and a muscular component. The fibrous component is attached laterally to the medial ends of the tarsal plates as two limbs of a Y. It has a superficial and a deep component. The superficial component inserts medially on the frontal process of the maxilla just anterior to the anterior lacrimal crest, level with the upper part of the lacrimal sac. It has a definite inferior border but the superior border blends with the periosteum. The deep component leaves the deep surface just lateral to the anterior lacrimal crest and inserts into the posterior lacrimal crest behind the lacrimal sac. This deep component of the tendon is the main medial anchor of the lids. During blinking the deep heads of the pretarsal muscles (Horner's muscle) pull the medial ends of the eyelids medially, shortening the canaliculi, while the lacrimal fascia and sac wall are pulled laterally by contraction of the deep heads of the preseptal muscle. The puncta close and the tears in the ampullae of the canaliculi are forced medially and are sucked into the sac. As the deep insertions of the orbicularis muscle relax at the end of the blink the lacrimal fascia and sac wall move medially again, the medial ends of the lids move laterally, the puncta reopen and the ampullae refill with tears. Drainage of tears from the lacrimal sac into the nasolacrimal duct is not influenced directly by the lacrimal pump mechanism and is mainly due to gravity. Near the eyelid margin, a specialized bundle of striated muscle, the muscle of Riolan, lies more posterior than the main portion of the orbicularis and creates the gray line. The muscle of Riolan may play a role in Meibomian glandular discharge, blinking, and the position of the eyelashes.

Orbital Septum

The orbital septum (Fig. 1.15) is a fibrous, multilayered membrane beginning at the arcus marginalis along the orbital rim. The septum is continuous with other layers on the forehead and within the orbit. The orbital septum is the anterior most

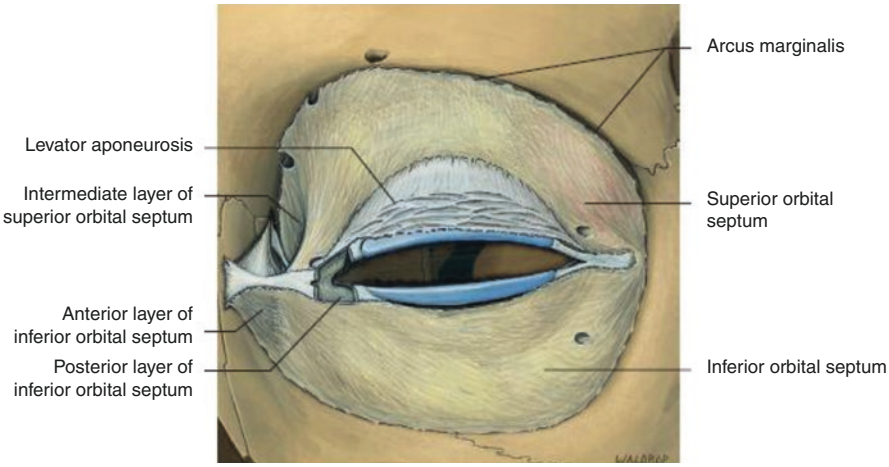

Fig. 1.15 Orbital septum

septal sheet of the orbital fascial system, and defines the anterior limit of the orbit. Within the upper eyelid, the septum forms a nearly continuous layer that separates the anterior eyelid lamellae from the posterior lamellae and from the deeper orbital structures. From the superior arcus marginalis the septum passes inferiorly between the orbicularis muscle and the preaponeurotic fat pockets. Distally, the septum is loosely joined to the levator aponeurosis. The point of insertion is usually about 3–5 mm above the tarsal plate. The more anterior layers of the septum gradually interdigitate distally with those of the levator aponeurosis [28]. After fusing with the aponeurosis, the anterior layer of the septum continues to extend downward over the distal aponeurosis and along the anterior tarsal surface [29]. The septum fuses with the anterior layer of the capsule-palpebral fascia 3–5 mm below the inferior border of the tarsus. The common fascial sheet then inserts onto the inferior tarsal edge [30]. Medially the septum divides into several layers and has an intimate relationship with the lacrimal drainage system. In the lower eyelid the anterior septal layer inserts onto the anterior lacrimal crest, and onto the inferior border of the fibrous medial canthal ligament. A posterior layer separates and passes posteriorly around the lacrimal sac. It is fused to periorbita along the orbital opening of the nasolacrimal duct, and also to the fascia of the lower lacrimal sac. In the upper eyelid an anterior layer of the orbital septum inserts onto the superior limb of the medial canthal ligament and onto the orbital process of the maxillary bone. Here it encloses the lacrimal sac fossa anteriorly, and is interrupted along the canthal ligament for penetration of Horner's muscle. Thus, the anterior layer of the septum forms an anterior fibrous wall to the lacrimal sac fossa. The anterior and intermediate layers of the orbital septum effectively isolate the lacrimal sac and duct within their own fascial compartment, separate from the eyelid and orbit. Laterally, the orbital septum passes slightly behind the bony orbital rim where it inserts onto the lateral canthal ligament, and the lateral

retinaculum at the orbital tubercle in company with the lateral horn of the levator aponeurosis [31].

Orbital Fat

Sub-orbicularis Oculi Fat Pad (SOOF) (Fig. 1.16)

This fat pad lies just below the lateral half of the inferior orbital rim and extends over the lower part of the body of the zygoma. It is in contact with the periosteum deep to the lower part of the orbicularis oculi muscle in the upper cheek. It is posterior to the deep layer of the SMAS lining the deep surface of the orbicularis muscle. As the SMAS descends from the lower lid tissues, it is thickened into a supporting sheet, the orbitomalar ligament (also known as the orbicularis retaining ligament), which has attachment also to the inferior orbital rim periosteum.

The Retro-Orbicularis Oculi Fat Pad (ROOF)

This fat pad, lies deep to the skin and thin subcutaneous fat layer of the brow, the orbital part of the orbicularis muscle and the lower fibers of the frontalis muscle. It is enclosed between the superficial and deep layers of the deep galea aponeurotica as these descend into the upper lid. An additional deep attachment of the row fat to the supraorbital periosteum is more secure medially than laterally. The brow fat may extend inferiorly on the anterior surface of the orbital septum. The SOOF and ROOF pads communicate at their lateral ends through fat overlying the lateral orbital rim and the lateral canthal tendon. These fat pads are separated from the orbital fat pads by the orbital septum and, in the lower lid, also by the layers of the SMAS (orbitomalar ligament) at the orbital rim.

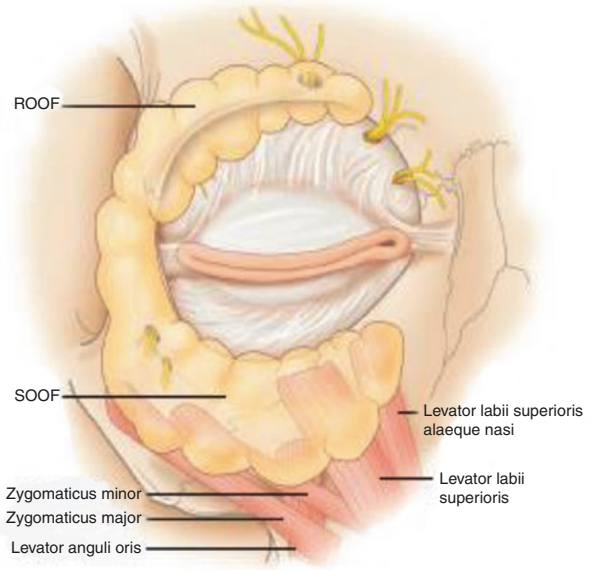

Fig. 1.16 Soof fat layers

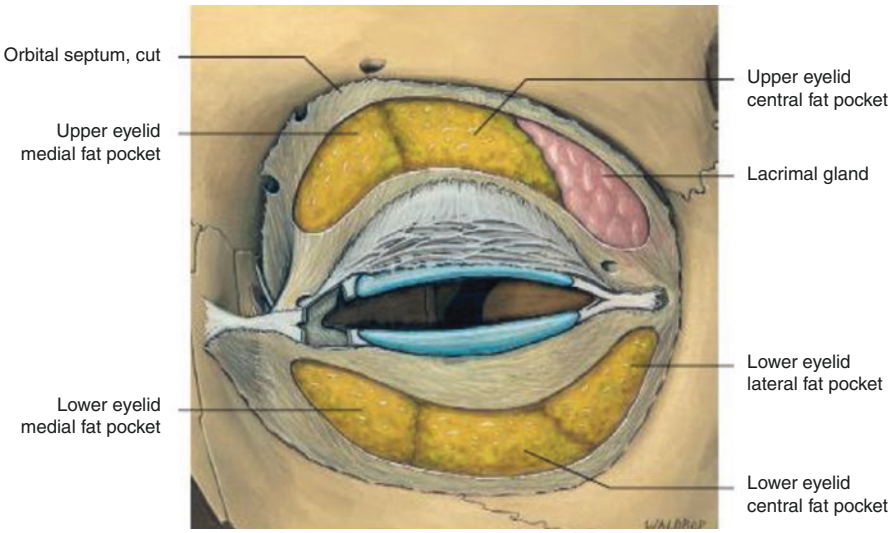

Fig. 1.17 Eyelid preaponeurotic fat pockets

The Post Orbicular Fascia (Fig. 1.17)

This plane is an avascular loose areolar layer between the orbicularis muscle and the orbital septum-levator aponeurosis fascial complex (upper lid) or the capsulopalpebral fascia (lower lid). It extends to the eyelid margin where blends with the gray line. Within the lid it allows bloodless dissection and identification of the underlying orbital septum. On the eyelid margin, the gray line marks the approximate anatomic separation of the anterior skin–muscle lamella from the posterior tarso-conjunctiva lamella. This fascial space is also responsible for the easy accumulation of fluid and blood in the eyelid following surgery or trauma. The postorbicular fascial plane is best defined beneath the pretarsal portion of the orbicularis muscle. Under the preseptal portion, this plane becomes more complex and contains a thin layer of fibroadipose tissue continuous with the deep brow fat pad [32]. In the upper eyelid there are two fat pockets: nasal and central. In the lower eyelid, there are three fat pockets: nasal, central, and temporal. The central orbital fat pad is an important landmark in both elective eyelid surgery and lid laceration repair because it lies directly behind the orbital septum and in front of the levator aponeurosis.

Retractors

The retractors of the upper eyelid are the levator muscle with its aponeurosis and the superior tarsal muscle (Müller muscle). In the lower eyelid, the retractors are the capsulopalpebral fascia and the inferior tarsal muscle.

Upper Eyelid Retractors

The lesser sphenoid wing just above the annulus of Zinn, superolateral to the optic canal gives the origin of the levator palpebrae superioris muscle (Fig. 1.18). The

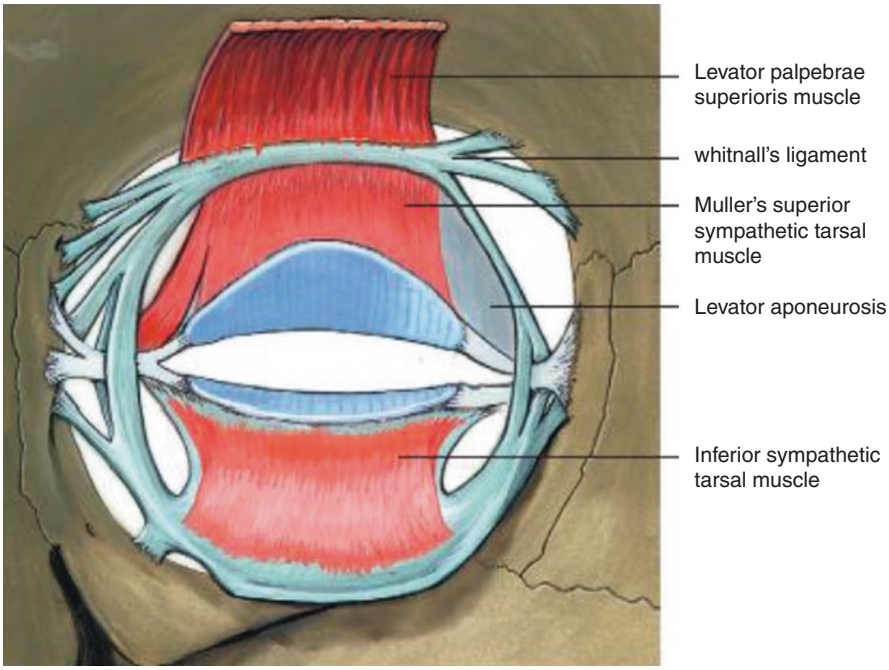

Fig. 1.18 Levator aponeurosis and Müller's tarsal muscles, interior orbital view

muscle is about 36 mm in length, measuring 4 mm in width at its origin, widening to 8 mm in the mid-orbit [33]. Along the anterior third of the levator muscle, posterior to Whitnall's ligament, a thin sheet of fibrous tissue separates and interconnects the levator muscle sheath with the superior rectus muscle. More anteriorly this becomes thicker until it completely envelopes the levator, fusing with a similar covering around the superior rectus muscle it is referred to this as the "conjoint fascial sheath" [34]. The forniceal suspensory ligaments are a fibrous attachment that run downward about 2 mm from the conjoint fascial sheet to the superior conjunctival fornix. Just behind the superior orbital rim the levator muscle widens to about 18 mm and is divided into two layers, superior and inferior, separated by connective tissue. The superior layer continued into the levator aponeurosis, and the inferior layer passed into Müller's smooth muscle [35]. Here a thickened condensation is seen within the muscle sheath around the levator muscle. This structure runs horizontally across the superior orbit and attaches medially to the fascia around the trochlea, and laterally onto the capsule of the lacrimal gland and periosteum of the frontal bone. This condensation is firmly adherent to the levator muscle sheath along its medial and lateral surfaces, but is only loosely attached centrally. It forms the superior transverse orbital ligament of Whitnall. The levator muscle is innervated by the superior division of CN III, which also supplies the superior rectus muscle. A superior division palsy, resulting in ptosis and decreased up gaze, implies an infraorbital disruption of CN III. The peripheral arterial arcade is found between

the levator aponeurosis and the Müller muscle, just above the superior tarsal border. This vascular arcade serves as a useful surgical landmark to identify the Müller muscle.

Lower Eyelid Retractors

The retractors of the lower lid are equivalent to the retractors of the upper lid (the levator and Müller's muscles). They develop from the capsulopalpebral head of the inferior rectus muscle. But unlike the upper lid retractors, they are vestigial, containing little muscle. They arise from the sheath of the inferior rectus muscle and consist of the capsulopalpebral fascia (equivalent to the levator) and the inferior tarsal muscle (equivalent to Müller's muscle). As they pass forward the lower lid, retractors split to enclose the inferior oblique muscle, and where they reunite, they blend with thickened fascia on their inferior aspect. This is Lockwood's suspensory ligament that inserts into the orbital walls close to the canthal tendons. The septum fuses with the lower lid retractors about 2–3 mm below their insertion into the lower tarsal border. The angle between the posterior aspect of the septum and the lower lid retractors contains a pad of orbital fat—the medial fat pad—similar to the preaponeurotic fat in the upper lid. The pull of the lower lid retractors depresses the lid in downgaze and helps to maintain the upright position of the tarsal plate.

Tarsus

The tarsal plates (Fig. 1.19) form the skeleton of the eyelids. They are made of dense fibrous tissue with some elastic tissue. The upper eyelid tarsal plates measure 10–12 mm vertically in the center of the eyelid; the maximum lower eyelid tarsal plate measurement is 4 mm. The tarsal plates have rigid attachments to the periosteum through the canthal tendons medially and laterally. The tarsal plates may become horizontally displaced with age as a result of stretching of the medial and lateral supporting tendons. Both tarsal plates are usually 1-mm thick and taper at the

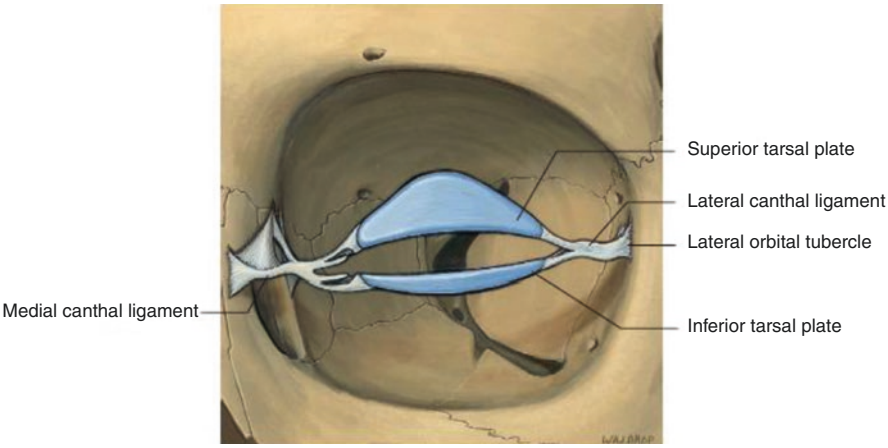

Fig. 1.19 Tarsal plates with medial and lateral canthal ligaments

medial and lateral ends as they approach the canthal tendons. Holocrine sebaceous glands, the Meibomian glands lie within the substance of the tarsal plates. In the upper lid the lower fibers of the levator aponeurosis insert into the lower part of the tarsal plate and Müller's muscle is attached to the proximal border. In the lower lid, the lower lid retractors insert into the proximal border. The tarsal conjunctiva is firmly attached to its posterior surfaces.

Conjunctiva

The conjunctiva is composed of non-keratinizing squamous epithelium. It forms the posterior layer of the eyelids and contains mucin-secreting goblet cells and the accessory lacrimal glands of Wolfring and Krause that are found mainly between the upper tarsal border and the upper fornix, especially laterally. The lacrimal gland ducts empty into the lateral part of the upper fornix. The superior and inferior fornices extend almost to the orbital rims. The lateral fornix extends to approximately 14 mm from the limbus but the medial fornix is shallower. Fibrous tissue support reaches the fornices and in the superior and inferior fornices "suspensory ligaments" can be identified. They are extensions of the common sheaths between the upper or lower lid retractors and the superior or inferior rectus muscles.

Blood Supply of the Eye Lid (Fig. 1.20)

The dorsal nasal artery pierces the septum above the medial canthal tendon to supply the skin of the root of the nose and the lacrimal sac. It gives origin to the medial palpebral arteries if these have not arisen separately from the ophthalmic artery. The two medial palpebral arteries enter the lids above and below the medial canthal

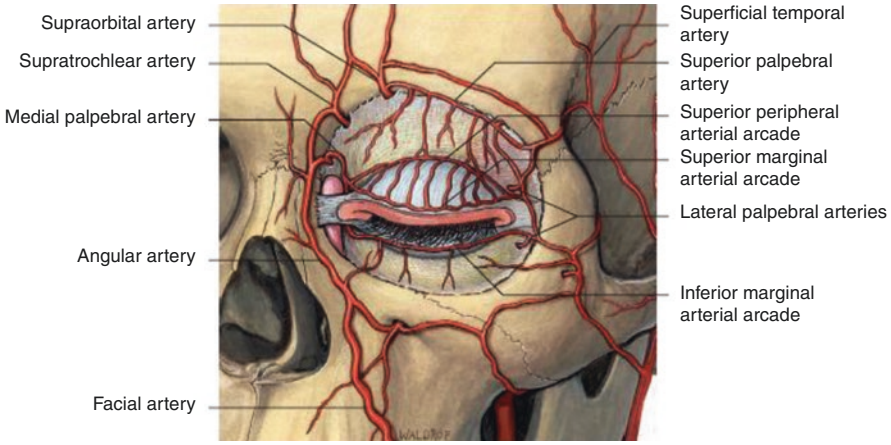

Fig. 1.20 Eyelid arterial supply

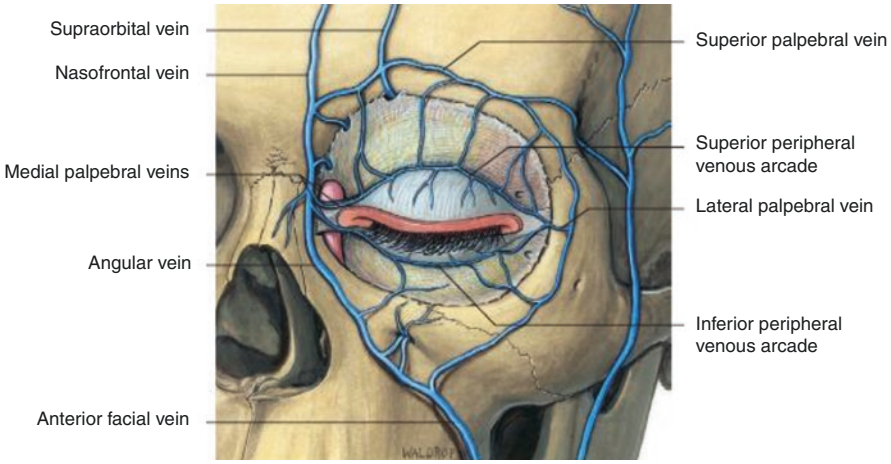

Fig. 1.21 Eyelid venous drainage

tendon. In the lids the medial and lateral palpebral arteries anastomose to form arcades within the submuscular connective tissue on the surface of the upper and lower tarsal plates 2–4 mm from the lid margins. In the upper lid, a second arcade is formed at the upper border of the tarsal plate. The supratrochlear artery pierces the septum with the supratrochlear nerve, winds upwards into the mid-forehead and supplies it. It anastomoses with the supraorbital artery. Blood from the external carotid system reaches the lids through anastomoses with the infraorbital and facial arteries, mainly via the angular artery, and the superficial temporal artery.

Venous Drainage (Fig. 1.21)

The veins of the lids are found mainly in the region of the fornices. They drain to the venous network of the middle third of the face. The angular vein is formed by the anastomosis of the supraorbital and supratrochlear or frontal veins at the upper inner angle of the orbit. It drains posteriorly into the superior orbital vein and inferiorly into the facial vein. It lies about 8-mm medial to the inner canthus where it can often be seen through the skin. Venous blood also drains to the inferior ophthalmic vein.

Lymphatic Drainage of the Lids (Fig. 1.22)

The preauricular and parotid lymph nodes drain the lateral two-thirds of the upper lid and the lateral third of the lower lid. The submandibular nodes drain the medial third of the upper lid and the medial two-thirds of the lower lid.

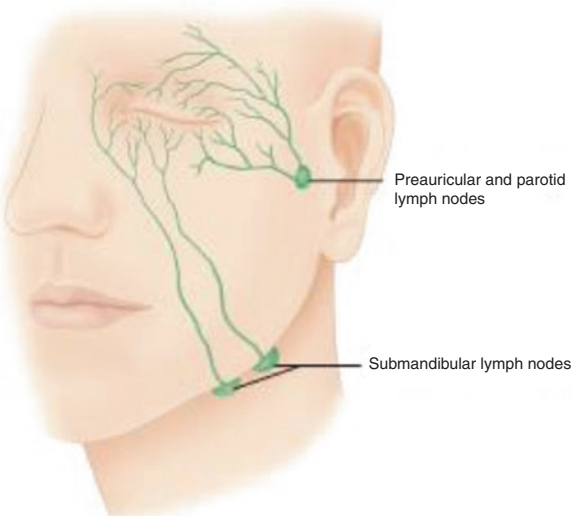

Fig. 1.22 Lymphatic drainage of the eyelids

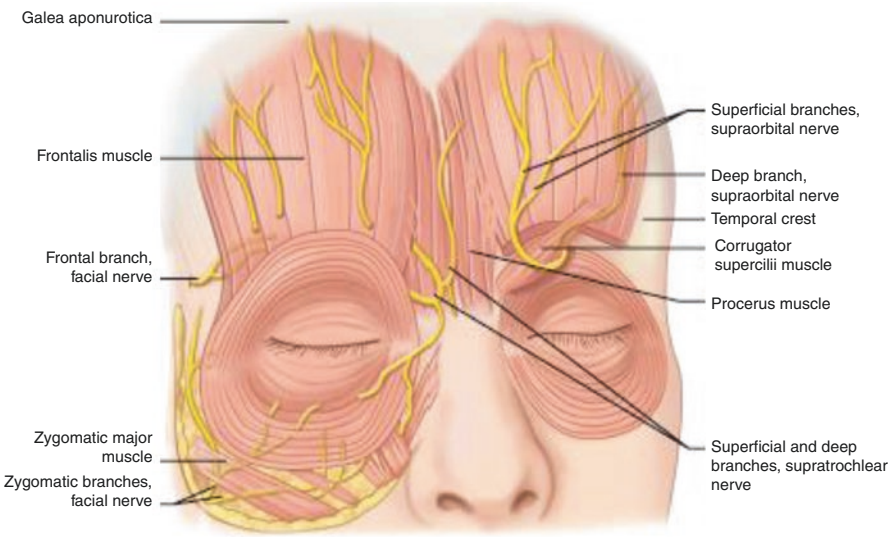

Fig. 1.23 Nerve supply of the lid

Nerve Supply to the Lids and Face

Motor Supply (Fig. 1.23)

The muscles of facial expression are supplied by branches of the facial nerve. Within the face the branches lie deep to the muscles of facial expression then penetrate the deep layer of the superficial musculo-aponeurotic system (SMAS) to innervate the

orbicularis muscle and the other muscles of facial expression. After emerging from the stylo-mastoid foramen the facial nerve gives origin to the posterior auricular branch which passes upwards and posteriorly to supply the occipitalis muscle and posterior auricular muscles. The trunk passes forward and enters the substance of the parotid gland where it divides into branches that emerge from the anterior border of the gland to supply the muscles of facial expression, including the frontalis and platysma muscles. Two of these branches, sometimes known as the upper and lower zygomatic branches, are of particular importance in the periocular region. The upper branch crosses the zygoma approximately at its midpoint, halfway between the outer canthus and the tragus, and enters the temporoparietal (superficial temporal) fascia and travels within it into the forehead, passing about 1.5 cm above the tail of the brow. Here it is known as the frontal branch of the facial nerve. Its surface marking is important during surgery in the forehead. It innervates the frontalis and orbicularis muscles, also the corrugator and procerus muscles, just above the superior orbital rim. The lower branch crosses the zygomatic bone to supply the orbicularis fibers of the lower lid and the upper fibers of the elevators of the upper lip. Having reached the lids, the terminal branches of the nerve turn at right angles to the muscle bundle to approach the lid margins, except medially where they run in the line of the muscles. There is extensive cross innervation between the branches of the facial nerve. The levator palpebrae superioris muscle is supplied by the third cranial nerve. It enters the orbit from the lateral wall of the cavernous sinus. It passes through the tendon ring lateral to the optic nerve and divides into superior and inferior branches. The superior division of the nerve traverses and supplies the superior rectus muscle before supplying the levator at the junction of its middle and posterior thirds. Müller's muscle is supplied by sympathetic nerves. Cranial preganglionic sympathetic fibers leave the CNS in the anterior spinal nerve roots of the intermediate region of the spinal cord, T1 to L1, and ascend the sympathetic chain to the superior cervical ganglion level with the second and third cervical vertebrae. Cranial postganglionic sympathetic fibers originate in the superior cervical ganglion and travel with the internal carotid artery and its branches to supply the structures of the cranial cavity and the orbit. The ciliary ganglion is attached anatomically to the nasociliary nerve lateral to the optic nerve near the back of the orbit. Preganglionic parasympathetic fibers originate in the Edinger Westphal nucleus in the midbrain and travel to the orbit with branches of cranial nerve III. They synapse in the ciliary ganglion and the postganglionic fibers travel in the multiple short ciliary nerves to pierce the sclera around the optic nerve and supply the sphincter muscle of the iris. Sympathetic postganglionic fibers from the superior cervical ganglion pass through the ciliary ganglion without further synapse and travel in the long and short ciliary nerves to enter the eye and supply the dilator muscle of the iris.

Sensory Supply

The lids and the contents of the orbit are supplied by the ophthalmic and the maxillary divisions of the trigeminal (fifth cranial) nerve. The ophthalmic division of the trigeminal nerve divides into the lateral wall of the cavernous sinus into the lacrimal, frontal, and nasociliary nerves. These pass through the superior orbital fissure

into the orbit. The lacrimal nerve runs forward along the superior border of the lateral rectus muscle to supply the lacrimal gland in its anterior two-thirds, it is accompanied by the lacrimal artery. It pierces the septum and supplies sensation to the lateral part of the upper lid and conjunctiva. The parasympathetic innervation of the lacrimal gland travels with the zygomatic nerve from the sphenopalatine ganglion and joins the lacrimal nerve just posterior to the gland. The frontal nerve is the largest of the three branches. It passes forward between the periosteum of the orbital roof and the levator muscle. Anteriorly, it divides into the supratrochlear and supraorbital nerves. The supratrochlear nerve ascends over the medial orbital rim with the artery, deep to the orbicularis muscle, to supply the medial part of the lid and conjunctiva and the skin of the forehead. The supraorbital nerve continues to the supraorbital notch which it passes through with the artery medial to it. It divides into superficial and deep branches. The superficial branch winds around the corrugator muscle and ascends more medially, superficial to the frontalis. The deep branch remains deep to the corrugator and ascends more laterally, deep to or through the frontalis. These branches supply the upper lid and conjunctiva, and the forehead and scalp as far as the vertex. The nasociliary nerve crosses medially above the optic nerve with the ophthalmic artery. It gives origin to several branches and then divides into the anterior ethmoidal nerve and the infratrochlear nerve. The anterior ethmoidal nerve passes via the anterior cranial fossa to terminate as nasal nerves. These supply the tip of the nose including the anterior part of the nasal septum. The infratrochlear nerve passes below the trochlea to supply the medial ends of the lids and conjunctiva, the lacrimal sac, and the root of the nose. There are several communications between the terminal branches of the ophthalmic nerve around the eye. They also communicate with the infraorbital nerve, a branch of the maxillary division of the fifth cranial nerve. The maxillary division of the trigeminal nerve passes forward from the trigeminal ganglion to the foramen rotundum through which it enters the pterygopalatine fossa. The infraorbital nerve branches forward and travels in a groove, then a canal, in the floor of the orbit to reach the infraorbital foramen. It branches to supply the skin and conjunctiva of the lower lid, the lower part of the side of the nose and the upper lip. The zygomatic nerve, a branch of the maxillary nerve, enters the orbit through the inferior orbital fissure. It follows the lower part of the lateral orbital wall where, after communicating with the lacrimal nerve, it divides into the zygomaticofacial and zygomaticotemporal nerves. The zygomaticofacial nerve exits anteriorly on the zygomatic bone to supply sensation to the malar area of the cheek. The zygomaticotemporal nerve exits in the temporal fossa and supplies sensation to the anterior temporal region.

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Aging of the Orbit and Rejuvenation Options

2

H. Dabbous, R. Chalhoub, N. Kawa, and N. Soueidan

"No eyes that have seen beauty ever lose their sight"

Jean Toomer

Introduction

The human face has been a central element throughout history. In addition to it being important in the description of beauty, it is the main element that portrays emotions and recognition [1, 2]. The face is the part of the body in which signs of aging are first noticed by both patients and people around them [3]. Early signs of aging of the face tend to primarily involve the periorbital and midface area [4]. It is not uncommon to see patients in their mid 20s to early 30s seeking advice regarding rejuvenation of the periorbital area, in order to prevent or treat early signs of aging. This is mainly the case when under-eye bags and wrinkles start to become more prominent, since these factors can make patients look older than their actual age [5].

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The periorbital region is composed of muscles, ligaments, fatty tissue, vessels and nerves, overlying a bony infrastructure. Intrinsic aging of the face and periorbital area is multifactorial in origin and includes remodeling of the cranial bone, gravity induced tissue descent, fat atrophy, and deterioration in the appearance of the skin [6]. Sun exposure, tobacco and alcohol use, comorbid medical conditions, extremes in body mass index (BMI), and medication use are common extrinsic causes of facial aging and have been shown to cause an acceleration in aging of the skin and subcutaneous tissues [7, 8].

Intrinsic Facial Aging

There are two main theories of intrinsic facial aging that have been advanced.

The volumetric or static theory suggests that there is a change and overall loss of volume [9] in the different compartments of the face, mainly a retrusion at the level of the cheek and a protrusion at the level of the lower eyelid [10]. This is combined with changes in the skin at the level of the eyelid, which gradually thins out and becomes darker in color as one ages.

In contrast, the gravitational, or dynamic theory supports the idea that volume in the face is not lost with age, but is rather shifted downward by gravity [11]. This is believed to be due to the combined effects of downward gravitational pull, the increased laxity of retaining facial ligaments as patients grow older, as well as changes in the resting tone of muscles of the face [6, 9]. The periorbital area, which is rich in retaining ligaments, is not affected by gravity as much as the midface and lower face, and aging in that area is thereby mostly due to volumetric changes [6].

Considering both the volumetric and gravitational theories together, and taking into consideration each of their consequences on the aging of the face and, more specifically the periorbital area, could possibly explain the changes witnessed with age [3].

Main Periorbital Changes Seen with Aging

The eye of a young patient manifests as having the medial canthus in a slightly lower position compared to the lateral canthus, thereby forming an upward slope from medial to lateral [6]. In addition, the lid to cheek junction is smooth, with a minimal concave depression of the lower eyelid in comparison to the convex protrusion of the cheek. In a youthful appearing patient, the malar prominence is covered by malar fat [6]. In the next sections, we will go over the distinct components of the periorbital structure, each of which contributes to the aging process.

Skin

One of the first signs of aging in the face includes sagging skin in the area of the lateral eyebrow, accompanied with ptosis of the lateral eyebrow and upper eyelid. In addition, skin redundancy and laxity in the latter area is also noted and is known as

dermatochalasia [9]. It has been shown that the advent of dermatochalasia increases with increasing age, and that men are more likely to suffer from this condition than women [3]. Dermatochalasia can tighten the space between the iris and eyelid, leading to an aged appearance, in addition to causing excessive skin redundancy in the lateral brow, thereby contributing to progressive loss of vision in the superior lateral fields [3, 9]. In addition, ptosis of the lateral brow leads to a flatter appearing eyebrow, caused by loss of the lateral arch. The frontalis muscle does not extend to the lateral brow, and with age, the lateral ligament of the brow becomes lax, leading to worsening ptosis [9]. Aging causes the margin of the lower eyelid to migrate downward, and that, along with the medial migration of the lateral canthus, changes the shape of the eye to a more circular form, more commonly found in elderly adults [12].

By the fourth decade of life, patients start to develop fine wrinkles at the lateral canthus, and the tear trough begins to form below the eyelid. As the aging process takes its course, wrinkling of the skin gradually becomes more noticeable to the naked eye, and pigmentation starts to take place, with a loss of skin elasticity and weaning of the shiny glow. These changes are mainly due to the atrophy of skin layers with age, and the decrease in the amount of collagen production, as well as deterioration in the elastic properties of the skin (disorganized layers of collagen and elastin). The loss and redistribution of fat with age leads to the uncovering of the vessels at the level of the periorbital area, conferring a bluish hue to the skin in the periorbital area [13]. Festoons can also appear in the area of the cheek caused by skin redundancies [6].

Special Consideration to Skin Discoloration with Age

In addition, under eye circles, also known as periocular hyperpigmentation, start to become a concern as patients age, since they usually give the impression that the patient is tired, sleep deprived and sad. These usually appear as semicircular macular lesions, ranging from light to dark brown in color, at the level of the periorbital area [14, 15]. Many factors come into play and contribute to the formation of infraorbital dark circles. This includes skin pigmentation and skin laxity, translucency of the skin allowing underlying vessels to tint the area with a resulting violet hue [4, 16], as well as hollowing caused by deepening of the tear trough [4]. The violaceous appearance of the lower periorbital area can be exacerbated by hormonal changes and menstruation in females [16]. Further contributors to skin pigmentation include melasma, triggered by hormonal changes in women, and yellowing of the skin with appearance of age spots [17].

Huang et al. [18] proposed a classification for periorbital hyperpigmentation. They divided under-eye circles into four types:

- Pigmented type: brown colored macular lesion below the eyes
- Vascular type: blue, pink or purple under-eye hue with possible surrounding eyelid edema
- Structural type: skin colored lesions that look like shadows formed by the anatomy of facial contours
- Mixed type: further subdivided into:

- Pigmented vascular
- Pigmented structural
- Vascular structural
- Combination of all three types (pigmented, vascular and structural).

In order for one to differentiate between a vascular or structural etiology of lower eyelid discoloration on physical exam, the patient's skin can be stretched at the level of the eyelid. Increase in the discoloration with such a maneuver would indicate thin skin and increased lower eyelid vascularity as the etiology, whereas with shadowing effects, skin stretching will lead to the disappearance of the periorbital hyperpigmentation [19].

Periorbital dark circles can also be associated with lower eyelid bags and skin edema leading to puffiness in the area, further contributing to periorbital aging.

Infraorbital palpebral bags can be due to multiple contributing factors, including malar fat pad descent, orbital fat prolapse, skin laxity and photoaging, extravasation of fluid at the level of the eyelid leading to edema, and orbicularis hypertrophy triggered by muscle over activity [20].

Some authors suggested a genetic background as one of the causes of periorbital hyperpigmentation, stating that in some patients, pigmentation can be noticed as early as in childhood [21]. The same authors also found that factors such as stress, lack of adequate sleep and rest, and medical comorbidities or illness can lead to an increase in the amount of pigmentation [21].

Oculodermal melanocytosis, also known as Nevus of Ota is a congenital cause of periorbital pigmentation [16], whereas Nevus of Hori is an acquired cause thought to be secondary to hormonal changes, dermatitis and photoaging. This usually involves the malar area, but that can often extend superiorly and involve the periocular area [22, 23].

Length of eyelashes, and the quality and distribution of eyebrow hair play an important role in the physical attractiveness of one's eye. However, they also play a role in apparent aging, whereby the distance between the sclera and the eyelash roots correlate highly with a patient's perceived age [12].

Fat

The superior periorbital area contains three major fat pads: the preaponeurotic, preseptal and galeal fat pads. The orbital septum delineates between the periorbital fat pad posteriorly, and the preseptal fat pad anteriorly. The galeal, or retro-orbicularis oculi fat pad is located below the skin of the eyebrow, and appears more prominent in the area of the lateral brow. With age, the galeal fat pad shifts inferolaterally causing fullness in the superolateral visual field with visual restriction [9].

The inferior periorbital area also contains three major fat pads: the medial, central and lateral fat pads, found immediately posterior to the orbital septum [9, 24]. These also gravitate downward as patients age due to weakening of the septum, thereby leading to anterior prolapse [24], and giving the impression of a lower eyelid "eyebag" [3]. The lower eyelid fat pad most commonly involved in protrusion is the central fat pad, followed by the lateral and less commonly the medial fat pad [3].

By the fifth decade of life, the lower eyelid fat pads begin to protrude and herniate, and an increase in the amount of periorbital fat takes place, with the subsequent formation of a lower eyelid bulge [6].

An additional contributor to the aged appearance of the face is descent of the malar fat pad in the cheek area, causing a decreased projection [25]. Adipose tissue of the midface loses volume with age, and shifts downward by gravity. This further contributes to pseudoptosis of the periorbital area [26].

The protrusion of lower eyelid fat is suggested to be caused by inferior displacement of the globe due to laxity in surrounding tendons, ligaments and fascia, leading to downward compression and displacement of the orbital fat anteriorly [27].

Muscle and Ligaments

Effectively, it has been advanced that ligaments in the periorbital area become lax with age, due to repetitive muscular contraction, leading to weaker support and stretching of the ligaments, with subsequent ptosis [28, 29].

Muscles become thinner as patients grow older. However, the orbicularis oculi is minimally affected in comparison to the rest of the facial muscles [30], and it is mainly prolapse of the midface and cheek area that is witnessed, whereas the periorbital area remains more or less stable in terms of muscle mass.

The lacrimal gland plays an important role in periorbital aging, as it starts to prolapse with age leading to lateral hooding caused by weaker support from its suspending ligaments [9].

The tear trough, an osteocutaneous ligament, becomes more demarcated as one grows older. It widens laterally and medially with age, and reveals the inferior orbital rim underneath [6]. This is also due to soft tissue ptosis and gravitational pull of the cheek tissues downward, leading to a demarcation of the nasojugal groove [3, 31].

The combination of soft tissue descent at the level of the cheek, and the prolapsing fat pad at the inferior lid, lead to further accentuation of the nasojugal groove [32, 33].

Bone

With older age and with the advent of menopause in women, periorbital bone thins out and starts to resorb, leading to a loss of projection of the periorbital area and an increase in the orbital aperture and orbital dimensions [24, 34]. The maxilla retrudes and undergoes rotation posteriorly [9]. This is contrasted by the herniation of infraorbital fat pads.

Extrinsic Facial Aging

Photoaging and Ultraviolet (UV) Light Exposure

Despite the midface area being the most commonly involved in photoaging due to its prominence, the periorbital area is not spared from this process. With increasing

exposure to UV light, the skin develops more wrinkles and becomes coarse, but also gets dry, lax and atrophic. Furthermore, skin lesions such as telangiectasias, actinic keratosis, and pigmented macules, among others, start to develop. This process is termed photoaging [6]

Excessive pigmentation of the skin can be congenital, but more commonly occurs due to photoaging, drug use [35], or dermatitis and irritation [36]. Trauma can also lead to skin pigmentation through blood extravasation and hemosiderin deposition in the area involved [4]. These factors all play a role in the development of under eye circles.

Eyelid skin is the thinnest in the body, reaching a thickness as low at 0.2 mm, and making it very susceptible to ultraviolet radiation, thereby triggering skin mottling and pigmented changes [4].

Both UV-A and UV-B light play an important role in the aging of the skin. UV-A causes long wavelength injury and reaches the dermis, or middle layers of the skin [17], thereby leading to tissue laxity and decreased elasticity [37]. On the other hand, UV-B causes short wavelength injury to the exposed skin [17] and affects the epidermis, or outer layer of the skin, leading to the formation of premalignant lesions in that area [38]. Skin exposed to the sun suffers from more inflammation and neovascularization compared to sun-protected skin [39], and there is an impaired organization of elastin and collagen in photoaged skin [17]. Sunscreen plays a very important role in preventing photoaging, with a small added advantage for physical sunscreen over chemical since the former leads to less contact sensitivity and skin irritation in patient who have delicate skin [4]. It should be noted that compared to darker-skinned individuals, fair skinned patients have a greater tendency to get affected by photoaging, and their skin sustains more damage upon sun exposure [17].

Smoking and Tobacco Use

Many studies have shown that smoking can lead to premature aging, whereby the formation of wrinkles begins early on, accompanied by skin color change to a grayish hue [40–42]. It is interesting to note that premature aging of the skin was found to be proportional to the patient's pack years [43].

Cigarette smoke contains multiple toxic chemicals and substances which are absorbed by skin cells and lead to the formation of free radicals [44]. These free radicals can be very toxic to the cells in our body, especially when they accumulate in large amounts.

When evaluating the effect of cigarette smoke on tissue oxygenation in the periorbital and perioral area, it was found that there is a significant decrease in the amount of oxyhemoglobin in the periorbital area of smokers, thereby leading to malfunction of the cellular mitochondria and subsequent cellular malfunction [44]. One of the most worrisome substances found in cigarette smoke is carbon monoxide, which reduces oxygen supply to the tissues to a significant extent, leading to a

reduction in blood flow metabolism of the involved area. These changes can eventually lead to early cell degeneration, manifesting as wrinkled and pale skin [44].

The changes caused by cigarette smoke were thereby found to have negative repercussions on the skin of patients, leading to effects similar to those encountered upon excessive sun exposure [45].

Interestingly, it was also found that the combination of sun exposure and tobacco use was found to age the skin to a greater extent than independent exposure to each of those factors [46]. A synergistic effect on skin aging was found when these two factors were present [43].

Seasonal Allergies, Irritants and Contact Dermatitis

In patients with atopy and allergies, as well as skin conditions such as contact dermatitis or lichen planus, the periorbital area can get inflamed, and subsequently suffer from postinflammatory hyperpigmentation [47, 48]. In addition, in patients with allergies, continuous eye rubbing and skin scratching leads to inflammation of the periorbital area and eyelid edema, further contributing to the aged appearance of the periocular area [16].

Other Extrinsic Factors

Drugs such a prostaglandin analogues used in patients with glaucoma have been found to cause periocular hyperpigmentation within 3 to 6 months of continued use, with complete resolution of skin changes once the drug is stopped [49].

Excessive exposure to sunlight and ultraviolet radiation was found to worsen the hyperpigmentation in patients with under-eye dark circles [50].

In addition, lifestyle also plays a big role, with sleep deprivation, stress, excessive alcohol consumption and tobacco use leading to worsening hyperpigmentation and a subsequent aged appearance of the face [51].

Rejuvenation Options for the Periorbital Area

Different types of anti-aging treatments and aging prevention options exist for the periorbital area, ranging from herbal preparations, to energy-based devices, injectable and surgical procedures. These play a main role in decreasing the emotional dissatisfaction associated with the aging process, in addition to giving patients a more youthful appearance.

Over the years, thousands of topical products have become available in the market. These are thought to tackle different aspects of periorbital rejuvenation, be it for prevention or for treatment purposes. For the most part, these non-invasive treatments target skin pigmentation, texture, volume, hydration and sun protection.

While these treatment options provide a great deal of day-to-day skincare, they are often combined with more invasive procedures to grant patients with optimal outcomes. More details can be found in Chap. 9.

Next in line after topical therapies are chemical peels, the use of energy based devices such as laser and ultrasound and radiofrequency devices, and the use of injectables including mainly hyaluronic acid gel fillers and botulinum toxins. These options are slightly more invasive than topical treatments, but have been found to give excellent results when used adequately. They can also be used in combination with each other, or in combination with topical therapies for more optimal results.

Skin resurfacing includes the use of chemical peels, mechanical resurfacing, also known as dermabrasion, and laser resurfacing.

It mainly consists of causing chemical, mechanical or thermal and ablative injuries to the different skin layers, in an attempt to stimulate affected areas, and lead to better texture and consistency as the skin attempts to heal itself.

Chemical Peels

There are different types of chemical substances used in chemical peels and skin resurfacing, including salicylic acid, glycolic acid, trichloroacetic acid, Jessner solutions (which is a combination of resorcinol, salicylic acid and lactic acid mixed in ethanol), phenol, Baker Gordon formula (which consists of phenol, tap water, septisol and croton oil) [4, 52, 53].

Combining those different chemicals and using different amounts of each to create varied solutions can lead to the formation of peels that act at different skin depths. Thereby, chemical peels can be subdivided into superficial, medium and deep peels based on the concentration of different constituents and the method of application [53, 54].

In addition, based on the extent of reach of the peel, different effects can be witnessed on the skin, ranging from exfoliation and lightening to epidermal thickening and de novo collagen formation [55, 56]. All of these effects occur subsequently to caustic liquefaction of tissues by the chemicals being applied [55]. The ultimate aim of peels, regardless of their depth of action, is skin rejuvenation and a youthful appearance through the treatment of skin affected by photoaging, as well as the target treatment of wrinkles, scars and pigmentation [54].

Superficial peels act mainly on the epidermis and have the advantage of causing minimal irritation and reactive hyperpigmentation compared to deeper acting peels [54]. The main side effects of these peels are erythema, dermatitis, skin irritation and burning, all of which usually resolve with time. The main pathologies targeted by superficial peels include superficial scarring, photoaged skin, and pigmentary skin changes [57].

When using superficial chemical peels, repeated application and treatment is needed before one starts seeing results, and treatment is thereby more time consuming, when compared to medium and deep chemical peels [56].

Chemical peels that reach medium depth usually reach the upper part of the reticular dermis. These types of peels act on photoaged skin and early wrinkles [53]. They can lead to the production of collagen de novo and are thereby very effective in the treatment of periorbital aging due to sun exposure [57]. Side effects include crusted skin, inflammation and edema, in addition to irritation and burning sensation [58].

Deep chemical peels reach the middle part of the reticular dermis and are used for photoaged skin, late and deep wrinkles, as well as premalignant lesions such as actinic keratosis [54]. Side effects encountered with deep peels include formation of scars, changes in skin pigmentation, changes in the texture of the skin and lower eyelid ectropion, as well as the development of potential heart, lung and kidney side effects when phenol is used in the peel [59].

When treating the periorbital area with chemical peels, protection of the eyes is of utmost importance and petroleum jelly can be used to that purpose [54]. One must also take care not to spill or splash the product involuntarily over the patient's face as this can lead to unwanted exposure to the product and will leave marks on the areas involved.

Mechanical Resurfacing

Mechanical resurfacing consists of forming microscopic abrasions to the most superficial skin layers. This can include the use of a motor driven device releasing crystals of aluminum oxide, termed microdermabrasion, the use of sandpaper that is repeatedly passed onto the periorbital area with varying force using one's hand, termed manual dermabrasion, or motorized dermabrasion [60]. Motorized dermabrasion is the least suitable form to be used in the periorbital region due to the likelihood of injury since the skin in that area is very thin and control of eyelid motility can be difficult. On the other hand, manual dermabrasion is the most suitable method for the periorbital area since it allows very specific control of the depth of tissue involved and the force being applied to the area [60].

Lasers

Lasers are one of the most popular and widely used methods for treatment and rejuvenation of the periorbital area. They can be categorized into ablative and non-ablative lasers, with the former type causing destruction of superficial skin layers and thereby leading to better cosmetic results and patient satisfaction, since they allow tissue remodeling and regrowth to occur [61]. However, this comes at the expense of more side effects, since ablative lasers are considered to be more invasive and slightly more harmful to tissues compared to their non-ablative counterparts.

Since different lasers have different wavelength, they can act on different chromophores and at different tissue depth, in addition to their ability to be used in the treatment of different skin lesions.

Nonablative Lasers

These include the most commonly used pulsed KTP laser (potassium titanyl phosphate, 532 nm), pulsed dye laser (585 nm), Nd:YAG laser (neodymium-doped Yttrium aluminum garnet, 1320 nm) and diode laser (1450 nm) [62].

The main advantage these lasers confer is a lack of epidermal injury due to their low depth of penetration, thereby leading to a fast recovery and minimal side effects [52, 62]. They mainly work by heating the superficial skin layer without sloughing off the epidermal layer.

Ablative Lasers

The main ablative lasers used in rejuvenation of the periorbital area include the carbon dioxide laser; considered the gold standard for periorbital rejuvenation; as well as the Erbium:Yttrium-Aluminum-Garnet (Er:YAG) laser [54].

Usually, treatment with laser should involve the whole face in order to avoid forming lines of demarcation. However, the lower eyelid region is an exception to this rule, and can often be treated on its own with very low risk of demarcation areas[52].

CO2 Laser

The CO2 laser has a wavelength of 10,600 nanometers, and its target chromophore is water [13]. Its use on the tissue surface will lead to skin tightening due to evaporation of tissue, stiffening of the collagen and eventually de novo collagen formation and deposition [54]. It is considered the gold standard for treatment of the periorbital area [54] since it was found to lead to very satisfactory results, all the while being safe and causing minimal side effects.

The CO2 laser's main side effects include skin reactions such as irritation, erythema, edema, scarring, and also changes in pigmentation and ectropion of the lower lid [54] commonly seen in patient with a history of blepharoplasty [63].

Er:YAG Laser

The Er:YAG laser has a wavelength of 2910 nm and its target chromophore is water, similar to the CO2 laser [54]. However, due to its longer wavelength, the Er:YAG laser penetrates tissues more superficially compared to the CO2 laser, and also leads to less heat formation and less tissue vaporization [54]. This is mainly why its use has been advocated for superficial wrinkles while CO2 laser is more commonly used for deep wrinkles [64, 65]. However, when it comes to the periorbital area, both lasers have been found to be equally effective in the treatment of both superficial and deep rhytids [66].

Advantages of the Er:YAG laser over the CO2 laser include decreased incidence of skin reactions [54] due to the decreased intensity of vaporization and interadermal heat formation. While Er:YAG usually leads to a faster recovery, this comes at the expense of less collagen tightening and the possibility of needing more sessions when using this laser compared to the CO2 laser.

Fractional Laser

This method uses either ablative or nonablative lasers, but instead of delivering thermal injury to the whole area affected by aging, columns of tissue are targeted, leaving unaffected skin in between [54]. When using the nonablative lasers, the epidermis is left intact [67] whereas with the use of the ablative laser, the epidermis is sloughed and stimulated to heal.

The advantage of using fractional versus continuous laser for skin resurfacing includes a more rapid recovery since parts of the skin are left intact and can trigger faster reepitheliaziation of the surrounding treated area [54]. In addition, when targeting only a column of skin, the laser is allowed to penetrate slightly deeper, thereby causing better targeted thermal injury which leads to more skin tightening and de novo collagen creation [67].

Side effects caused by the fractional laser are similar to those seen with the continuous laser, but usually are less extensive and last for shorter periods of time. One of the downsides of using fractional laser therapy is the need for multiple session spaced four weeks apart in order to achieve the desired result [54].

Radiofrequency Devices

These devices mainly rely on the creation of heat at the level of the dermis, through the delivery of energy to the skin surface. They mainly lead to de novo collagen formation, as well as tightening of the collagen already present in skin, allowing for the decrease or disappearance of wrinkles and overall younger appearance of the skin [68]. Radiofrequency devices are very similar to nonablative lasers, but they produce faster results. Their side effect profile is similar for that of nonablative lasers [62].

Injectables

Fillers

With increase in age, volume loss in certain facial areas takes place, and the periorbital area is specifically affected by this process, with the deepening of the tear trough and the laxity of periocular ligaments, as was discussed at the beginning of this chapter. To counteract for this volume loss, injection of substances to fill the spaces and hollows created in the face as a result of aging is commonly performed. This can lead to a more youthful appearance and give the face a healthier overall contour.

The most commonly used substance to reach adequate cosmetic results and counteract the aging process is hyaluronic acid. It is especially useful in the periorbital area and can lead to excellent results in the hands of an experienced physician.

Hyaluronic acid is a glycosaminoglycan disaccharide that is found in human skin, synovial fluid and vitreous fluid [54] It is a molecule that binds water very avidly and remains bound to it until it is degraded. This allows the molecule to keep giving the face volume until it completely disappears [54]. Common areas injected include the brow, the upper eyelid and the tear trough.

It is very important to inject only small quantities of the product and to avoid overcorrecting the defect as this can lead to patient dissatisfaction. In addition, if the midface area is going to be injected, it should be targeted prior to the treatment of the periorbital area since the former can reduce the depth of the tear trough and thereby will lead to less product quantity used in the latter [54].

Common side effects include ecchymosis, erythema and mild edema, which can be encountered with any face injection. More serious side effects can occur from the inadvertent injection of material into blood vessels, leading to necrosis of the injection site, and also embolization of material and occlusion of arteries. In the periorbital area, this is of particular concern since the ophthalmic artery can get affected, leading to permanent loss of vision [52]. Fortunately, these side effects are rare and become even rarer in experienced hands.

Neuromodulators

Botulinum toxin is one of the most widely used injectables worldwide, and was shown to have very adequate results in the area of the face, and more specifically the periorbital area [54]. Patient education is crucial prior to such procedure due to its non-reversible effects. Botulinum toxin injections last 6 months on average, at which time retreatment must take place.

In the periorbital area, botulinum toxin can be used to decrease rhytids, as well as to reshape the brow, increase the palpebral aperture, and eliminate lines at the level of the lateral canthus [54].

Contraindications to the use of botulinum toxin include neurological diseases related to disturbances in acetylcholine release or re-use such as Lambert-Eaton syndrome, Myasthenia gravis and amyotrophic lateral sclerosis (ALS) [54].

Side effects include pain, erythema or ecchymosis at the injection site, headaches [52] and the possibility of eyebrow or eyelid ptosis, as well as facial asymmetry in the periorbital region [69].

Surgical Approaches

The periorbital region is easily manipulated using different surgical options. Blepharoplasty is the most common cosmetic procedure performed. Upper and lower eyelid blepharoplasties differ significantly in their procedure and their indications. Upper eyelid blepharoplasty primarily entails recreating upper eyelid volume consistent with younger age while lower eyelid blepharoplasty aims at creating a smoother junction between the lower lid and cheek.

The brow lift is another surgical intervention that aims to correct eye brow position and flatten out forehead rhytids or crows-feet.

Another widely used technique is autologous fat transfer, that consists of using the patient's own fat, processing it, and injecting it into either the upper, or more commonly the lower eyelids for volume replacement.

An in-depth discussion of the various surgical techniques will be further covered in Chap. 8.

Conclusion

Aging of the face is a process that involves both intrinsic and extrinsic factors, with each playing a different role on a different area. The periorbital region is of utmost importance in the process of aging as it leads to patient dissatisfaction at an early age, before the rest of the face starts showing signs of aging.

This area is very commonly looked at, and can almost immediately reflect changes that occur with lack of sleep, stress, ultraviolet exposure and smoking.

Main intrinsic factors include changes in bone width, fat descent and loss of fat volume, changes in skin pigmentation, and development of laxity in ligaments and tendons of the periocular area. These unfortunately cannot be controlled by the patient. However, the changes due to extrinsic factors, which include photoaging and skin changes caused by tobacco use, as well as periocular changes caused by allergic reactions and various types of skin conditions can be controlled through avoidance of exposure to aging factors and treatment of comorbid conditions. Since the periorbital area is so involved with the aging process, it has been an area of focus in the research and development of rejuvenation options. Many methods exist to reverse changes that occur with aging, if not completely, at least to some extent. These include topical therapies, the use of chemical peels, laser and radiofrequency devices, injectables, and finally surgical options. All of these methods have been shown to have good result, and they can sometimes be used in combinations.

It is up to the physician to offer the patient all the available options, explaining which will benefit the specific areas that need to be targeted, in order to come up with an adequate cosmetic result, with which the patient will be satisfied.

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Eye Medications and Its Effect on Orbital Fat and Cosmesis

3

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In this chapter, different eye medications that could affect eye cosmesis or orbital fat will be discussed. These medications includes; preservatives that are present in eye drops including artificial tears and glaucoma drop, active ingredients in glaucoma medications itself and peribulbar injections of steroids and there effects on the eye.

Adverse Reactions to Preservatives Present in Different Eye Drops

Dry eye is a multifactorial disease of the ocular surface, resulting in discomfort, visual disturbance, and tear film instability, with potential damage to the ocular surface. Dry eye disease (DED) occurs along with an increased osmolality of the tear film and subacute inflammation of the ocular surface [1]. Stress to the ocular surface, including environmental and genetic factors, infection, endogenous stress, and antigens are the main triggers. Proinflammatory cytokines, chemokines, and matrix metalloproteinases lead to the expansion of autoreactive T-helper cells, which infiltrate the ocular surface and lacrimal gland, resulting in a vicious circle of damage to the ocular surface and inflammation [2]. A wide range of management options exists for DED, including artificial tears (ATs), anti-inflammatory agents, immunomodulators, occlusive devices, and environmental modifiers [3]. To date, the most common treatment of DED consists in the regular use of ATs. A large number of products are available, combining in various proportions a limited number of ingredients such as glycerin, polyvinyl alcohol, propylene glycol, hydroxypropyl guar, carbomers, cellulose derivatives, and sodium hyaluronate. The ATs can

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be presented in low, medium, or high viscosity (gels) preparations. Most of the ATs contain preservatives in order to maintain the sterility of eye drops in multidose containers. The preservatives act in a totally unspecific manner as a detergent or by oxidative mechanisms and thereby cause damage not only to contaminating bacteria and other microorganisms but also to the cells of the ocular surface. It has also been demonstrated that they also affect the contact lenses' physical properties, the trabecular meshwork, and the retina. Benzalkonium chloride (BAK) is the most commonly used preservative in ophthalmology, even though it is considered as the most toxic. New preservatives, as Purite or Polyquad have unfortunately, several toxic and inflammatory effects not less than BAK on the ocular surface [4].

Eye drops including glaucoma local treatment contain main therapeutic agents, along with various additives. Additive compounds may facilitate preparation, stabilize the solution or suspension, and/or increase product safety. Common additives include solubilizing agents, thickening agents, isotonizing agents, preservative agents, buffering agents, and stabilizing agents. Adverse reactions to eye treatments is caused by either the main active agent or the additive agents, particularly preservatives. A preservative is an additive agent that extends the shelf-life of a drug. Preservatives may have bacteriostatic or sterilizing properties and often accentuate product transparency. Most preservatives also act as surfactants which destabilize bacterial cell membranes. This causes destruction of the cell membrane, inhibition of cell growth, and reduction of cell adhesiveness. However, preservatives also exert these effects on normal corneal and conjunctival cells, resulting in ocular surface disorders (OSD) which is characterized by an inadequate quantity of tears, an unstable tear film secondary to poor quality of tears, ocular surface breakdown, and/or symptoms such as irritation, burning, foreign body sensation, dryness, photophobia, fatigue, and fluctuating visual acuity. OSD include superficial punctate keratitis, corneal erosion, conjunctival allergy, conjunctival injection, and anterior chamber inflammation [5, 6]. OSD symptoms can be debilitating and often severe, affecting a patient's quality of life and ability to work [7]. Patients using anti-glaucoma eye drops usually have lower Schirmer's test scores and reduced tear break-up times that may be the cause of ocular surface disorders. Many glaucoma medications use benzalkonium chloride as a preservative. Other agents include parabens, chlorobutanol, sodium chlorite, and a boric acid plus D-sorbitol plus zinc chloride fixed combination, preservative. Among these, benzalkonium chloride is most frequently associated with adverse reactions. Additionally, benzalkonium chloride has been reported to be involved in the appearance of macular edema after cataract surgery [8]. There are many compounds which cause preservative-induced superficial punctate keratitis but benzalkonium chloride is often the cause [9]. Thereafter, when this condition develops, switching the patient to eye drops with preservatives other than benzalkonium chloride, or eye drops without preservatives (unit dose instillation containers or membrane filter-incorporated eye drop bottles) is often beneficial. As an example in cases where latanoprost formulations with benzalkonium chloride were changed to latanoprost formulations without preservatives, IOP remained stable and 42.9% of patients had improvements in corneal epithelium disorders [10]. Reducing

benzalkonium chloride exposure was often sufficient to result in ocular surface improvements and this in case where patient switched to a combination. A deleterious effect of BAK has been demonstrated both in vitro as well as in vivo [11]. A concentration of 0.007% of BAK induces a lysis of 50% of cultured epithelial cells in less than 2 min [12]. Numerous reports have demonstrated that prolonged use of topical ocular medications preserved with BAK may exacerbate symptoms and signs associated with OSD and have adverse effects on the conjunctiva and cornea. These effects include the induction of subclinical inflammation, reduction of corneal epithelial barrier function, destabilization of the tear film, and an overall higher incidence of patient complaints of dryness and irritation in users of BAK-containing eyedrops [7]. BAK exerts its damaging action mainly through a direct cytotoxic mechanism, accentuated by the cumulative effect of repeated administrations of preserved eyedrops [13]. Alternative preservative could be used, as an example polyquaternium, is known to have less corneal toxicity, as well as less rupture of cellular junctions, when compared to BAK [14].

Adverse Reactions to Main Agents in Glaucoma Eye Drops

Glaucoma is a chronic, progressive disease in which retinal ganglion cells degenerate, and subsequent, gradual reductions in the visual field ensues. The ultimate objective of glaucoma treatments is, to stop visual field defect deterioration. Intraocular pressure (IOP) reduction is the only proven treatment to prevent visual field defect progression [15, 16]. Eye drops, oral medications, laser therapy, and surgery have all been used to decrease IOP in glaucoma patients. Among these therapies, topical treatments are the first choice because they have the highest efficacy and the lowest incidence of adverse reactions. Eye drops used in managing glaucoma decrease eye pressure by helping the eye's fluid to drain better and/or decreasing the amount of fluid made by the eye. There are currently several types of IOP-lowering eye drops used to treat glaucoma. These include parasympathomimetic drugs, sympathomimetic drugs, β-blockers, carbonic anhydrase inhibitors, prostaglandin analogs, α-adrenergic agonists and rho kinase inhibitors. In addition, combination drugs are available for patients who require more than one type of medication. Adverse reactions are divided into those affecting only the eye and those causing systemic reactions. Adverse reactions associated with each type of eye drop are detailed to follow.

Prostaglandin Analogs

Prostaglandins lower IOP by accelerating uveoscleral outflow. Prostaglandin analogs that are currently available include latanoprost, travoprost, bimatoprost, and tafluprost. They are often the first drug therapy used because they have been widely successful in decreasing IOP, rarely cause systemic side effects, and only need to be administered once a day. Isopropyl unoprostone is a prostaglandin analog that

reduces IOP via a different mechanism and when compared to other prostaglandin analogs has a lower IOP-lowering effect with a lower incidence of adverse reactions.

Ocular Adverse Reactions

Conjunctival allergy, conjunctival hyperemia, corneal epithelial disorders, and blepharitis are characteristic adverse reactions associated with prostaglandin analogs. Patients receiving these drugs might have eyelash bristling/lengthening, vellus hair, eyelid pigmentation [17], iris pigmentation [18], and deepening of the upper eyelid sulcus (DUES) [19].

In the beginning of treatment with prostaglandin analogs, patients sometimes have intense conjunctival hyperemia, but this gradually diminishes over time. As shown in a meta-analyses of several systematic reviews; conjunctival hyperemia occurred significantly less often with latanoprost than with travoprost (odds ratio = 0.512) or with bimatoprost (odds ratio = 0.32) [20]. In another meta-analyses, conjunctival hyperemia was more likely to occur with bimatoprost than with latanoprost (relative risk = 1.70), or travoprost (relative risk = 1.19) [21]. Furthermore, latanoprost use was 1.45 times more likely to induce conjunctival hyperemia than travoprost. On the other hand, other systematic reviews have shown that conjunctival hyperemia was more likely to occur with travoprost (relative risk = 5.71) or bimatoprost (relative risk = 1.59 times) use than with latanoprost use. This was less likely to occur with travoprost (relative risk = 0.82 times) than with bimatoprost [22]. Conjunctival hyperemia was evaluated and graded in eyes in which latanoprost was currently being used. Medication regimens were left unchanged or patients were switched from latanoprost to bimatoprost or travoprost [23]. Twelve weeks later, there were no differences in conjunctival hyperemia change score for any of the three eye drop types examined. The reported incidence of conjunctival hyperemia differs between various prostaglandin analogs, occurring more often with bimatoprost use than with other prostaglandin analogs.

The incidence of eyelash lengthening/bristling may also differ between various prostaglandin analogs. In a study where only one eye was administered a prostaglandin analog, eyelash lengthening/number increase occurred 54%, 46%, 26%, and 46% more often in the eye treated with bimatoprost, travoprost, latanoprost, and tafluprost, respectively. Differences between individual drugs were not significant [20]. In another study, eyelash changes in the lower lids were measured after administration of latanoprost only in one eye. Eyelash length was 6.95 ± 0.91 mm in the treated eye and 5.83 ± 0.76 mm in the untreated eye, a difference that was statistically significant [24]. Gel suspensions with and without bimatoprost were also applied to each upper eyelid [25]. After 6 weeks of daily application, the length of the longest eyelash was compared to that measured at baseline. The eyelashes in the bimatoprost group grew 2.0 ± 1.5 mm, significantly more than those in the bimatoprost-free (control) group, which only grew 1.1 ± 1.1 mm. 1.1 ± 1.1 mm. In another study, four types of prostaglandin analogs were administered to rabbits for 1 month [26]. In the bimatoprost and tafluprost groups, eyelashes grew significantly longer, but in the travoprost and latanoprost groups, eyelash length did not

significantly change. Casson and Selva [27] described a patient whose trichomegaly secondary to the chronic use of latanoprost resulted in eyelash ptosis that obstructed his visual field and required a bilateral eyelid anterior lamellar transposition procedure. Eyelash length and increase in length was especially remarkable in the bimatoprost group. Therefore, bimatoprost had been used for cosmetic reasons as an eyelash enhancer [28].

All prostaglandins seem to have similar effects on eyelid pigmentation. It is known that eyelid pigmentation changes caused by latanoprost resulted from markedly increased melanin levels. An increase in tyrosinase activity was thought to cause these changes because tyrosinase was involved in this melanin increase, which occurred at the RNA level [20]. Iris pigmentation often occurs in Europeans and Americans, in whom iris pigments are green-brown, yellow brown, blue-brown, and/or of mixed color [29].

The occurrence of DUES with prostaglandin analog use was first reported with bimatoprost use in 2004 by Peplinski and Albiani Smith. They reported upper eyelid sulcus deepening and dermatochalasis involution in three patients who were unilaterally treated with bimatoprost, this was attributed to a possible effect of bimatoprost on Muller muscle [30]. In another study five patients in whom chronic daily unilateral treatment with bimatoprost 0.03% caused upper eyelid sulcus deepening, clinically apparent relative enophthalmos, and involution of dermatochalasis. They hypothesized that preaponeurotic and deep orbital fat atrophy are responsible for the majority of these periocular changes. The author documented that these adnexal changes were not evident prior to starting treatment with bimatoprost. Among patients for whom the medication could be stopped, partial or complete reversal of the clinical picture was observed in 3–6 months [31]. Romano and colleagues showed that bimatoprost induced smooth muscle contraction [32]. Some patients with Prostaglandin-Associated Periorbitopathy (PAP) have inferior scleral show, which could be related to contraction of the inferior eyelid's smooth muscle retractors. In terms of atrophy, the number of a person's fat cells increases from birth until young adulthood and then remains relatively constant thereafter [33]. Thus, it is the volume of lipid fat per cell that dictates one's physical appearance from middle age onward.

Fat metabolism is under intense regulation by hormones, mainly insulin, catecholamines, and natriuretic peptides, and paracrine factors such as cytokines, adenosine, and prostaglandins [34].The FP prostanoid receptor is thought to mediate, at least in part, the pharmacologic effect of bimatoprost as evident by the lack of IOP response in FP-prostanoid receptor knockout mice [35]. FP-receptor activation has been associated with inhibition of preadipocyte differentiation in several cell lines [36] that are prevented from expressing adipocyte-specific genes and accumulating fat droplets. Furthermore, FP-receptor agonists have been shown to down-regulate fatty acid binding protein expression, which is important for the uptake of free fatty acids and triglyceride synthesis in adipocytes [37]. In addition, pharmacokinetic studies of a single topical administration of 0.1% bimatoprost in male cynomolgus monkeys indicate that eyelid specimens contain more than 2000 times higher

concentrations of bimatoprost compared with aqueous and more than 16 times higher concentrations compared with iris and ciliary body [38], which indicates significant periorbital absorption of the medication. The DUES incidence differs among the various prostaglandin analogs. Prostaglandin F2alpha can inhibit fat production [39]. Therefore, it was thought that prostaglandin analogs reduced orbital adipose tissue mass, resulting in DUES. In a study, in which one eye was administered a prostaglandin analog and one eye was left untreated, photographs of the face were taken and DUES was evaluated using a score. The condition occurred in 60%, 50%, 24%, and 18% of patients using bimatoprost, travoprost, latanoprost, and tafluprost, respectively [22]. The condition was noted significantly more often in patients using bimatoprost and travoprost than in patients using latanoprost and tafluprost. The score risk ratio increased 3.67 times with bimatoprost, 3.34 times with travoprost and 1.42 times with latanoprost [40].

In anamnestic cases involving corneal epithelium herpes, herpes was reported to recur and deteriorate with latanoprost administration [41].Therefore, caution should be used when prescribing prostaglandin analogs in these patients. Macular edema has also been reported after latanoprost administration following cataract surgery [42]. In these cases, the blood–aqueous barrier broke down during cataract surgery. There is currently no need to routinely discontinue prostaglandin analog use after cataract surgery, but discontinuation should be considered in eyes within intraoperative blood–aqueous barrier breaks.

Beta Blockers

The β-blocker eye drops sometimes contain both α1-blockers and β-blockers, which reduce IOP through different mechanisms. The β-blockers control aqueous humor and α1-blockers accelerate uveoscleral outflow. The β-blockers currently available are timolol, carteolol, betaxolol and metipranolol. The only available α1-blocker plus β-blocker combination eye drops are nipradilol and levobunolol. Systemic side effect includes: low blood pressure, reduced pulse rate, and fatigue. Beta blockers can also cause a shortness of breath in people who have a history of asthma or other respiratory disorders. Additionally, beta blockers can change cardiac activity by decreasing the amount of blood the heart pumps out, which may reduce the pulse rate and/or slow down the heart's response rate during exercise. Rare side effects include reduced libido and depression. Systemic side effects of beta blockers can be minimized by closing the eyes following application or using a technique called punctal occlusion that prevents the drug from entering the tear drainage duct and systemic circulation.

Ocular Adverse Reactions

Ocular adverse reactions to β-blockers include conjunctival allergies, conjunctival injection, corneal epithelium disorders, blepharitis, and ocular pemphigoid. Additionally, corneal sensitivity may be reduced because of the local anesthetic

effect (membrane-stabilizing effect) of betaxolol. The subsequent reduction in reflective tearing may lead to corneal epithelium disorders. Carteolol has intrinsic sympathomimetic activity so administration of this drug does not lead to a reduced corneal sensitivity. Therefore, carteolol administration was associated with fewer cases of corneal epithelium disorders than timolol [43]. Timolol is available in a preservative-free formulation.

Alpha Agonists

Alpha agonists reduces the IOP by controlling aqueous formation and increasing uveoscleral outflow [44]. Sympathetic α2-receptor agonists currently available included brimonidine and apraclonidine. Systemic adverse reactions associated with long-term sympathetic α2-receptor agonist use included decreases in blood pressure and pulse, drowsiness, dizziness, and dry mouth [45].

Ocular Adverse Reactions

Ocular adverse reactions associated with long-term sympathetic α2-receptor agonist use included conjunctival hyperemia, pupil dilation, and allergic conjunctivitis [46]. Alphagan P has a purite preservative that breaks down into natural tear components and may be better tolerated in people who have allergic reactions to preservatives in other eye drops.

Carbonic Anhydrase Inhibitors (CAIs)

Carbonic anhydrase inhibitors reduce IOP by inhibiting the ciliary epithelium and controlling aqueous formation. Acetazolamide, an internal carbonic anhydrase inhibitor, has been used to date, but is associated with a high incidence of adverse reactions, including dysesthesia of the fingers and around the lips, frequent urination, lassitude, anorexia, weight reduction, urolithiasis (kidney stones), metabolic acidosis, and hematopoietic cell restraint anemia [47].

Dorzolamide and brinzolamide eye drops are used topically with few systemic side effect.

Ocular Adverse Reactions

Ocular adverse reactions associated with carbonic anhydrase inhibitors include conjunctival allergy, conjunctival hyperemia, corneal epithelial disorders, blepharitis, Stevens–Johnson syndrome, and toxic epidermal necrosis [48]. Dorzolamide is viscous and has a fairly acidic pH (pH = 5.5–5.9), which generally causes ocular irritation. Foreign body sensation and blurred vision often occur in patients receiving brinzolamide because intraocular transitivity is slightly poor [49]. Moreover, carbonic anhydrase naturally exists in the corneal endothelium, and caution is needed in patients with corneal endothelial disorders [50].

Parasympathomimetic Drugs, Cholinergic (Miotic)

When parasympathetic nerves are stimulated, the ciliary muscles constrict. The scleral spurs are subsequently pulled backwards to open up the trabecular meshwork, the resistance to aqueous outflow is reduced, and IOP was decreased. In eyes with closed-angle glaucoma, parasympathomimetic drugs caused constriction of the sphincter pupillae, iris flattening and iris clearance from the trabecular meshwork. This opens the angle and decreases IOP. One currently available parasympathomimetic drug is pilocarpine. Four administration a day is required and patients using this medication often have adverse reactions. Therefore, it is used sparingly and generally when no other alternative exists. Systemically Increases in parasympathetic nervous system activity of the internal organs may result in higher secretory gland activity and cause stress on smooth muscles. As a result, drooling, sweating, diarrhea, nausea/vomiting, stomachache, asthma, bradycardia, hallucinations and depression may occur with parasympathomimetic medication use. It is also present in the form of Pilocarpine HCl 1%, 2%, 4%, Carbachol 0.75%, 1.5%, 3%, Pilocarpine HCl gel 4%.

Ocular Adverse Reactions

Ocular adverse reactions associated with parasympathomimetic drugs included miosis-caused aphose, visual field constriction, and night vision loss [51]. Near sightedness could also occur because of stress on ciliary muscles and patients may be conscious of haze. Ocular pemphigoid, cataract, and retinal detachment may also occur.

Rho Kinase Inhibitors

Netarsudil is a new class of glaucoma drug that increase the drainage of intraocular fluid. It is prescribed once-daily (p.m.), it is in the form of an ophthalmic solution 0.02% (Rhopressa) and it is approved in the United States for lowering elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. It is a Rho kinase (ROCK) inhibitor that lowers IOP primarily by increasing trabecular outflow, produces statistically and clinically significant reductions in mean IOP from baseline, with comparable effects on nocturnal and diurnal IOP. In three phase III trials of patients with elevated IOP, the ocular hypotensive efficacy of once-daily netarsudil 0.02% met the criteria for non-inferiority to twice-daily timolol 0.5% at all-time points over 3 months in patients with baseline IOP < 25 mmHg. The most frequent adverse event (AE) was generally mild conjunctival hyperemia, the severity of which did not increase with continued dosing [52]. Ina study by Serle et al. [53]. There were no Netarsudil-related systemic safety issues .The most frequent adverse events were ocular: conjunctival hyperemia, conjunctival hemorrhage, and cornea verticillata. They stated that conjunctival hyperemia was an extension of the pharmacology of ROCK inhibitors, which cause

vasodilation of blood vessels by inducing relaxation of vascular smooth muscle. Most part the hyperemia was mild, transient, and self-resolving, Conjunctival hemorrhage was similarly relatively mild and self-resolving, and typically was described by investigators as small petechial hemorrhages. Cornea verticillata was typically scored as mild with no associated decrease in visual function.

Combined Medications

Combination can offer an alternative for patients who need more than one type of medication. In addition to the convenience of using one eye drop bottle instead of two, there is decreased exposure to preservatives. There may also be a financial advantage. Some types are also available in generic form and also as a preservative-free formulation. Side effects of combined medications may include any of the side effects of the drug types they contain.

Steroid Injection

Steroid injection is indicated in treatment of chalazions [54], uveitis, iritis and management of macular oedema. It is also used in treatment of adnexal hemangioma [55].

In addition to the systemic complications of steroids, injection around the eye also poses the risk of local complications including globe perforation [56], intractable elevated intraocular pressure [57], conjunctival or corneoscleral melting [58], vascular occlusion from embolisation or pressure induced optic nerve compression [59], proptosis or fat atrophy [60].

The mechanism of lipomatosis after administration of local corticosteroid injection has not been clearly established. Glucocorticoids have been shown to directly cause hypertrophy of retroperitoneal adipose tissue in adult rats [61]. On the other hand, triamcinolone acetate injections also cause local fat atrophy [62]. In particular, periorbital steroid injections have been reported to result in subcutaneous lipoatrophy [63]. Histopathologic findings have demonstrated a reduction of subcutaneous adipose tissue [64]. The degree of atrophic change has also been correlated with the dosage of the corticosteroid injection [65]. Residual steroid along the needle tract has been hypothesized to cause lipolysis of subcutaneous tissues [66]. The different anatomically specific responses of subcutaneous and retrobulbar fat to local administration of corticosteroids may play a role in determining fat atrophy or fat production. An immune-mediated reaction and multiple steroid component interaction are other possible mechanisms for orbital lipomatosis secondary to retrobulbar steroid injection. Both anaphylactic and delayed-hypersensitivity reactions have been reported secondary to local triamcinolone acetonide use [67]. Delayed-hypersensitivity reactions typically are seen within days of corticosteroid injection [68]. In addition, histopathologic findings revealed no evidence of granulomatous

issue or fibrosis. The triamcinolone acetonide injection also consists of 0.99% benzyl alcohol, 0.75% carboxymethylcellulose sodium, and 0.04% polysorbate. One or more of these components could contribute to the fibrosis. Mechanical trauma may also have contributed to the clinical presentation. Inferotemporal needle insertion may disrupt the framework between the anterior and posterior compartment and radial septa within retrobulbar fat defined by Koorneef [69]. Consequently, the lack of supporting structure can cause laxity and herniation of retrobulbar fat along the inferior orbital rim. This mechanism could explain the observation of inferior herniation of fat but not proptosis. The ptosis and proptosis observed most likely represent the mass effect of lipomatosis on the globe and eyelid. Radiographic imaging demonstrated generalized adipose hypertrophy in the retrobulbar fat compartment. Subsequently, the biopsied mass may represent normal adipose tissue forced to herniate by pressure from increased retrobulbar fat. Orbital lipomatosis is a potential complication of retrobulbar steroid injections. Although the exact mechanism has not been clearly established, the pathophysiology may involve the local action of corticosteroids on retrobulbar fat. Omesh et al. [70] postulated that retrobulbar lipomatosis can develop over 2 months with an injection of 60 mg triamcinolone acetonide. They found in addition to ptosis and proptosis, two of five patients had erythema of the lower eyelid suggestive of mild inflammation.

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Soft Tissue Fillers for the Periorbital Region

4

Ahmed Sadek, Dalia Elshebl, and Ahmed Nagaty

Introduction

The peri-orbital region is one of the most eye-catching regions of the face and has a considerable portion in the formation of others impression of our overall facial looks regarding youthful and healthy looks. It is also one of the most affected regions by facial expressions, sun damage, weight changes and aging. Aging of the face is a sophisticated and dynamic process, with downward displacement of tissues, deflation, and external cutaneous changes with individual variation in each patient [1] and the peri-occular region is much affected by aging which involves multi-layer changes including skin (epidermis and dermis), fat compartments, muscle, and bones. Facial fillers have been and still used as an important technique that is very helpful in minimizing changes mainly caused by aging and weight loss over the years by restoring fullness to the peri-occular areas that have undergone volume loss by weight loss or loss of support by ligaments relaxation and soft tissue sagging secondary to ageing.

Understanding the anatomy of the upper and lower eyelids and the lid-cheek junction and respecting layered arrangement of the facial anatomy is crucial to perform safe and effective surgical and non-surgical procedures especially when fighting the signs of facial aging [2].

In young age, the periocular area consists of well-toned, elastic skin without sun damage, a full, well-demarcated brow without descent, a crisp and visible upper

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eyelid crease with minimal dermatochalasis, and a tight, well-positioned lower eyelid with minimal laxity or excess skin [1] and the junction between the lower eyelid and the cheek appears to be smooth without any irregularities [3].

With aging process, the upper eye lid undergoes volume loss, with deflation and hollowing of the upper eyelid, thereby exposing the superior orbital rim leading to appearance of sunken, hollowed eye, with a deep superior sulcus. Drooping of the brow and dermatochalasis may be present, obscuring the pretarsal platform and the eyelid crease [1]. The lower eyelids undergo weakening of the orbital septum and pseudo herniation of the lower lid fat pads which lead to dark circles and eyelid bags formation. The decent of the midface/suborbicularis oculi fat and malar fat pads aggravate the condition, thereby baring the inferior orbital rim. In the areas of skin attachment to deeper structures, focal loss of volume along the orbital rim may uncover deeper facial contours and resemble the decent of soft tissue [4–7]. The lid-cheek junction is more apparent in old age due to fat redistribution which increase with aging process [8–10].

The most common deformity that occurs due to these changes is a relative depression near the medial orbit in the area of the lower eyelid-midface transition. Tear trough deformity is defined as shadowing in the area of the orbitomalar ligament. An additional surface depression may be formed in the area of the confluence of the lower eyelid retractors, orbital septum, and tarsal plate, known as the septal confluence. Another focal area of depression in the midface is formed by the malar ligament, which limits the suborbicularis oculi fat [11–13].

The tear trough represents the boundary between the nasolabial fat compartment and the medial aspect of the lower eye lid, however, the tear trough is separated from the upper margin of the superficial nasolabial fat compartment by the nasojugal groove. The size of the triangular shaped space between the two superficial fat compartments (nasolabial vs. medial cheek) increases with aging process due to the volume loss of the subcutaneous medial cheek fat and the downward displacement of the nasolabial fat compartment. Fillers can be used for the treatment of volume loss and downward shift of facial fat compartments to achieve recontouring and/or restoring volume deficiencies in this area [2].

The orbicularis oculi muscle can be identified in the same level in the lower eye lid and in the cheek as the superficial musculoaponeurotic system (SMAS), although these two parts are separated by the orbicularis retaining ligament [3]. Superficial fat compartment of the face lies superficial to orbicularis oculi muscle. This compartment is divided into the medial cheek fat compartment (the malar fat pad) which is near to the lateral aspect of the lower eyelid and the superficial nasolabial fat compartment which is near to the medial aspect [2].

Deep to the orbicularis oculi muscle the sub-orbicularis oculi fat (SOOF) can be identified. The orbicularis retaining ligament and the zygomatico-cutaneous ligament represent the upper and lower boundary of SOOF respectively [3]. This deep fat compartment is connected via the temporal tunnel to the inferior temporal compartment, which is bounded superiorly by the lateral orbital thickening and inferiorly by the McGregor's patch [14]. The SOOF extends 2–4 mm medial to the

mid-pupillary line forming the deep lateral boundary of the tear trough which consists of 3 layers only: skin, muscle and periosteum. The SOOF is divided into medial and lateral compartments [3].

The anatomy of the periorbital region presents difficulties for soft tissue filling:

1. First, the skin overlying bone is very thin. As a result, irregularities of contour, such as lumps, are difficult to conceal.
2. Similarly, because the filler is close to the surface, any color irregularity or low-grade inflammation will be more apparent.
3. Finally, the periorbital area is characterized by delicate functional relationships and complex 3-dimensional contours that represent a focal point for facial aesthetics.

Therefore, many experienced practitioners who do not hesitate about injecting fillers into the thicker areas of the face, such as the perioral area or cheek, are reluctant to fill the periorbital area [15].

Indications

Volume deflation of the periorbital area which is caused by tissue and fat loss should be assessed carefully. This process leads to more hollowness due to loss of eyelid support at the inferior orbital rim. Surgical techniques aim to excise excess tissue and lift can lead to a deep superior sulcus, accentuating the superior orbital rim. A precised approach aim to deliver filler to focal hollows in selected patients to smoothen surface depressions and mask bared deep structures such as the orbital rim [7, 16–18].

Patient Selection and Planning

Orbital rim, septal confluence, and zygomatic areas are the major components of periorbital hollows [11]. Severity of each hollow should be assessed individually. In young patient with minimal hollow, 0.3 cc of filler per side may sufficient, but in an older patient with severe soft-tissue and bony volume loss, as much as 1 cc per side may be required to fill the area [15].

The quality of skin should be considered as patients with very thin or light-colored skin are more liable to color hue. However, for relatively “dry” malar mounds, significant improvement in contour is recognized when injecting orbital rim and zygomatic hollows [15].

Efforts have been exerted to analyze the tear trough properly in order to propose a treatment algorithm mainly by assessing soft tissue loss, fat herniation and skin laxity or excess as Turkmani’s, Burton’s and Hirmand’s (Tables 4.1, 4.2, and 4.3).

Table 4.1 Turkmani's morphology related classification [19]

Type	Caused by:
Hill	Superficial infraorbital fat pad herniation.
Valley	Fat reduction and skin changes.
Hill-Valley	Weakening of the orbital portion of orbicularis oculi muscle and its retaining ligaments, followed by fat reduction and skin changes.
Hill-Valley Hill-Valley	Series of changes in portions of orbicularis oculi muscle and its retaining ligaments.
Mixed	A range of any of the 4 previous deformities.

Table 4.2 Barton's grading system based on anatomic analysis [20]

Grade	Description
0	Absence of medial and lateral lines demarcating the orbital rim, and smooth, youthful contour without a transition zone at the orbit-cheek junction.
I	Mild, subtle presence of a medial line or shadow, smooth lateral transition of lid-cheek junction.
II	Moderate prominence of a visible demarcation of the lid-cheek junction, extending from medial to lateral.
III	Severe demarcation of the orbit-cheek junction, with obvious step between the orbit and the cheek.

Table 4.3 Hirmand's classification system of the tear trough [21]

Class I	Limited to tear trough or medial orbit.
Class II	Medial and lateral depression apparent.
Class III	Full depression visible circumferentially at the orbital rim.

Therapeutic options should be adjusted depending on the deformity identified in each patient:

- Type 1 deformity: non-surgical techniques, i.e. minimally invasive applications (e.g. soft tissue fillers);
- Type 2 deformity: non-surgical or surgical techniques;
- Type 3 deformity: surgical approach is necessary with great importance to preserve the function of the orbicularis oculi muscle. Preoperative meticulous clinical assessment is the key of any surgical approach to type 3 deformity [2].

We recommend filler injection for grade I & II and Valley deformities.

Contraindications

As everyone might think, not everyone is suitable for soft tissue augmentation by filler injections. Periorbital filler injections, inspite of being an aesthetic procedure that is carried by the aesthetic dermatologist or surgeon, has been proven not to be

Table 4.4 Contraindications of periorbital filler injections

Absolute contraindications	Relative contraindications
– Unrealistic expectations – Mental disturbance – Dysmorphophobia – Very thin skin or skin atrophy – Active infection (viral, bacterial, yeast, parasites) – Allergy/hypersensitivity to the product constituents or excipients – Glabellar necrosis – Allergy to lidocaine	– Active inflammatory dermatitis – Tuberculosis – Wegener's granulomatosis – Immune suppression – Transplant patients – Patients with inflammatory bowel disease – Impaired renal or hepatic function – Thyroid dysfunction – Cachectic or catabolic status

suitable for all those who are indicated for having this procedure based on medical grounds. These contraindications are either absolute ones which totally make the procedure unsuitable for the patient at least till treatment of this particular contraindicating condition and relative which gives the physician the chance to weigh benefits versus and risks and perform the procedure at his own risk based on his assessment of the case and his experience and scientific background (Table 4.4).

Filler injection is an elective procedure and may not be medically suitable to every patient seeking treatment. Patients with preexisting conditions that limit the use of dermal fillers should be avoided (Table 4.4). In aesthetic practice, this area is often neglected. In doubtful patients, physician treatment decision is taken cautiously by the physician who have full assessment of the patient [22].

Expected outcome of the treatment should be explained to the patients to avoid unrealistic expectation. Also, the limitations and risks of filler injection should be discussed in detail. Filler injection of inadequately informed patients could lead to problems and patient dissatisfaction [23].

Contraindications related to the chosen filler should be adhered to because some patients have previously showed allergy to product constituents or excipients. Treatment of patients with multiple or severe allergies and those with a history of anaphylaxis should be avoided [22].

Also, where data are available on a particular product or technique, the physician should take care not to postulate the results or assume that they are transferrable. Even if these results obtained only in one area of the anatomy [24].

Patients who have signs of an underlying mental disturbance or body dysmorphic disorder should be dealt with caution [22].

Patients with previously abnormal thin skin or skin atrophy, such as corticosteroid-induced skin atrophy due to long-term use of topical or peroral steroid, or with conditions such as anetoderma, vermiculate atrophoderma, or rheumatoid arthritis-associated skin thinning of the dorsum of the hands, are not suitable candidates for superficial or medium-depth injection of fillers. Very thin skin with many fine wrinkles on the eyelids and in cheeks is also a contraindication for certain types of fillers [25].

Infections in the area to be treated, or surrounding skin, can be exacerbated by filler injection. Also, filler may be contaminated by the infecting organism in the

nearby area. Thus, treatment of patients with an ongoing skin infection in the area to be treated or in the close vicinity of it should be avoided [26]. Viral infections such as herpes simplex virus (HSV) and perioral human papilloma virus (HPV); mollusca contagiosa; bacterial infections with streptococci or staphylococci, such as impetigo; yeast infections; and extensive pityrosporum folliculitis make the patient an unsuitable candidate for treatment. Also, the presence of severe *Propionibacterium acnes infection* or parasitic mite infestation, such as massive demodex folliculorum infestation stands against treatment with filler [22].

When active HSV is evident, treatment should be postponed, and a prophylactic antiviral therapy (acyclovir, valaciclovir, or famciclovir) prescribed to prevent reactivation and spread of HSV. Prophylactic antiviral to patients with known history of HSV episodes should be considered to prevent virus reactivation when treating the perioral area and lips [27, 28].

Treatment of patients with infections such as sinusitis, periodontal disease, ear, nose, or throat infections, or dental abscesses should be deferred until the condition has resolved [29]. Clinical evidence is emerging indicating that these infections might subsequently invade implanted filler areas, inducing biofilm reactions. Later, the possibility of transition from infection to an established hypersensitivity via toll-like receptors increase, since these molecules have been incriminated in the development of many pathological conditions, including infectious diseases, tissue damage, and autoimmune and neurodegenerative diseases [30].

Active inflammatory dermatitis such as atopic dermatitis, allergic contact dermatitis, "status cosmeticus", or seborrheic dermatitis should be judged by treating physician. According to the severity of the condition and its proximity to the treatment area, treatment decision is made by the physician [22]. Patients with allergies, rosacea, or preexisting malar edema may not be good candidates for hyaluronic acid injection because they have an underlying tendency for fluid retention [8]. Hyaluronic acid have tendency to absorb fluid which may be accentuated by these preexisting conditions and can worsen the fluid accumulation [31].

Dermal filler treatment can also aggravate more generalized skin conditions or connective tissue disease and might not be suitable in some of these conditions. Examples include lupus erythematosus, mixed connective tissue disease, conditions that cause Koebner response such as lichen planus. Uncontrolled immune deficiencies, such as graft versus host disease may also be adversely affected by dermal filler injection, or conversely might affect the behavior of the filler in the tissue [22]. Immune depression or suppression is not an absolute contraindication of any type of filler [25], however poly-L-lactic acid should not be used [26].

The use of fillers in patients with normal wound healing is not contra indicated, even though they may have an underlying systemic disease. No association has been established between use of fillers and autoimmune diseases so patients with HIV, rheumatoid arthritis, diabetes, or scleroderma may be treated by filler if they have normal wound healing [25, 26].

Conditions such as tuberculosis, Wegener's granulomatosis, transplant patients, patients with inflammatory bowel disease (Crohn's disease or ulcerative colitis), substantial food intolerance, repetitive urinary infections or impaired renal or

hepatic function, thyroid dysfunction, and cachectic or catabolic status need careful assessment of each individual patient [22].

Disorders of hemostasis or coagulation, for example, coagulopathies, protein C deficiency, hemophilia, and hemoglobin disorders such as thalassemia, need a careful assessment, and an accurate clinical picture of their severity and management must be obtained [22].

Treatment Plan

A detailed history and physical examination focused on identifying the areas of volume deficiency is performed. Signs of edema and fluid retention should be assessed. Skin changes such as sun damage, wrinkles should be noted, as it will not be affected by filler injection and will need supplemental treatment. Informed consent is obtained [1].

Patients should be instructed on the longevity of the filler to be injected, informed on the other required procedures and home treatments needed in cases of combined causes of per-orbital problems or more advanced cases. They should also know that it is a 15 min procedure with a possible touch up on the re assessment visit after 2 weeks.

Before the availability of synthetic hyaluronic acid fillers, volume replacement have been limited to autogenous fat grafting that requires harvesting, solid implant placement, and fillers such as collagen and silicone. New synthetic fillers have provided a practical solution to the problem of volume loss with an acceptable safety, tolerability, and efficacy profile [32–36].

Hyaluronic acid is a glycosaminoglycan disaccharide formed of alternating units of D-glucouronic acid and *N*-acetyl-D-glucosamine. Its uniform structure across species, decreasing the likelihood of immunogenicity, and it is normally present in human tissue, including the skin and synovial joint fluid [36–39].

For injectable fillers, hyaluronic acid is modified through cross-linking in order to strengthen its mechanical properties and increase resistance to breakdown. Various products are available with specific characteristics including particle size, degree and method of cross linkage, concentration of cross-linked/free hyaluronic acid, and resistance to deformation. The degree of modification is characterized by the formation of cross-linkage (bond between two strands) and pendant (bonding present at only one end). The concentration and degree of cross-linking are the main factors that affect longevity of the product [37, 38, 40].

There are many Food and Drug Administration-approved hyaluronic acid fillers available on market with similar approved indications. Periocular filler injection is generally considered “off label” [39].

The authors recommend the use of hyaluronic acid fillers for correcting tear trough deformities, but items of concentration, elasticity, viscosity, cohesivity, and cross-linking shall be considered first. The authors recommend using filler of low to average concentration of hyaluronic acid, average elasticity, viscosity, cohesiveness and cross linking (Fig. 4.1).

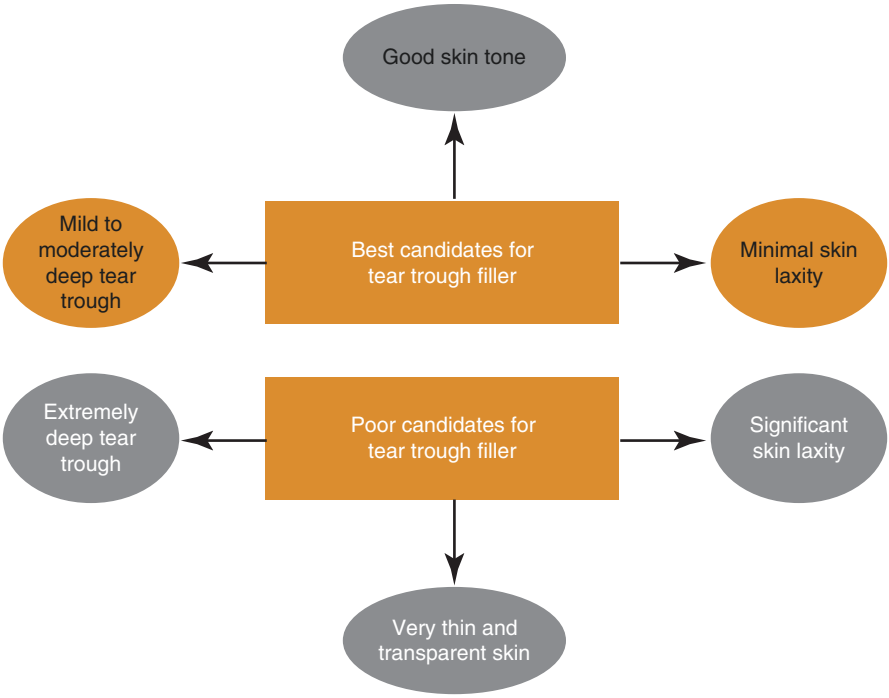


Fig. 4.1 Good and poor candidate for tear trough injection

Patient's Awareness

Patients should be informed about the assessment of his condition, possible treatment modalities, risks, side effects, prognosis and cost of all alternatives and when decided on performing filler injections, he shall be informed specifically about the specific risks which in spite of being rare include bruising, contour irregularities, color change, fluid accumulation and rarely loss of vision. Patients on anticoagulant drugs may have increased bruising [15].

Side Effects

Hyaluronic acid fillers have low rates of side effects without significant down time.

- Common side effects include bruising, redness, pain during the injection, contour irregularities, and filler visibility/bluish hue (Tyndall effect) [13, 18, 32, 33]. Also, under- or over filling are common side effects of filler injection. Tissue edema or acute hemorrhage may initially mask inadequate filling. Furthermore, hyaluronic acid will absorb water leading to more apparent edema due to the very thin skin of the eyelids. As such, the final result of injection takes several days to stabilize. If additional volume is required, a retouch injection can be done to adjust contour. Mild overfilling can be managed with massage to homogenize

and/or disperse the hyaluronic acid. However, if the desired effect is not achieved by massage, hyaluronidase can be injected to disintegrate the excess hyaluronic acid [41–45]. When edema persists with minimal response to hyaluronidase, this may be associated with protein contaminants in the filler [41].

Complications

- Serious complications are rare, however early recognition is vital to minimize its consequences. Arterial occlusion presents with immediate blanching and pain, while venous occlusion may be delayed in presentation with violaceous discolouration and dull aching pain. Treatment of both conditions start with vigorous massage, warm compresses, and nitroglycerin paste. Lastly, in spite of being extremely rare, loss of vision has been reported from embolization of filler material to the central retinal artery [41–48]. A linear, feathered deposition of filler or the use of blunt cannula have been suggested to minimize these risks [1]. Vascular risks doesn't have to develop directly after injecting the blood vessel but may occur due to compression after placing a relatively large filler bolus next to or above a small vessel causing its compression.
- Delayed complications include persistent nodularity, infection, and angioedema occur days to weeks post injection. Non-inflammatory nodules may resolve by firm, gentle massage, while inflammatory nodules mostly need antibiotic coverage and incision drainage due to infectious etiology [41–48] (Table 4.5).

Management of Complications

Undesirable results may include color show, contour irregularity, or poor 3-dimensional shape which are not permanent problems [49, 50].

A bluish hue due to Tindal effect in the injected area is a common complication, especially in fair-skinned patients. Most often, this is not obvious and not even

Table 4.5 Injection techniques to avoid complications

Injection techniques to help avoid complications:
• Understand periorbital anatomy.
• Treat with local anesthesia with epinephrine to vasoconstrict blood vessels.
• Inject small volumes per pass and <0.1 ml in any one area.
• Keep the tip of the injection instrument moving.
• Attempt aspiration prior to injection.
• Use low injection pressure, do not force injection, especially in areas of previous scarring, injection or surgery.
• Consider the use of blunt cannulas but remember they do not eliminate the risk.
• Smaller needles and cannulas are more likely to penetrate vascular walls.
• Always know where the tip of the needle or cannula is in 3-dimensions, including depth (can use non-dominant hand to protect globe and feel tip of the cannula prior to injection).

noticed by the patient. Deep injection of the material may decrease this effect, but does not eliminate it. Lumps or contour irregularities are commonly present because of thin eyelid tissues that reveal every contour of the filler. However, most patients find the result acceptably smooth. Irregularities can be adjusted by injecting additional filler to seal depression or injecting hyaluronidase to dissolve excess material in elevation points, or a combination of the two. Adjustment of the injection could be done between the second week to the fourth week [15].

Redness or increased vascularity over the sites of the injection is rare. Pigmentation of lower eyelid circles will not improve by Hyaluronic acid gel injection and may even worsen the condition [15].

Occasionally, diffuse non-inflammatory edema in the lower eyelid may follow hyaluronic acid gel injections, it seems to be lymphedema than an inflammatory reaction. It may persist for many weeks after the injection and incompletely respond to hyaluronic acid elimination by hyaluronidase injections. Injection of hyaluronic acid gel in patients who have tendency towards periorbital fluid retention should be approached cautiously [15] (Table 4.6).

Pre-treatment

A full medical treatment history is mandatory, putting in consideration that any defined interactions, certain immunosuppressive agents and steroids should flag up the need to understand the patient's medical history more clearly. Even agents that interfere with cytochrome P450 should be considered as signals to proceed with caution [22].

Table 4.6 The authors recommend the following algorithm to dealing with possible vascular complications following filler injections

How to deal with vascular complications:
• DO NOT PANIC!!!!
• Stop further injection.
• Try to aspirate what has been just injected, sometimes it works
• Withdraw the needle out.
• Ask the assistant to prepare 1 cc of hyaluronic acid (150 IU) in an insulin syringe.
• Ask patient to chew 2 aspirin 75 mg tablets.
• Apply warm compresses, massage and apply nitroglycerin ointment, gel or patch to the area of vascular occlusion.
• Inject 1 cc of hyaluronidase enzyme mixture previously prepared (1500 IU over 10 cc saline) to the area of vascular occlusion.
• If needed, inject low molecular weight heparin.
• Wait for 1 h, if the patient does not improve inject another 1 cc of hyaluronidase enzyme mixture and wait another hour, inject up to 4 cc (1 cc per h).
• Ask the patient for a re consultation after 24 h, then if needed, inject 1 cc of hyaluronidase enzyme mixture every 24 h up to 3 cc (1 cc per day).
• Hyperbaric oxygen therapy can help as well.

Patients should discontinue anti-inflammatory and antiplatelet agents a week prior to treatment (if medically appropriate) to minimize bruising. A list of foodstuffs, herbal supplements, and over-the-counter medications to avoid may be beneficial for them [51–53].

Although there is weak evidence that antiplatelet therapy may be continued safely in the perioperative period [54], there are few publications discussing the issue systematically, and esthetic practitioners are warned to be mindful of the bleeding risk that applies to individual patients [55]. Patients with cardiovascular stents or taking anticoagulants in the long term need careful consideration, and explanation of the risks is a must [56].

Skin anesthesia may be done with ice, cold air, topical anesthetic, or focal vibration. Infraorbital and supraorbital nerve block could be performed, local infiltrative anesthesia should be avoided because it may distort tissue, complicating filler injection [1].

Treatment

Filler injections in the periorbital region can be injected either supra or infra orbitally. Injecting the upper eyelid is relatively very safe in a plain away from vessels and nerves, however injecting the tear trough deformity requires special caution to avoid injury or injecting by mistake the infra orbital vessels or the lacrimal sac. Because of the very thin skin of the upper and lower eyelids, mild contour and color irregularities may be more noticeable. Depositing significant amounts of filler in one location increase the chance of color and surface irregularities. To minimize lumps and irregularities, filler should be injected in a linear, feathered, thread-like pattern. Digital pressure is used to evenly distribute the filler. If bruising occurs, gentle focal pressure is applied to the area [1].

In the upper eyelid, fillers can be injected supra orbitally in the lateral part to elevate the tail of the eyebrow and allow some degree of stretching of the upper eyelid skin which are appreciated feminine aesthetic signs. Injection is performed while the patient is looking down, a 30-gauge needle is used to penetrate the skin at the superolateral orbital rim. The needle is advanced deep to orbicularis oculi muscle towards the inferior border of the superior orbital rim. Another safer method was performed through an initial puncture with a larger gauge needle, followed by insertion of a blunt cannula. A small amount of filler (0.1 ml) is deposited in linear pattern in the supra periosteal plane. After the needle is withdrawn, the filler is gently, but firmly shaped by digital pressure to equally distribute the material. Additional filler can be placed in a feathered, linear droplet fashion and the process repeated until the required volume has been delivered to the deficient area. Injury to the supraorbital neurovascular bundle must be avoided. For patients with prominent lateral orbital rim, filler can be delivered along the lateral orbital rim and sub-brow in a similar fashion (0.1–0.5 ml) [1].

In the lower eyelid, fillers can be injected to correct the tear trough deformity via a 30-gauge needle to puncture the skin to reach the desired plane. The needle is advanced in the sub orbicularis plane in the hollowed areas overlying the inferior

orbital rim. Filler is delivered, using multiple passes to place the filler in a linear, feathered fashion (0.3–0.5 ml). The needle is then withdrawn, and gentle, yet firm digital pressure is utilized to distribute the filler in the desired shape [1].

The MD Codes modality of filler injections was created by Dr. Mauricio De Maio (MD codes™), and its rejuvenation codes mentioned for the infra orbital region starts by the concept of enhancing the support of lower periorbital area. It is vital to perfectly know the facial anatomy and to start the treatment plan by the Ck1 (zygomatic arch), Ck2 (zygomatic eminence), and Ck3 (anteromedial cheek—mid-cheek) points followed by the Tt1 (central infraorbital), Tt2 (lateral infraorbital), and Tt3 (medial infraorbital) points [57].

With tear trough patients nearly 0.5 ml of filler should be used on each side to treat Ck points:

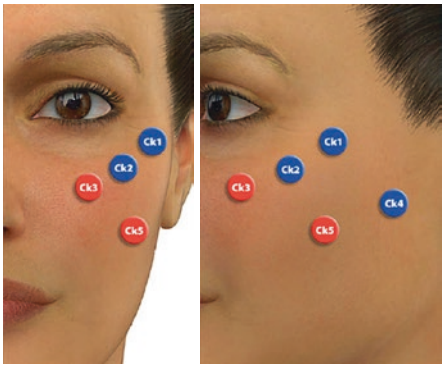
- Ck1 = 0.1 ml
- Ck2 = 0.1 ml
- Ck3 = 0.3 ml

Slight upwards and backwards traction should be exerted on the skin before injecting Ck1 and Ck2 points supra periosteally. By this way, lifting effect is achieved in this area. Because of the proximity of the zygomaticofacial artery and veins, aspiration is a must before injecting these 2 points [57].

Ck3 must be injected in the subcutaneous level to compensate the subcutaneous tissue loss which increase with ageing. Pinching the skin perpendicularly after aspiration should be done before each injection due to the proximity of the infraorbital artery and veins to Ck3 [57] (Fig. 4.2).

Hence the periorbital area support has been improved, moving to the Tt points in the lower orbital area on each side

- Tt1 = 0.2 ml
- Tt2 = 0.2 ml
- Tt3 = 0.1 ml



Code	Injection area
Ck1 (L1)	Zygomatic arch
Ck2 (L2)	Zygomatic eminence
Ck3 (L3)	Anteromedial cheek
Ck4	Lateral lower cheek / parotid area
Ck5	Submalar

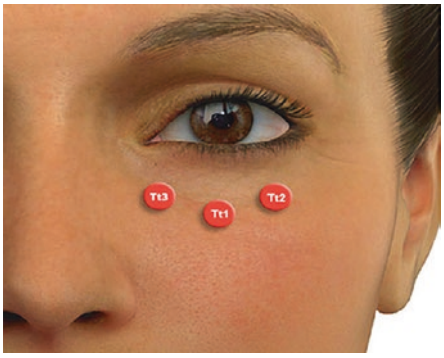
Fig. 4.2 Anterior and lateral cheek injection points face map. Courtesy of Allergan and Dr. Mauricio de Maio [58]

In this step of the treatment, the needle was advanced until touching periosteum while perpendicular pinching on the skin was done. Then the material was deposited in the retromuscular layer after aspirating with the syringe. Injection is performed 1–2 mm below the lower orbitary edge because above the orbital rim is the orbital septum and behind it the infraorbital fat. If the filler is injected into the infraorbital fat, the periorbital lower depression worsen and the solution to this problem would be more difficult [57] (Fig. 4.3).

Peng & Peng have created standardized categorization, evaluation, and treatment protocol for the management of tear troughs with fillers through determining three categories of traits: A (Atrophy), B (Bulging), L (Laxity) via a 6-step evaluation process (Tilt, Snap, Smile, Squint, Pull, Push), their treatment protocol is simplified for each category (with 6 major injection points and a variety of injection depths and volumes) achieving satisfactory results. Refer to Table 4.7 for a summary of these categories [59].

Table 4.8 shows a summary of ABL categories, injection sequence, injection depth, and testing.

Tear trough modality can also be injected by cannula which is more recommended for not so much experienced injectors. The insertion point for the cannula is marked 2 cm inferolateral to the left lateral canthus and cleaved with a 21-gauge needle guide. 22–25G 50-mm cannula is inserted and advanced beneath the orbicularis oculi muscle towards the medial canthus, remaining within the area cephalad to tear trough ligament (TTL). Retrograde injection of a monophasic product with a low concentration of hyaluronic acid filler (20 mg/ml, cross-linked) is done to the



Code	Injection area
Tt1	Central infraorbital
Tt2	Lateral infraorbital
Tt3	Medial infraorbital

Fig. 4.3 Typical tear trough injection points face map. Courtesy of Allergan and Dr. Mauricio de Maio [58]

Table 4.7 ABL category system

Atrophy	Bulging	Laxity
A0: No atrophy	B0: No bulging	L0: No laxity
A1: Tear trough	B1: Eye bags	L1: Cheek laxity
A2: A1 + PMG	B2: Malar festoon	L2: Lower eyelid laxity
A3: A2 + Anteromedial cheek deficiency	B3: B1 + B2	L3: L1 + L2

Table 4.8 Summary of injection sequence, depth, and testing

Category		Injection sequence	Injection depth	Testing
A	1	Tt1 + Tt3	Tt superficial or deep. Superficial in areas of tight ligament-bone attachment [Pull]-Tt3	Observation
	2	Tt1 + Tt2 + Tt3		
	3	Ck3 → Tt1 + Tt2 + Tt3	Tt same as above. Ck3: deep cheek fat pad or periosteum with bony deficiency, deep fat pad otherwise	
B	1	Ck3 → Tt1 + Tt2 + Tt3		
	2	Ck1 → Ck3 → Tt1 + Tt2 + Tt3	Malar festoon as no go area (no Ck2)	
	3	Ck1 → Ck3 → Tt1 + Tt2 + Tt3		
L	1	Ck1 + 2 → Ck3 → Tt1 + Tt2 + Tt3	Ck3, Tt same as above. Ck1 + 2: deep on periosteal level.	Observation, [Tilt], [Snap]
	2	Ck1 + 2 → Ck3 → Tt1 + Tt2 + Tt3		
	3	Ck1 + 2 → Ck3 → Tt1 + Tt2 + Tt3		
Treatment planning			[Smile] helps determine expression impact [Push] helps simulate postinjection appearance and help differentiate surgical and nonsurgical options	

Table 4.9 Comparison of using cannula vs. needle for tear trough filler injections

Cannula	Needle
Better when injecting to compensate volume and release fibrotic ligamentous structure.	Better for making fine contours.
Recommended for injection into the deep fat layer under the orbicularis oculi-muscle.	Recommended for injection into the subdermal area above the orbicularis oculi-muscle.
Safer, longer and causes less bruising or swelling recommended to avoid vascular compromise.	Easier to pass through layers. Not recommended for beginner injector specially in periorbital area

preseptal space from the medial canthus to the insertion point. Gentle digital pressure is to be applied to distribute the product evenly upon withdrawal of the cannula [60].

During the procedure, beginning from the insertion point, the unimpeded advancement of the cannula within the space that no structures pass proves that the cannula is in the preseptal space. Upon withdrawal of the cannula from the preseptal space, prominent resistance is felt because of neighboring anatomical structures such as muscles, ligaments, and fat. The texture of the bone can be felt when the cannula passes over the periosteum that forms part of the floor of the preseptal space [60] (Table 4.9).

Other modalities of injection have been described by many authors as mentioned in Table 4.10 [61].

Table 4.10 Hyaluronic acid injection techniques

Technique	Characteristic
Lambros [62]	The injection takes place deep in the dermis. The needle goes through the skin at the most lateral extent of the tear trough, advancing fully to medial aspect, leaving a small amount of product. Pressure is applied to flatten the injection site.
Kane [63]	The deepest part of the medial tear trough is treated first. A miniscule amount of hyaluronic acid filler is injected at each pass in a cephalad and caudal direction.
Stutman and Codner [64]	A deep injection is performed next to the periosteum in order to reduce the visibility of the product. The injection is performed below the medial insertion of the orbicularis muscle and is continued in a lateral and inferior direction to the orbicularis retaining ligament. Soft massage is then performed to avoid irregularities at injection sites.
Steinsapir and Steinsapir [65]	Injections are in the subperiosteal plane inferior to the orbital rim. Pressure is applied to the needle before applying the HA to prevent passage to other planes. Serial punctures are made to cover the entire region.
Glaser and Patel [66]	This is a similar injection technique to that described by Steinsapir. However, with this technique, the hyaluronic acid filler is injected in a plane between the periosteum and the orbicularis oculi in order to improve the aesthetic outcome.
Sharad [67]	The injection is performed through a point in the pupillary midline, 1 cm below the orbital rim. The injection begins in a diagonal direction to the medial canthus, injecting the HA in a subperiosteal fashion. Then, the direction of the needle changes vertically (up), then in a lateral manner, leaving small aliquots of product in these areas as necessary.
Trevidic [68]	A cannula is used to inject from the lateral to medial tear trough deformity. Leaving small amounts of product makes this procedure safer, with less risk of vascular or nerve injury and less generation of edema.

Post Treatment

No special care has to be taken following tear trough filler injections except for advising on no manipulation of the filler or exposure to temperature extremes. Proper illustration of warning signs shall be performed to patients in order to increase their awareness.

Documentation

Well-focused pretreatment photographs should be taken, not only for assessment of treatment effects and any adverse effects but also for medicolegal purposes [23, 56].

Our patient have a tear trough deformity grade 1 treated with cannula technique. Before and after treatment photographs were taken for documentation (Fig. 4.4).

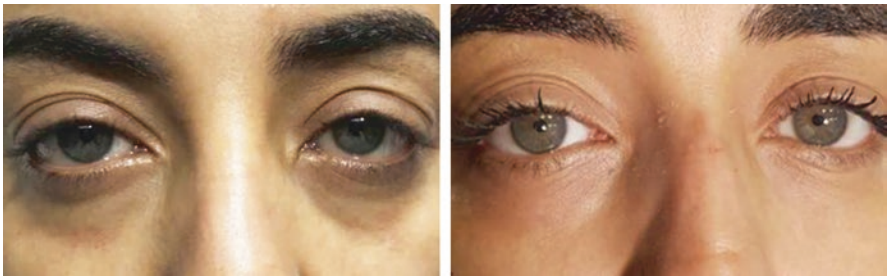


Fig. 4.4 Tear Trough deformity grade 1 treated with cannula technique. Before and after treatment

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Neuromodulators in Periorbital Rejuvenation

5

Anthony V. Benedetto

Introduction: Periorbital Region and Botulinum Toxin (BoNT) Injections

Injections of botulinum neurotoxin (BoNT) to diminish wrinkle lines in the upper face and periorbital area are the only indications approved for cosmetic rejuvenation by the Food and Drug Administration (FDA) in the United States of America (USA) [1–4]. These anatomical sites include, in particular, frown lines of the glabellar (central brow), lateral canthal rhytides (crow's feet) and horizontal forehead lines. The face is the only location in the body where muscles insert into the undersurface of the skin. So, when facial muscles contract, they move the skin of the face in different directions. This allows one to either raise or lower the eyebrows in a smile or frown, open or shut the eyes to protect or sharpen one's vision, and so on. The different directions in facial skin movement is accomplished by muscles contracting in opposing directions, yet in complementary fashion, by elevating (levators) or lowering (depressors) facial skin. These competing movements by agonistic and antagonistic muscles contracting intentionally or unintentionally cause horizontal, vertical, diagonal or radial wrinkling of the different parts of the face, specifically of the cosmetic units of the face. Thus, nonverbal communication can be expressed with the slightest contraction of one or a combination of facial muscles (i.e. by "mimetic facial muscles"). Also, one must always understand that every single individual patient is different, one from another, and facial movements are idiosyncratic to that patient and rejuvenation should be appropriately tailored to an individual's needs and requests. This is particularly true when rejuvenating the periorbital region with the BoNTs (Fig. 5.1).

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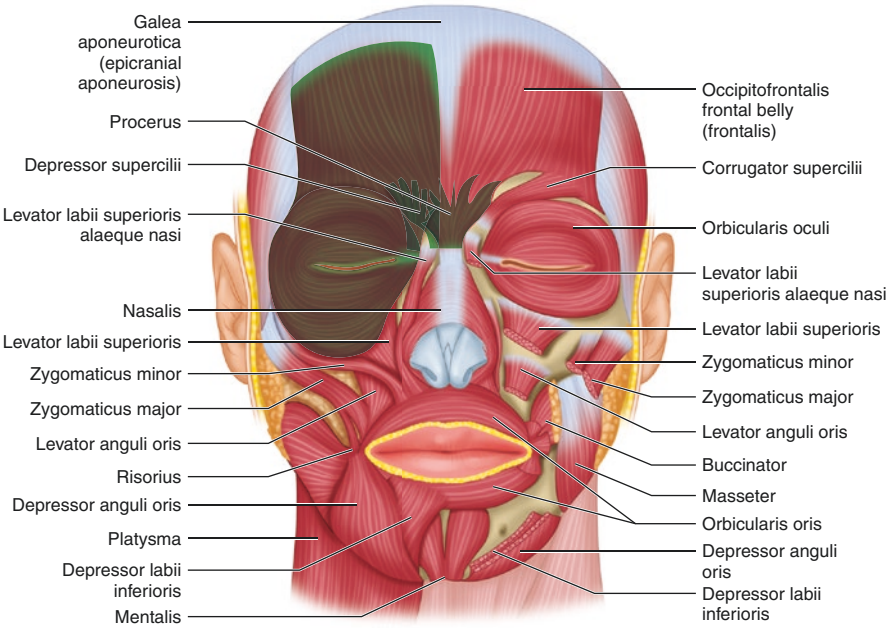

Fig. 5.1 The mimetic muscles of the face

Practical Anatomy for Injecting the BoNTs

Contracting any of the mimetic muscles of the face will wrinkle the skin perpendicular to the direction of muscle contracture. For example, muscles which contract in a horizontal direction because their muscle fibers are oriented horizontally will cause vertical wrinkle lines on the face. Muscles that produce horizontal wrinkle lines have muscle fibers oriented vertically and contract in a vertical direction.

There are five periorbital muscles surrounding the bony orbit, some of which cause horizontal and others vertical wrinkle lines around the orbit (Fig. 5.2). Those that cause vertical wrinkling of the central brow are the *corrugator supercilii* and the medial horizontal fibers of the orbital portion of the *orbicularis oculi*. The horizontal wrinkles of the central brow and the root of the nose are caused by the contractions of the *procerus, depressor supercilii* and the medial vertical fibers of the orbital portion of the *orbicularis oculi* (Fig. 5.2). These four muscles (corrugator supercilii, depressor supercilii, procerus, and the orbital portion of the orbicularis oculi) are considered the depressors of the periorbital area. However, there is only one levator of the periorbital area, inclusive of the brow and the forehead, namely, the *frontalis* (Fig. 5.2). All five periorbital muscles, levator and depressors, must be treated with BoNT if a successful outcome of upper facial and periorbital rejuvenation is to be realized. The specific locations of these five mimetic muscles can be seen in Fig. 5.2.

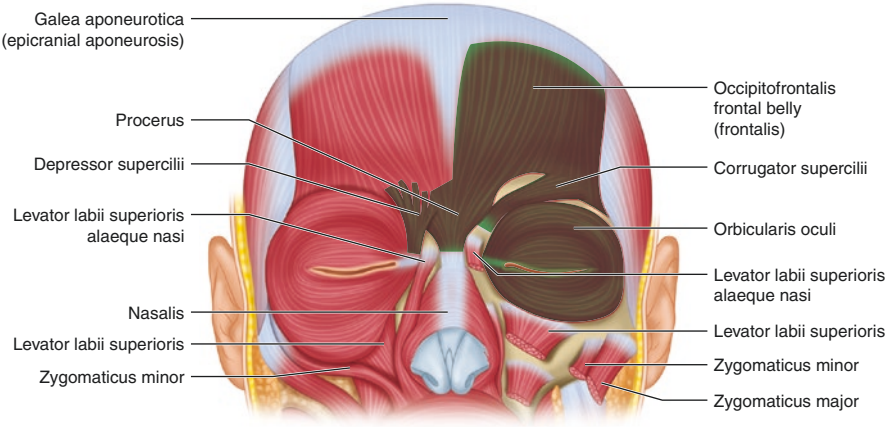

Fig. 5.2 Mimetic muscles of the periorbital area consist of a single brow elevator (the frontalis) and four depressors: the procerus, depressor supercilii, corrugator supercilii, and orbicularis oculi

The corrugator supercilii lies directly against the frontal bone medially just beneath the interdigitating muscle fibers of the superior aspect of the orbital orbicularis oculi, procerus, depressor supercilii, and frontalis. It typically travels upwardly and laterally at an oblique angle of approximately 30°, to emerge from beneath the interdigitating fibers of the frontalis and superior orbital orbicularis oculi and inserts underneath the skin into the soft tissue and dermis just above the middle of the eyebrow in the vicinity of the midpupillary line and the supraorbital notch or foramen. The corrugator supercilii lies directly above the supraciliary arch of the bony orbit and is the deepest of the five muscles (Fig. 5.2) [5]. When injecting the central brow and the corrugator supercilii, the needle must be placed deeply and through the other superficial muscles which lie above it (i.e. frontalis and orbicularis oculi) in order to reach and properly inject the corrugator supercilii. The other four muscles of the periorbital area can be treated with superficial or mid-dermal injections of BoNT (Fig. 5.2).

The horizontal lines of the glabella and nasal root are produced by the contraction of the vertically oriented fibers of the procerus, depressor supercilii, and the medial vertical fibers of the orbital orbicularis oculi. These three muscles also are referred to as the "medial brow depressors" (Fig. 5.2) [6].

The procerus is a thin ($\leq$1 mm thick), paired muscle, pyramidal in shape and centrally located in the midline of the glabella between the two eyebrows. The shape, size, and strength of the procerus will help determine the different types of glabellar frown lines that are created across the nasal radix (see de Almeida's glabellar frown lines, Figs. 5.3, 5.4, 5.5, 5.6, and 5.7) [7]. Its location 2–4 mm beneath the surface of the skin makes it an easy target for injections of BoNT (Fig. 5.8a, b) [4].

The orbicularis oculi is a flat, broad muscle whose fibers form a complete concentric elliptical ring around the orbit and over the eyelids. It encircles the globe, covering the eyelids and extending approximately 3 cm beyond the peripheral margins of the

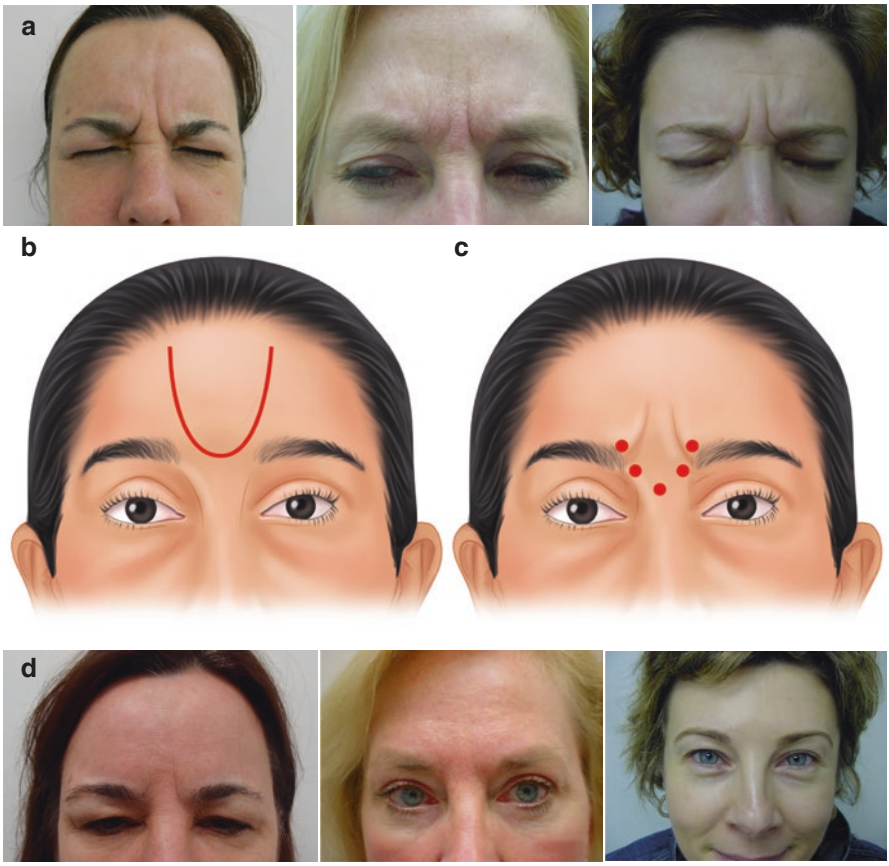

Fig. 5.3 (**a**) Mild to moderate approximation and depression of the medial brow forming the typical and one of the most commonly seen patterns of glabellar frown lines (the "U" pattern). (**b**) Commonly seen "U" type of glabellar contraction and resulting pattern of frown lines, also known as the 11s. Muscles involved: predominantly the corrugators and procerus. (**c**) Five-point pattern of injection for this commonly encountered glabella "U" pattern. (**d**) Same patients frowning at rest 2 weeks after onabotulinumtoxinA treatment

bony orbit, interdigitating with adjacent muscle fibers up into the forehead and down as low as the mid cheek. This sphincter-like muscle can be divided into three parts. The outermost fibers of the orbicularis oculi are called the *orbital* portion of the orbicularis oculi. Its fibers completely surround the bony orbit, superiorly, inferiorly, medially and laterally forming a wide sphincteric ring beyond the edges of the bony orbital rim (Fig. 5.9) [8–10]. A section of the medial aspect of the orbital orbicularis oculi, whose fibers have a conspicuously more vertical orientation, has been referred to as the "depressor supercilii" by some authors (Fig. 5.9) [6, 11–13]. Contraction of this medial aspect of the orbital orbicularis oculi (i.e. depressor supercilii) lowers the eyebrow downward and slightly medially. The medial, lateral, superior and inferior aspects of

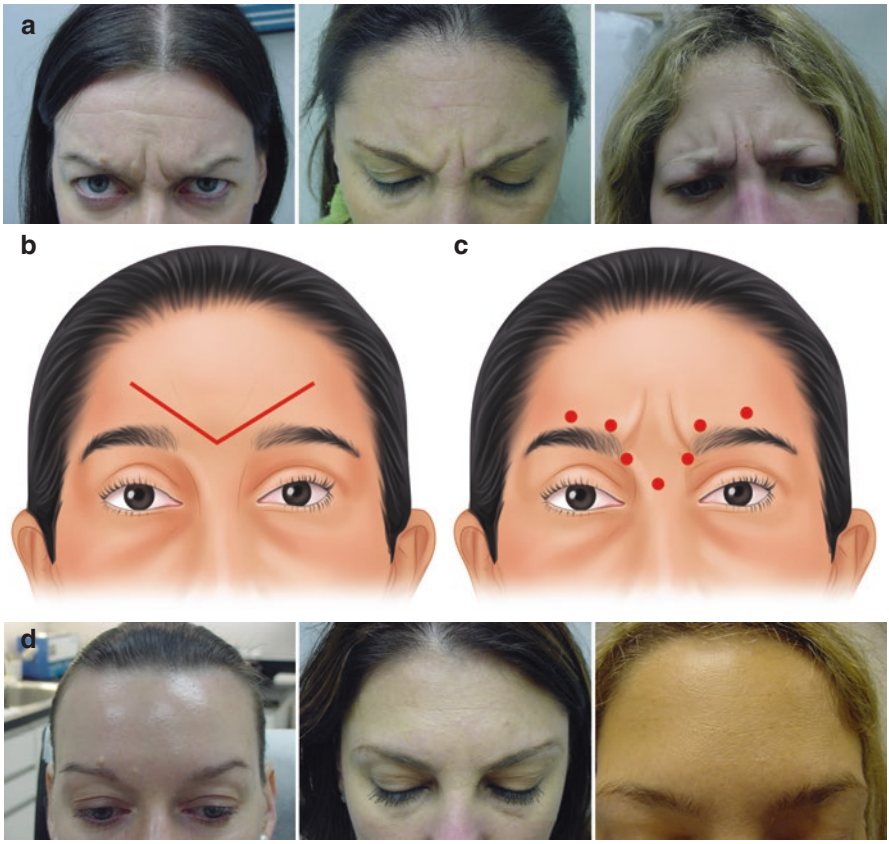

Fig. 5.4 (**a**) Moderate to severe approximation and depression of the medial brow forming the more commonly seen pattern variation identified by very deep glabellar frown lines (the "V" pattern). (**b**) Vigorous glabellar contraction and resulting "V" pattern of frown lines. Muscles involved: strong corrugators, procerus, and medial aspect of the orbicularis oculi. (**c**) Seven-point injection pattern for this exaggerated glabellar "V" pattern. Higher doses of BTX-A are usually needed for treatment. (**d**) Same patients 3 weeks after an onabotulinumtoxinA treatment

the periorbital region are the most often treated parts of the orbital orbicularis oculi which are injected with BoNTs to produce specific aesthetic effects [14].

The central inner portion of the orbicularis oculi which overlies the eyelids is identified as the *palpebral* portion of the muscle. The palpebral orbicularis oculi is further subdivided into *preseptal* and *pretarsal* parts (Fig. 5.9) [8, 10]. Contraction of the palpebral orbicularis oculi approximates the upper with the lower eyelids, either deliberately or involuntarily. The third portion of the orbicularis oculi is the *lacrimal* orbicularis oculi, which functions as an integral part of the lacrimal drainage system (Fig. 5.10). The three constituent portions of the orbicularis oculi are anatomically and physically confluent and act in unison as the eyelid protractors.

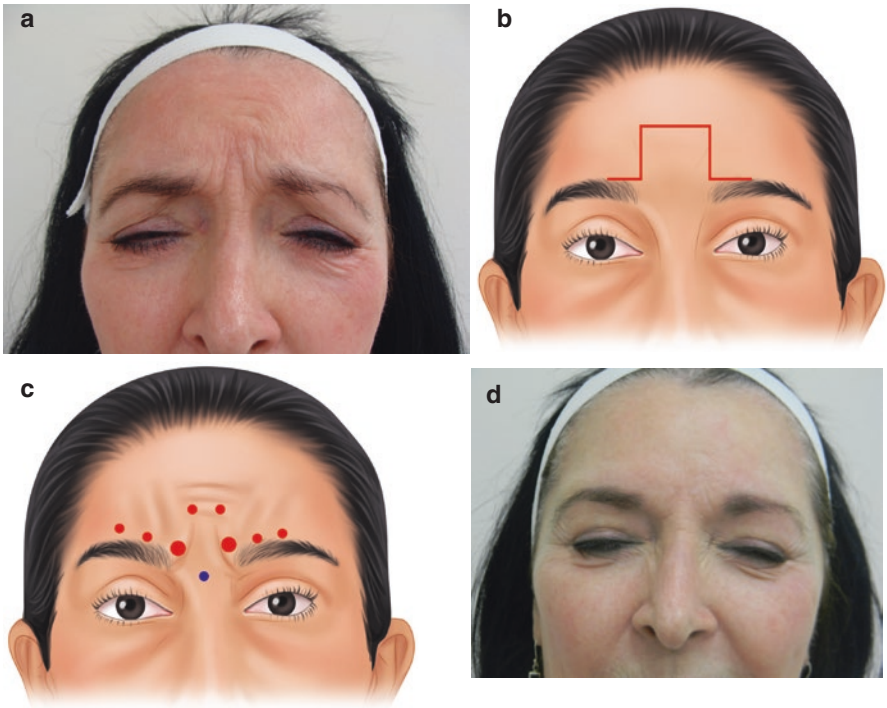

Fig. 5.5 (**a**) Adduction of the medial eyebrows and elevation of the center of the glabella along with depression of the mid and lateral brow forms the "omega" pattern of glabellar frowning. (**b**) The "omega" pattern of frown lines in outline form. Muscles involved: corrugators and lower central frontalis. (**c**) This eight-point pattern of injection is used for the glabellar "omega" pattern. Higher doses of onabotulinumtoxinA are needed for the corrugators and some units in the lower central frontalis and usually none for the procerus (blue, author's modification). (**d**) Same patient frowning 1 month after an onabotulinumtoxinA treatment

Available BoNT Products Their Preparation and Dosage

Botulinum toxin is found in nature surrounded by a group of neurotoxin-associated proteins (NAPs) which protect the neurotoxin from adverse environmental conditions and the proteolytic digestion in the gastrointestinal tract [15]. In the manufacturing process of commercial BoNT-A, some are produced complexed with NAPs and others without.

It is extremely important to understand that the specific units and dosages of the different BoNT-A toxins discussed here are proprietary for each manufacturer's individual product and cannot be dosed interchangeably. That is, the same number of units of one BoNT-A product absolutely must not be used with an identical unit dose of another manufacturer's BoNT-A to treat patients even if a dose ratio of equivalency is provided by the manufacturer as being 1:1 [1]. Allergan, Inc. plc was the first company to manufacture and distribute the first injectable BoNT-A (onabotulinumtoxinA), ie

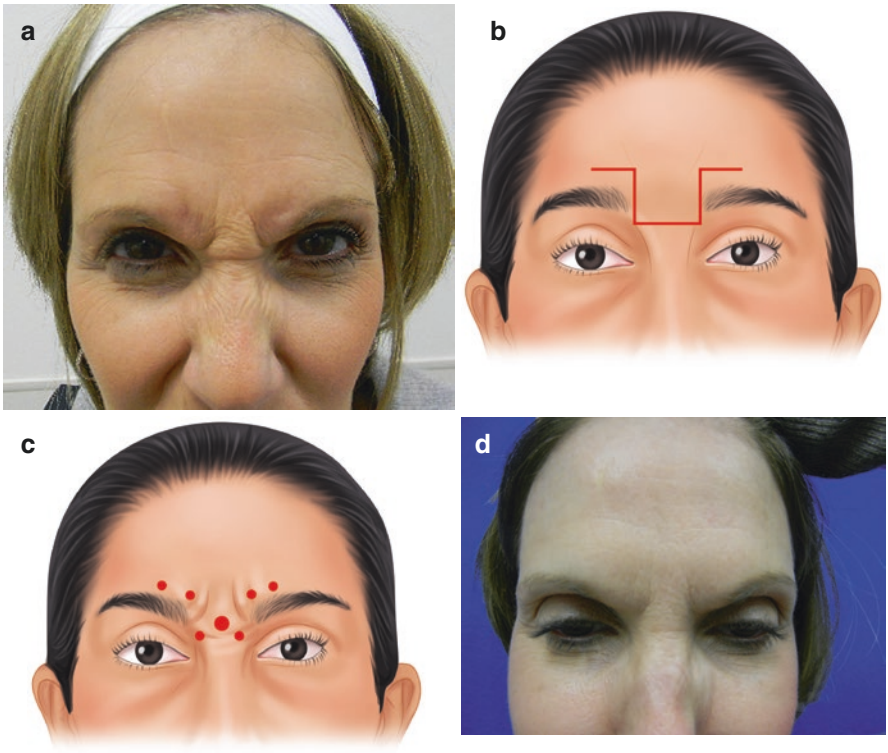

Fig. 5.6 (**a**) More depression than adduction of the medial brow forms the "inverted omega" pattern of glabellar frowning. Note the deep horizontal line at the root of the nose. (**b**) Less frequently seen type of glabellar adduction producing an "inverted omega" pattern of frown lines. Muscles involved: mostly the procerus and depressor supercilii. (**c**) A different seven-point pattern of injection for this uncommon glabellar "inverted omega" pattern. Higher doses of onabotulinumtoxinA are needed for the procerus. (**d**) Same patient frowning 2 weeks after an onabotulinumtoxinA treatment

BOTOX® for therapeutic and BOTOX® Cosmetic for cosmetic purposes. Hence, all subsequently produced BoNT-As have been measured against the Allergan product for comparable efficacy.

The reason for the dosing indecipherability of the different brands of BoNT-As is because the current cell-based potency assay used by Allergan is proprietary and different from other manufacturers' proprietary potency assays of their own BoNT, which vary according to vehicle, dilution scheme, and laboratory protocols [16, 17]. Therefore, when using any type of BoNT it is imperative that one learns how to administer that particular brand of BoNT independently of any conversion ratio, because individual muscles may respond in a distinctly different manner to certain formulations and specific serotypes of BoNT [16]. The science of the pharmacokinetics and pharmacodynamics of the BoNTs is still to be determined and the possibilities for future developments are virtually limitless [18–20].

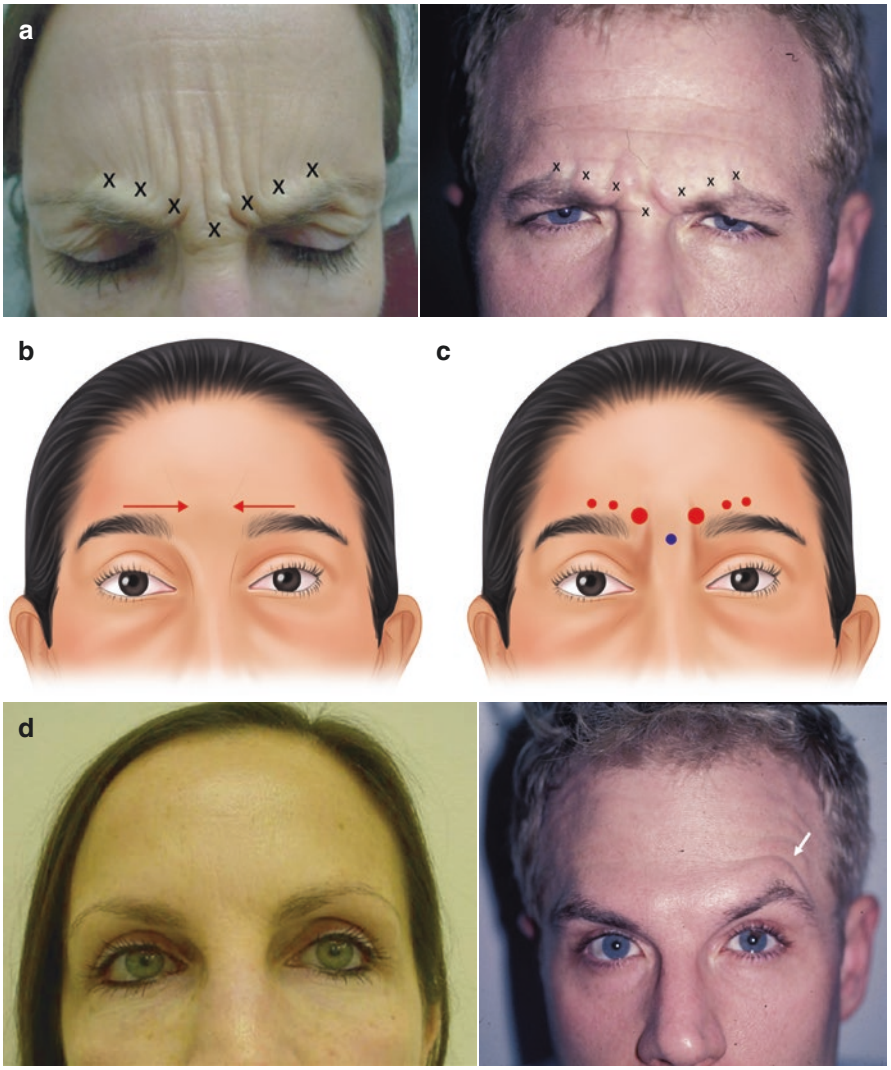

Fig. 5.7 (**a**) Adduction and approximation mainly of the eyebrows form this "converging arrows" pattern of glabellar "corrugated" frowning in both female and male patients. There is a little depression of the medial brow. (**b**) This is an uncommon type of glabellar contraction resulting in a "converging arrows" or "parallel lines" (author) pattern of frown lines. Muscles involved: mainly the corrugators and the upper mid horizontal orbital orbicularis oculi. (**c**) This seven-point pattern of onabotulinumtoxinA injections targets mainly the corrugators and the mid-section of the upper orbital orbicularis oculi (blue, author's modification). (**d**) Same patients 2 months after onabotulinumtoxinA treatment. Note the slightly higher elevation of the male patient's left eyebrow after treatment (known as a "Mephisto" brow)

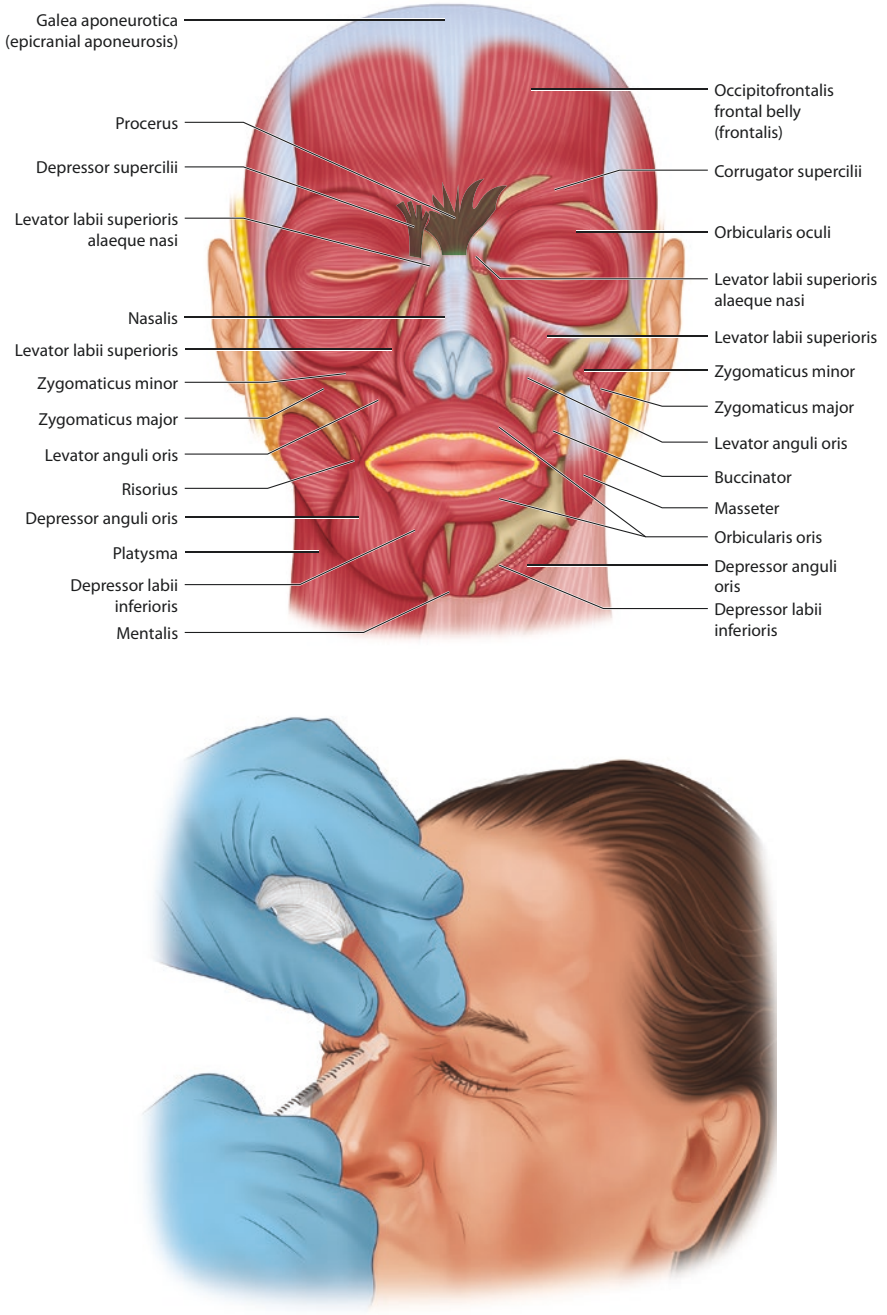

Fig. 5.8 The depressor supercilii is the diminutive muscle of the glabella. The procerus is the midline, deep muscle of the glabella

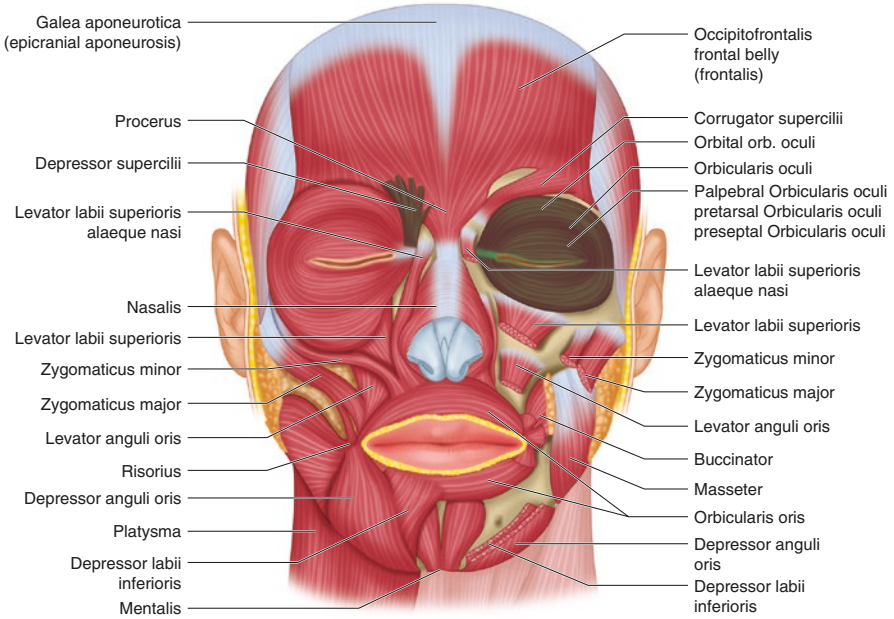

Fig. 5.9 The orbicularis oculi has different subdivisions and interdigitates with the other depressors and elevator of the glabella

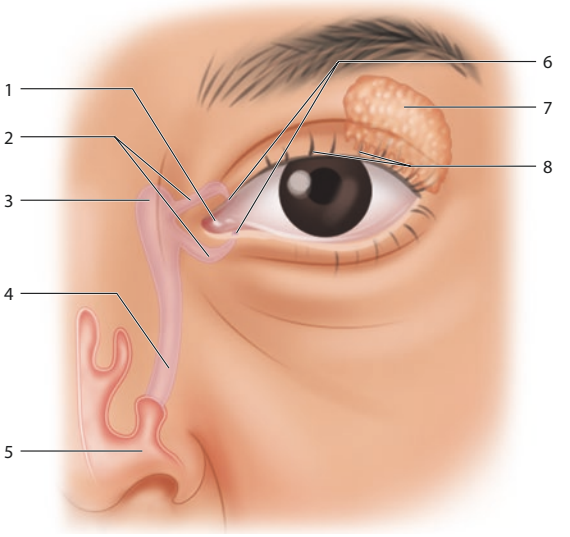

Fig. 5.10 Tears are produced by the main (orbital) and accessory (palpebral) lacrimal glands. The distribution of these tears over the surface of the eye is achieved by movements of the eyelids performing a wiping action of the marginal tear bed. The passage of tears into the nose occurs via the lacrimal drainage system, propelled by contractions of the orbicularis oculi. 1, plica semiluminaris and lacrimal lake; 2, lacrimal canals; 3, lacrimal sac; 4, nasolacrimal duct; 5, inferior nasal meatus; 6, superior and inferior lacrimal papillae and puncta; 7, orbital lacrimal gland; 8, palpebral (accessory) lacrimal glands

In 1989, the FDA approved BOTOX® for the therapeutic treatment of strabismus and blepharospasm [21]. By 2000, BOTOX® was approved by the FDA for the therapeutic treatment of cervical dystonia. In April 2002, the FDA approved BOTOX® for the cosmetic treatment of glabellar frown lines. This led Allergan to create the additional brand name of BOTOX® Cosmetic [1]. Both BOTOX® and BOTOX® Cosmetic are exactly the same product: they contain the same active ingredient in the same formulation, are manufactured by identical methods, and are only distributed under different names for different labeled indications and uses. BOTOX® is to be used for therapeutic purposes, whereas BOTOX® Cosmetic is to be used for cosmetic purposes [1, 22]. Subsequently, new and different formulations of BoNT-A other than BOTOX® and BOTOX® Cosmetic were approved for use in the USA for both therapeutic and cosmetic purposes. The first of these was DYSPORT®, which was approved by the FDA in May 2009 for therapeutic and cosmetic purposes [2, 23–25]. In July 2011, XEOMIN®, a non-complexed BoNT-A was approved by the FDA for therapeutic and cosmetic purposes [3, 26–28]. In February 2019, the FDA approved JEUVEAU™ only for cosmetic purposes [5, 29] (Table 5.1).

To distinguish between the current and future different formulations of BoNT from one another without mentioning their trade names, in April 2009, the FDA assigned nonproprietary names, a type of "generic" name, to the different formulations of the currently approved BoNTs, again emphasizing their uniqueness and lack of full equivalency. OnabotulinumtoxinA (OnaBTX-A) was assigned to BOTOX® and BOTOX® Cosmetic, also known as Vistabel® in certain countries in Europe, and Vistabex® in Italy. AbobotulinumtoxinA (AboBTX-A) was assigned to DYSPORT®, also known as Azzalure® in Europe and Reloxin® elsewhere. IncobotulinumtoxinA (IncoBTX-A) was assigned to XEOMIN®, otherwise known as XEOMEEN® in Belgium and Bocouture® in Europe and elsewhere. PrabotulinumtoxinA (PraBTX-A) now approved for distribution in the USA as Jeuveau™, is known as Nabota in Asia, Nuceiva in the EU and Canada. Botulinum neurotoxin type B (BoNT-B) known as Myobloc® in the United States and Neurobloc® in Europe was given the designation of RimabotulinumtoxinB (RimaBTX-B). Other BoNTs currently available for use in other parts of the world are found in Table 5.2.

All the currently available BoNT-As in the USA are distributed in some sort of powder form and require reconstitution before use. Each manufacturer's package insert has their own recommendations for reconstituting their proprietary BoNT-A, depending on the different quantity of product contained in the vial (Tables 5.1 and 5.2). Tables 5.3, 5.4 and 5.5 illustrate the variability of recommended volumes of reconstitution for each product according to the content of BoNT-A in each vial. Some products need to be kept refrigerated at specific temperatures after delivery; others can be stored at room temperature. After reconstitution, there are specific instructions for continued storage of each product, but most products must be kept refrigerated at certain temperatures, for a specific finite amount of time. The shelf life of a particular product can also vary, which can be different even for the same commercial product, depending on the quantity of product in the vial. For example, vials of onabotulinumtoxinA can be stored in their dry, powdered form in the refrigerator at a constant temperature of 2°C–8 °C for up to 36 months for the 100 U vial, but only 24 months for the 50 U vial [1]. Although the package insert for onabotulinumtoxinA recommends the reconstituted product be

Table 5.1 FDA-approved injectable BoNT brands available worldwide for aesthetic use

Product	Company	Country	Bacterial production strain	Manufacturing process	U/vial (product specific)[a]	Excipients (in vial)[b]
Dysport®/ Reloxin®/ Azzalure®	Ipsen/Galderma	France/ Switzerland	Hall NCTC 2916 Complexed with NAPs[c] (600–900kD[d])	Precipitation, dialysis, chromatography	125/300/500	0.125 mg HSA 2.5 mg lactose
Botox®/Botox® Cosmetic/ Vistabel®/ Vistabex®	Allergan, Inc. plc	USA/Ireland	Hall-hyper Complexed with NAPs (900kD)	Acid precipitations, dialysis	50/100/200	0.5 mg HSA 0.9 mg NaCI
Xeomin®/ Xeomeen®/ Bocouture®	Merz GmbH	Germany	Hall ATCC 3502 Complexed without NAPs (150kD)	Unknown	50/100/200	1 mg HAS 4.7 mg sucrose
Jeuveau®/ Nabota®/ Nuceiva®	Evolus, Inc/ Daewoong Pharmaceutical Co. Ltd.	USA/South Korea	Hall-hyper? Complexed with NAPs (900kD)	High-Pure Technology® (patented)	100u	0.5 mg HSA 0.9 mg NaCI

Source: Adaptation of Toxin Science Limited, 2019

Note: All products are either freeze dried (Dysport®, Xeomin® and Jeuveau® products) or vacuum-dried (Botox® products)

[a]The potency units of each product are specific to that product and are not interchangeable with those for other BoNT products

[b]*HSA* human serum albumin

[c]*NAPs* Neurotoxin-associated proteins

[d] kD kiloDaltons

Table 5.2 Approved (outside the USA) BoNT products from Asia (current as of 2018)

Product	Company	Country	Bacterial production strain	Manufacturing process	U/vial (product specific)	Excipients (in vial)[a]
BTXA®/Prosigne®/Redux®/ Lantox®/Lanzox®	Lanzhou Institute of Biological Products/Hugh Source Int'l	China	Hall-hyper	Crystallization, dialysis	50/100u	5 mg gelatin 25 mg dextran 25 mg sucrose
Meditoxin®/Neuronox®/Siax®/ Botulift®/Cunox®	Medytox, Inc	South Korea	Hall-hyper	Acid precipitations, dialysis	50/100/200u	0.5 mg HSA 0.9 mg NaCI
Innotox®/MT10109L (Liquid Product)	Medytox, Inc	South Korea	Hall-hyper	Unknown	25/50u	No human serum albumin (HSA) or animal products
Coretox®/MT10107 (Naked toxin—no NAPs)	Medytox, Inc	South Korea	Hall-hyper	Unknown	100u	Methionine Polysorbate Sucrose
Botulax®/Zentox®/Regenox®	Hugel Pharma	South Korea	CBFC26	Protamine sulphate DEAE sepharose Chromatography	50/100/200u	0.5 mg HSA 0.9 mg NaCI
Nabota®/Evosyal® (DWP 450)	Daewoong Pharmaceutical Co Ltd.	South Korea	Hall-hyper?	High-Pure Technology® (patented)	100u	0.5 mg HSA 0.9 mg NaCI

Source: By courtesy of Toxin Science Limited, 2017

[a]Concentrations of excipients may depend on number of units in vial

Table 5.3 Vial dilutions for onabotulinumtoxinA, incobotulinumtoxinA, and prabotulinumtoxinA for 100 unit vials

Diluent volume (0.9% sodium chloride)	U/0.1 mL	U/0.01 mL
1.0 mL	10.0 U	1.0 U
2.0 mL	5.0 U	0.5 U
2.5 mL	4.0 U	0.4 U
4.0 mL	2.5 U	0.25 U
5.0 mL	2.0 U	0.20 U
8.0 mL	1.5 U	0.15 U
10.0 mL	1.0 U	0.1 U

Table 5.4 Vial dilutions for abobotulinumtoxinA for 500 unit vials

Diluent volume (0.9% sodium chloride)	U/0.1 mL	U/0.01 mL
1.0 mL	50.0 U	5.0 U
2.0 mL	25.0 U	2.5 U
2.5 mL	20.0 U	2.0 U
5.0 mL	10.0 U	1.0 U

Table 5.5 Vial dilutions for abobotulinumtoxinA for 300 unit vials

Diluent volume (0.9% sodium chloride)	U/0.1 mL	U/0.01 mL
0.6 mL	50.0 U	5.0 U
1.0 mL	30.0 U	3.0 U
1.5 mL	20.0 U	2.0 U
2.5 mL	12.0 U	1.2 U
3.0 mL	10.0 U	1.0 U

used within 4 h, studies have shown that after reconstitution, the potency of onabotulinumtoxinA should remain consistent and unchanged for up to 6 weeks, and can be used without any noticeable change in clinical efficacy [2–5, 30–32].

Rimabotulinumtoxin-B has always been distributed in liquid form at the different doses. It is the first and only botulinum toxin available in a ready-to-use solution that does not require reconstitution. It remains stable up to 36 months refrigerated and up to 9 months at room temperature. It is currently available in three dosing volumes (2500 U in 0.5 mL, 5000 U in 1.0 mL, and 10,000 in 2.0 mL) with the same concentration (5000 U/mL).

There are clinical trials currently being conducted by Ipsen, the manufacturers of abobotulinumtoxinA and by Allergan, the USA distributors of a South Korean product called Innotox® (nivobotulinumtoxinA) (see Table 5.2), that are currently underway for FDA approval of a liquid formulation of their BoNT-A. Much of the variability of product reconstitution and toxin bioavailability will become standardized when these approvals are granted.

Table 5.6 Dose equivalence

Treatment zone	onabtxA: abobtxA (USA)		incobtxA: abobtxA (Russia)		incobtxA: abobtxA (international)	
Glabella	20:52.5	1:2.6	20:50	1:2.5	20:50	1:2.5
Crow's feet	10:25	1:2.5	12:20	1:1.7	20:22.5	1:1.1

Table 5.7 Recommendations on number of injection points for different BoNTs

Treatment zone	OnabotulinumtoxinA			IncobotulinumtoxinA		AbobotulinumtoxinA		
	Germany	France	USA	Russia	International	Russia	International	USA
Glabella	5–7	2–5	5–7	5–6	5–7	3–5	5	3–5
Crow's feet	3–5	2–5	2–5	3–4	2–5	3–6	3	3–4

Several studies have assessed the potential risk for contamination of reconstituted botulinum toxin. There is no evidence suggesting any serious or nonserious adverse events have been associated with the use and reuse of vials of onabotulinumtoxinA which have been reconstituted for more than 4 h and reused in the treatment of multiple patients [33]. In another study, the routine refrigerator storage of 100 unit vials of reconstituted onabotulinumtoxinA did not result in any microbial contamination even after serial re-extractions of the reconstituted solution from the same vials by different personnel. Storage of reconstituted onabotulinumtoxinA and subsequent multiple extractions from the same vial of botulinum toxin appears safe for clinical use for at least 7 weeks after reconstitution [33–35].

An extensive and complex study comparing the different national and international consensus reports and recommendations on the use and dosing of OnaBTX-A, AboBTX-A and IncoBTX-A in different Western countries of the USA, Russia, and Europe confirmed a lack of consensus on the use of all the BoNTs in different countries, as well as the absence of a unified consensus design (Tables 5.6 and 5.7) [36].

How to Inject: Dosage and Practical Important Points

When one performs injections of a BoNT or any other injectable in the periorbital area, both the patient and the physician should remain relaxed, comfortable, and without distractions. The patient should be in a sitting or semireclined position, approachable from both sides of a well-lit treatment table. Before injecting any particular brand of BoNT, a thorough pretreatment evaluation of the patient and his or her wrinkles should be performed. This should include examining the patient at rest and in full motion. While determining the dose for treating the medial periorbital area, lightly palpate the muscles of the glabella with the palmar surface of the fingertips of the nondominant hand as the patient

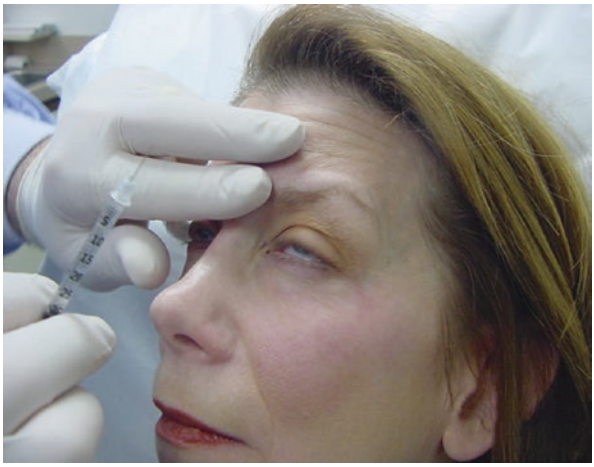

Fig. 5.11 Palpation with the palmar surface of the non-dominant hand fingertips helps determine the location and dose of BoNT-A to be injected

forcibly squints and frowns (Fig. 5.11). This will help ascertain the location, size, and strength of the individual glabellar muscles to be treated. When treating the glabella, there are FDA approved dosaging and standard injection points (Fig. 5.12b). While varying an injected dose of BoNT-A for each individual patient can produce a more delicate and refined result, neophyte injectors should initially adhere to the on-label dosing and approved injection techniques of the BoNT-A being used. As one develops expertise in treating patients, then one can develop his or her own injection technique and preferential dosing. The frequently used and standardized injection technique for treating the glabella is to inject a BoNT-A into five different sites with doses that have been approved by the FDA (Fig. 5.12). On-label dosing depends on the proprietary BoNT product being used (see Tables 5.6 and 5.7) [1–5, 17, 37–39]. As one becomes more adept at injecting the BoNTs, standard on-label dosing can be modified to best improve the pattern of the individual patient's wrinkles, especially when one is treating the variable glabellar patterns of wrinkles that can occur with different patients. Trinidade et al. have described five diverse patterns of glabellar wrinkles (Figs. 5.3, 5.3, 5.5, 5.6, and 5.7) [7]. For each of the distinct glabellar wrinkle patterns, variations in dosing and injection placement can enhance the final aesthetic outcomes (12A). Typically, because of the strength of their glabellar muscles, men require approximately twice the number of units and sometimes even more injection points (7 or more sites across the glabella and medial brow) to produce a desired effect which lasts at least 3–4 months (Fig. 5.13) [40–44].

There can be a noticeably high arching of the eyebrows of approximately 2–3 mm, caused by the levator action of the frontalis in those patients whose glabellar depressors have been substantially weakened, if the interdigitating muscle fibers of the frontalis immediately above the brow have not been weakened [45–49]. This is the result of the dynamic relationship between the brow depressors (corrugator supercilii, depressor supercilii, orbicularis oculi, and procerus) and their brow elevator (frontalis), the only levator muscle of the upper face (Figs. 5.1 and 5.2) [45, 47]. Ordinarily, the effects of a BoNT treatment of glabellar frown lines can last at least 3–4 months. Patients treated with a BoNT can experience some asymmetry for various reasons, particularly those who are treated for the very first time. Therefore, all patients should return for a post-treatment re-evaluation and possible touch-up injections within 2–3 weeks after any

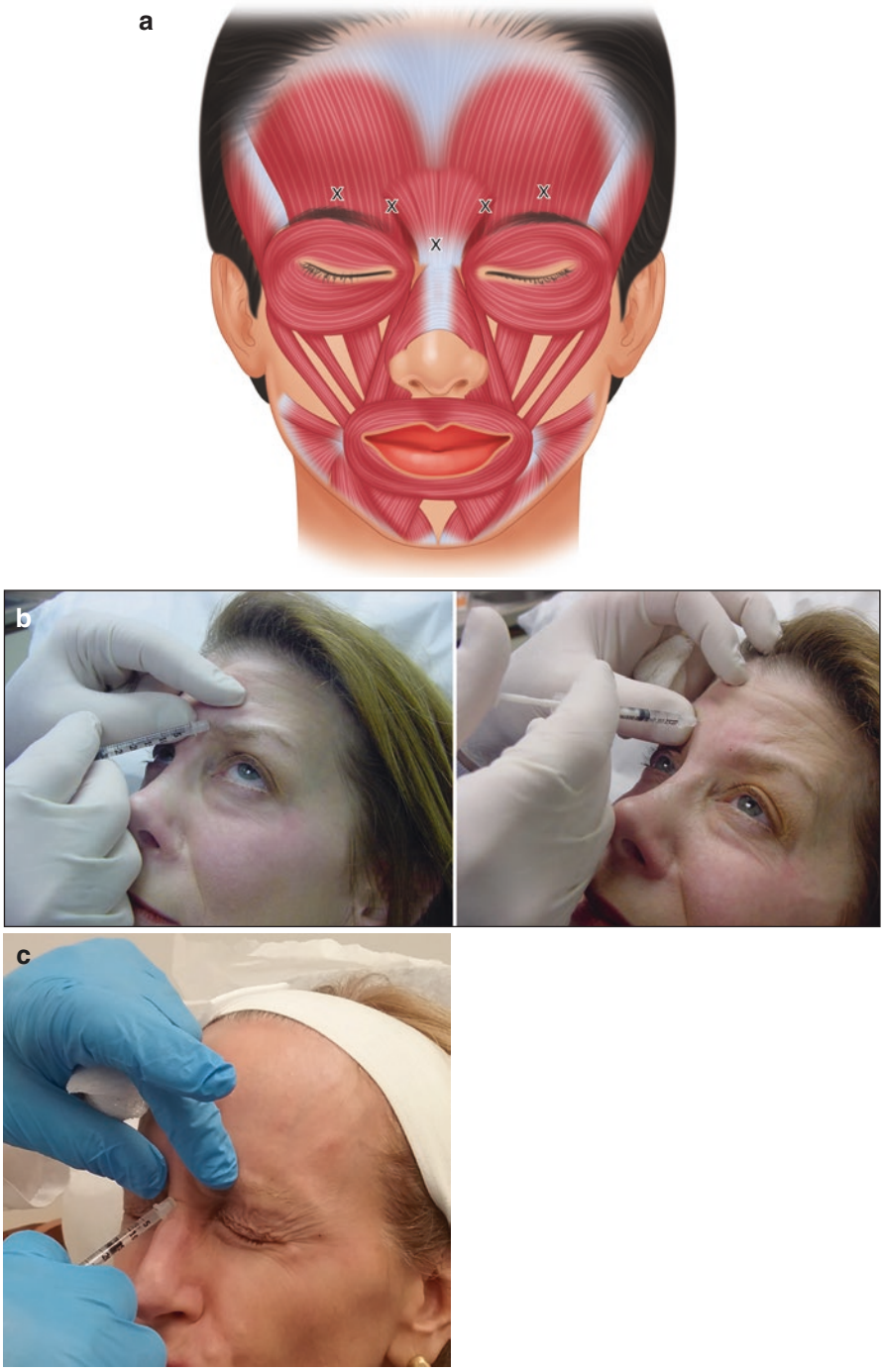

Fig. 5.12 (**a**) Standard five injection points for treating glabellar frown lines. (**b**) Technique of injecting the corrugator supercilii. (**c**) Injecting the procerus in the midline of the nasal root should be done deeply just above the bone

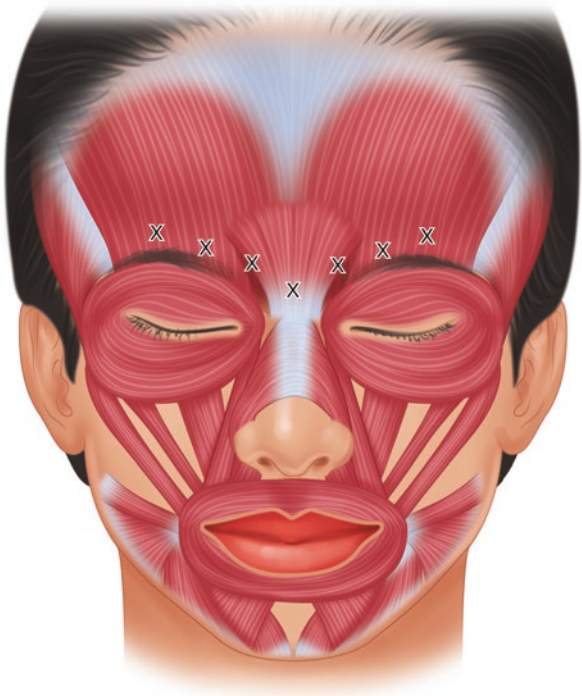

Fig. 5.13 Standard seven injection points for treating stronger glabellar muscles causing deeper furrows and frown lines

treatment session. Different BoNT-As may last longer than others for many different reasons. Also, frequent maintenance treatments with any of the different BoNT-As may eventually prolong the interval between subsequent treatments, especially after 2 or 3 years of regularly scheduled injection sessions every 12–15 weeks.

The lateral canthi are the other sites which can be treated on label, but specifically only with onabotulinumtoxinA (OnaBTX-A) and abobotulinumtoxinA (AboBTX-A) to enhance and rejuvenate the periorbital region. As with the glabella, the lateral canthi should be evaluated thoroughly before treatment by having the patient forcibly squint and then smile to show the full appearance of their teeth. This will cause the patient to display the extent of their wrinkles in the lateral canthal area. When injecting OnaBTX-A or AboBTX-A in a lateral canthus, one should stand on the opposite side of the treatment area with the patient facing toward the injector. This will allow the physician to approach the lateral canthus with the tip of the needle pointed lateral to and away from the patient's eye. Stretching the skin over the target area with the non-dominant hand under ample lighting enables the physician to visualize the multitude of blood vessels that lie just beneath the surface of the skin in this area (Fig. 5.14). While injecting OnaBTX-A or AboBTX-A around the lateral canthus, it is important to remain at least 1.5–2.0 cm lateral to the lateral bony orbital rim [1, 50, 51]. The approved recommended dose for the cosmetic treatment of lateral canthal wrinkles is 4 U of OnaBTX-A or 10 U of AboBTX-A injected into each of three sites subcutaneously in the lateral periorbital area 1.5–2.0 cm apart from each other for a total dose of 12 U of OnaBTX-A or 30 U of AboBTX-A at each lateral canthus (Figs. 5.15 and 5.16).

There are two injection patterns approved by the FDA for injecting OnaBTX-A in the lateral canthal area (Figs. 5.15 and 5.16). One injection pattern is indicated when

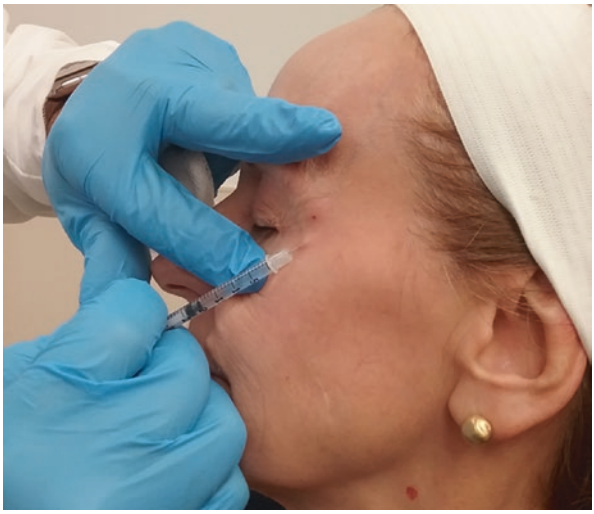

Fig. 5.14 Injecting crow's feet or lateral orbital orbicularis oculi. Note the injector stands on the opposite side, pointing and inserting the needle away from the lateral canthus and globe. Stretching the skin with the non-dominant hand assists in visualizing superficial periocular vasculature

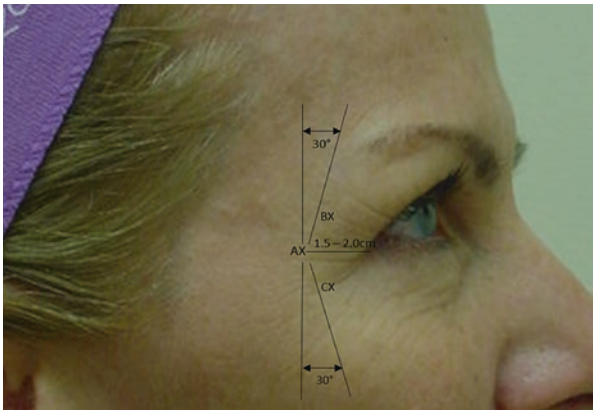

Fig. 5.15 This injection pattern is recommended for lateral canthal wrinkles that radiate outwardly in parallel lines starting from a point in the center of the lateral canthus. The starting point (AX) should be injected at least 1.5–2.0 cm lateral to the lateral canthus and bony orbital rim. The second injection point (BX) is approximately 1.5–2.0 cm superior to (AX) and placed at a 30° angle anteriorly, while always remaining 1.5–2.0 cm lateral to the bony orbital rim. The third injection point (CX) is angled in the same direction but inferior to injection point (AX), and must remain superiorly positioned to the upper border of the zygomatic arch (Frankfurt Plane) and no more medially to an imaginary vertical line that passes through the lateral canthus

the lateral canthal wrinkles radiate away from the bony orbit toward the temporal fossa symmetrically above and below the meridian of the lateral orbit. Injections of OnaBTX-A or AboBTX-A should begin from a starting point that is at least 1.5–2.0 cm lateral to the lateral bony orbital rim (Fig. 5.15: AX). This central injection starting point (point AX) should be where 4 U OnaBTX-A or 10 U of AboBTX-A is injected (Fig. 5.15: AX). The second injection point (point BX) (Fig. 5.15: BX) is where another 4 U of OnaBTX-A or 10 U of AboBTX-A is injected at a 30° angle, 1.5–2.0 cm superiorly and anteriorly from the first point (point AX) and approximately 1.5–2.0 cm

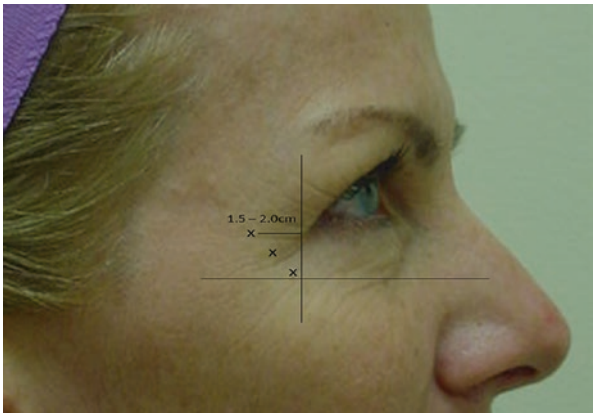

Fig. 5.16 This injection pattern is recommended for patients in whom the majority of lateral canthal lines appear below an imaginary horizontal line that bisects the lateral canthus. The 3 injection points should each be placed approximately 1.5–2.0 cm lateral to the lateral canthus, remaining superiorly positioned to the superior border of the zygomatic arch (Frankfurt Plane) and no more medially than an imaginary vertical line that passes through the lateral canthus

laterally from the bony orbital rim. The third injection of 4 U of OnaBTX-A or 10 U of AboBTX-A is placed 1.5–2.0 cm inferiorly and anteriorly to the first injection point at the same 30°angle (point CX) (Fig. 5.15: CX) and approximately 1.5–2.0 cm lateral to the bony orbital rim (Fig. 5.15: AX). With this third and inferiorly placed injection, it is imperative to remain superior to the upper border of the zygoma and lateral to an imaginary vertical line passing through the lateral canthus.

The second recommended injection pattern should be utilized for those patients whose lateral canthal rhytides are positioned primarily below the horizontal meridian of the lateral canthus (Fig. 5.16). The three injection points of 4 U of OnaBTX-A or 10 U of AboBTX-A each should be placed approximately 1.5–2.0 cm lateral to the lateral canthus and 1.5–2.0 cm from each other with the lower injection point placed no more inferiorly to the superior border of the zygoma and no more medially to an imaginary vertical line that passes through the lateral canthus (Fig. 5.16).

Since the skin of the periorbital area is thin, the tip of the needle should be inserted no more deeply than 2–3 mm below the skin surface, bevel pointing downward. Raising a wheal at each injection point is proof the injections are given at the proper depth (Fig. 5.17). This will allow the OnaBTX-A or AboBTX-A to spread slowly and evenly into the underlying lateral muscle fibers of the orbital orbicularis oculi. Men may need slightly higher dosing, approximately 15–20 U of OnaBTX-A per side for comparable results (Fig. 5.18) [1]. Because there also can be variable patterns of wrinkling of the lateral canthal lines in different patients, OnaBTX-A or AboBTX-A treatments should be individualized for each patient (Fig. 5.19). Depending on a patient's age and amount of skin laxity, the lower malar creases can continue over the malar aspect of the cheeks as far down as the corners of the mouth (Fig. 5.20). Characteristically, a patient can possess any one or multiple patterns of creases that can even be different in shape and severity from the right-to-left side of the face (Fig. 5.21) [52]. In addition, an individual can possess a certain amount of both static and dynamic wrinkles, but only the dynamic ones are

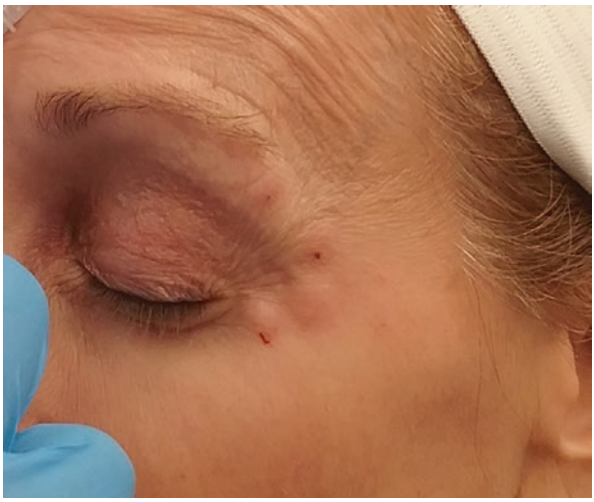

Fig. 5.17 Raising a wheal at each injection point will guarantee the injection is given at the proper depth in the crow's feet

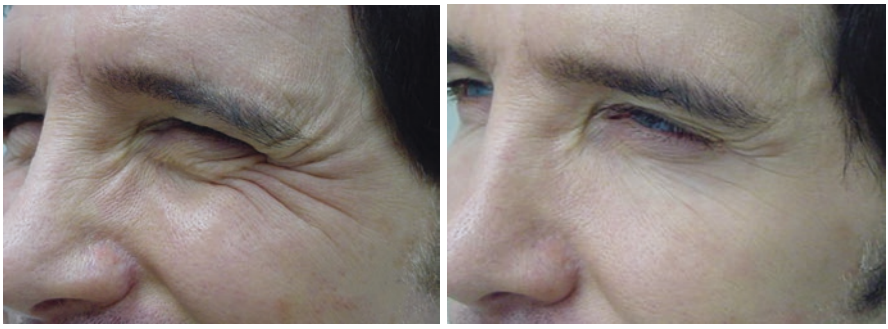

Fig. 5.18 Men may need slightly higher dosing than women, as was done in this patient with 18 U of onabotulinumtoxinA per side for comparable results. This patient is seen before and 1 month after treatment

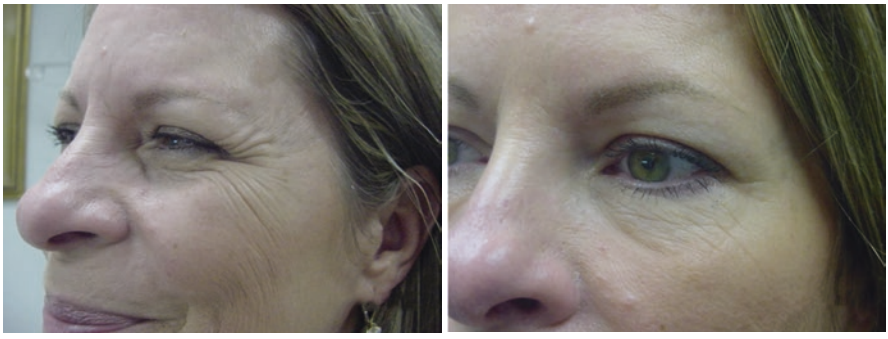

Fig. 5.19 This patient is seen before and 3 weeks after treatment for crow's feet

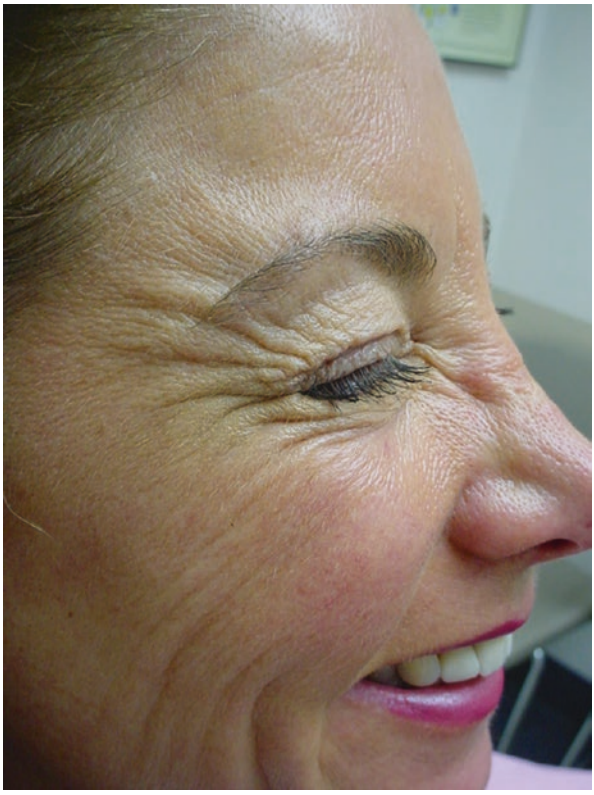

Fig. 5.20 With the lateral canthi, the lower malar creases can continue over the malar aspect of the cheeks as far down as the corners of the mouth

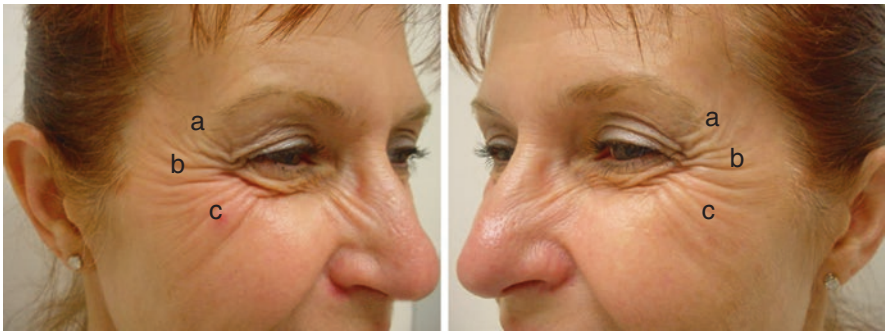

Fig. 5.21 Different patterns of crow's feet: (**a**) upper eyelid; (**b**) lateral; and (**c**) lower eyelid and malar creases of the left and right side of the face before treatment with onabotulinumtoxinA

reducible by injections of OnaBTX-A or AboBTX-A. With experience, a physician injector will develop the expertise to adjust the number of injection sites and dose of OnaBTX-A or AboBTX-A depending on the pattern, depth, and severity of lateral canthal wrinkling in conjunction with the thickness of the skin and the presence or absence of blood vessels (Fig. 5.22) [37–39, 51–54]. In order to avoid puncturing any one of the

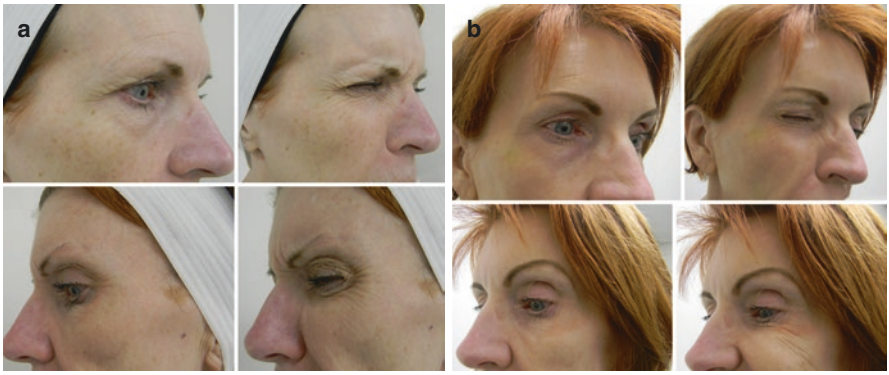

Fig. 5.22 This patient is seen before (**a**) and 1 month after (**b**) treatment of lateral canthal lines with onabotulinumtoxinA

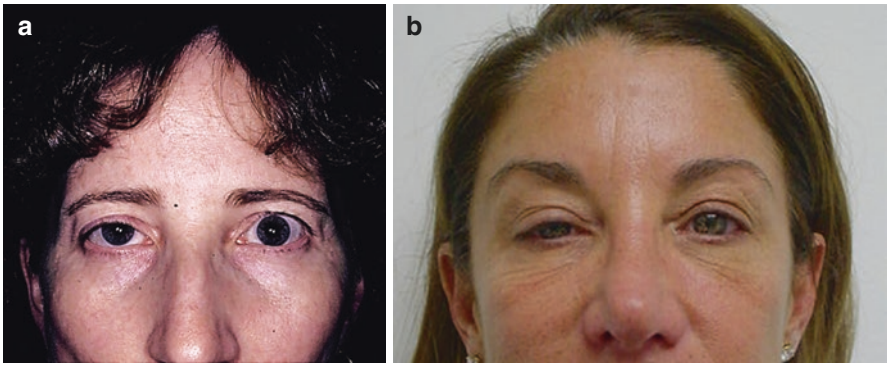

Fig. 5.23 (**a**, **b**) Upper eyelid blepharoptosis (over the right eye of both patients) is one of the most significant and frequently occurring complications seen when injecting any of the BoNTs in the periorbital region. Blepharoptosis is probably caused by the spread of injected BoNT through the orbital septum, weakening the levator palpebrae superioris

many superficial vessels found in and around the lateral canthus, injections of OnaBTX-A or AboBTX-A can be placed intradermally or subcutaneously, producing wheals on the surface of the skin (Fig. 5.17). One must avoid deep injections placed inferiorly to the upper border of the zygoma because this will adversely affect and weaken the upper lip levators (zygomaticus minor and major) and result in asymmetry in the lower face and dysfunctional perioral movements [55]. The duration of effect of OnaBTX-A or AboBTX-A treatments of the lateral canthi usually is about the same as that seen in other areas of the face. At least 3 months and sometimes up to 4 or more months with OnaBTX-A, but up to 6 months with AboBTX-A of diminished crow's feet can be obtained with the proper dosing and accurate placement of the injections. For some patients, the duration of effect is extended with repeated treatments of OnaBTX-A and AboBTX-A.

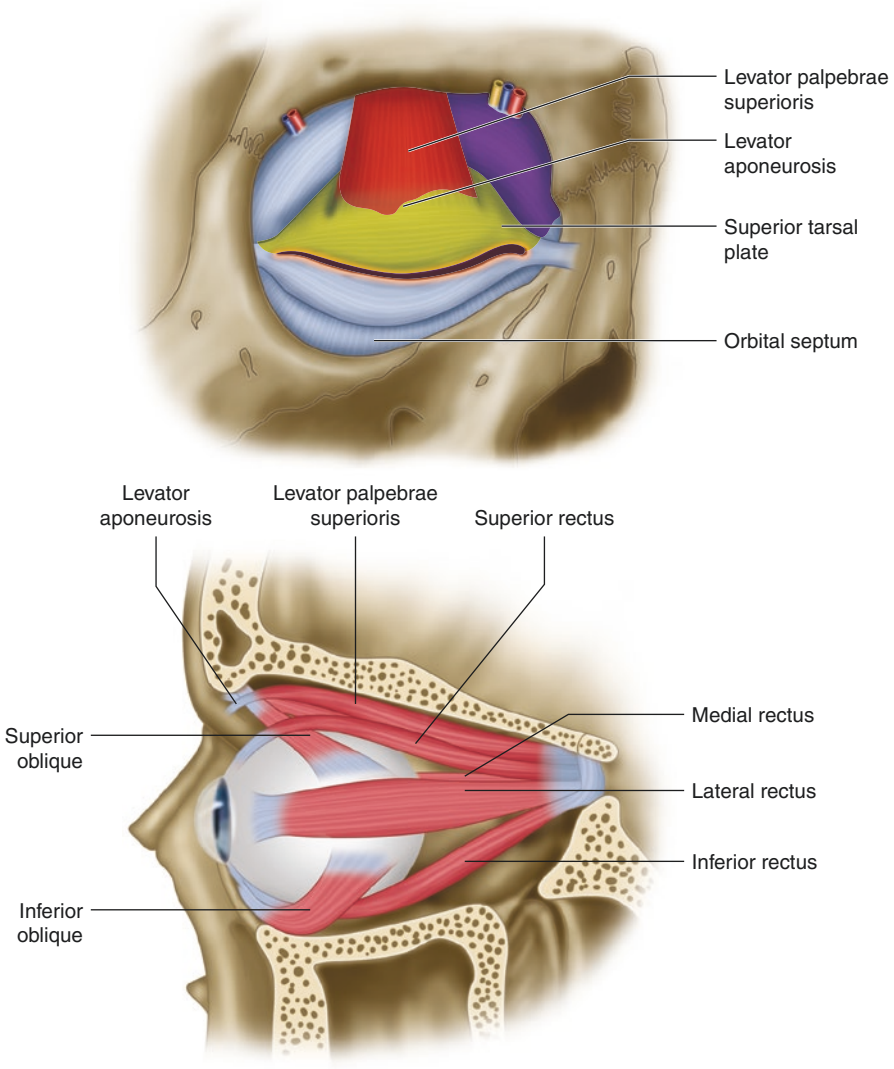

Fig. 5.24 Blepharoptosis can be caused by the spread of injected BoNT through the orbital septum, weakening the levator palpebrae superioris

Possible Complications and How to Handle Them

Upper eyelid blepharoptosis is one of the most significant and frequently occurring complications seen when injecting any of the BoNTs in the periorbital region (Fig. 5.23a, b) [22, 49, 56]. Blepharoptosis is probably caused by the spread of injected BoNT through the orbital septum, weakening the levator palpebrae superioris (Fig. 5.24). This can occur more frequently in older patients in whom the barrier function of the orbital septum is

weakened with age, or when large volumes of highly diluted BoNT-A are injected quickly, forcibly, deeply, low and close to the bony supraorbital margin at the midpupillary line. Occasionally at this location, some actual muscle fibers of the levator palpebrae superioris can extend anteriorly into the levator aponeurosis, allowing the injected BoNT-A easy access to functional muscle fibers thereby weakening the levator palpebrae superioris and causing ptosis of the upper eyelid (Fig. 5.23a, b). Unexpected blepharoptosis in a younger patient is usually the result of forceful injections of a BoNT-A placed too deeply in the area of the midbrow, particularly with high volumes. Another reason for inadvertent blepharoptosis is when a BoNT-A is routinely injected deeply into the skin at a fixed distance of 2 cm from the upper border of the eyebrows instead of 2 cm from the bony superciliary arch or ridge. The eyebrows commonly sit approximately 5 cm above the upper eyelid crease in women. Men's eyebrows usually grow directly over or below the superciliary ridge. There are some women, however, whose eyebrows rest just as low as men's. Therefore, instead of using the eyebrows as a point of reference for injecting BoNTs, one should use the upper orbital bony margin or rim as the reference point and not inject BoNT any lower than 3–4 cm above the upper margin of the bony orbit or 2–3 cm superior to the superciliary ridge or arch. Injecting a BoNT-A immediately above the eyebrows in men or women puts their levator aponeurosis at risk of exposure with the BoNT as the aponeurosis exits the superior margin of the bony orbit (Fig. 5.24). Any injection less than 3 cm above and away from the bony orbital rim, regardless of where the eyebrow sits over the superciliary ridge, will allow the BoNT to reach the levator aponeurosis directly or indirectly and weaken its distal muscle fibers and cause blepharoptosis.

Blepharoptosis is a 1–2 mm or more drop of the upper eyelid, obscuring the upper border of the iris (Fig. 5.23) [49]. Blepharoptosis can appear as early as 48 h and up to 7–10 days after an injection of a BoNT and can last 2–4 weeks or even longer. An antidote for blepharoptosis is the intraocular instillation of one or two drops of 0.5% apraclonidine (Iopidine®, Alcon Laboratories, Inc., Fort Worth, TX), an alpha-2-adrenergic agonist with mild alpha-1 activity. It will temporarily contract Müller's muscle (a nonstriated, smooth, sympathomimetic levator muscle of the upper eyelid), and raise the upper eyelid approximately 1–2 mm. If ptosis persists after 15–20 min, the instillation of an additional one or two drops may be required before the affected eyelid will elevate. This procedure can be repeated three to four times a day. Approximately 20% of patients can develop a contact conjunctivitis with the frequent use of apraclonidine. The mydriatic and vasoconstrictor phenylephrine (Mydfrin 2.5%, Alcon Laboratories, Inc., Fort Worth, TX, or Neo-Synephrine® HCl, 2.5% Ophthalmic Solution, USP, Paragon BioTeck, distributed by Bausch & Lomb [a division of Valeant, Laval, Quebec, Canada]) is an alpha-1 agonist that also can be used when apraclonidine is not available [37]. However, there are more potential side effects associated with the use of phenylephrine than with apraclonidine even when only the 2.5% ophthalmic solution is used. Phenylephrine can increase intraocular pressure, cause systemic allergic and urticarial reactions, local contact and irritant dermatitis and acutely exacerbate narrow angle glaucoma, cardiac arrhythmias, and hypertension. Because it also is a potent mydriatic, even one drop of phenylephrine will prevent the patient from accommodating as usual and visual acuity can be compromised. Ophthalmic mydriatics and vasoconstrictors because of their multiple side effects profile, should only be used on an as-needed basis when utilizing them just to elevate blepharoptosis.

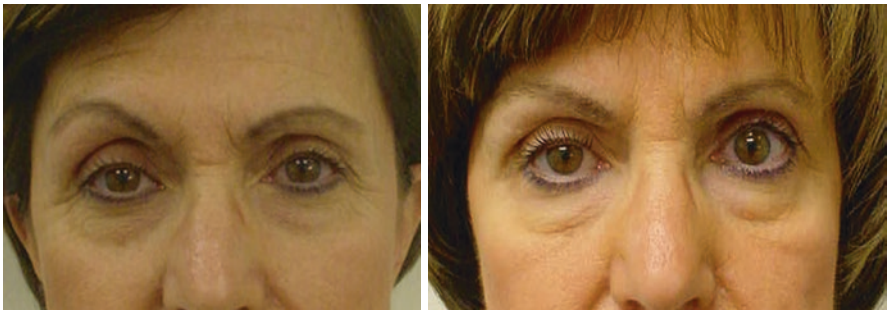

Fig. 5.25 Older patients with dermatochalasis of brow and eyelid skin lift the soft tissue of the brow to maintain their upper eyelids in a constantly raised position to compensate for a heavy, lax brow. When this 'compensatory brow lifting', made possible by the lower fibers of the frontalis, is weakened by injections of BoNT, the result is a 'secondary blepharoptosis', which became obvious in this patient after a BoNT treatment

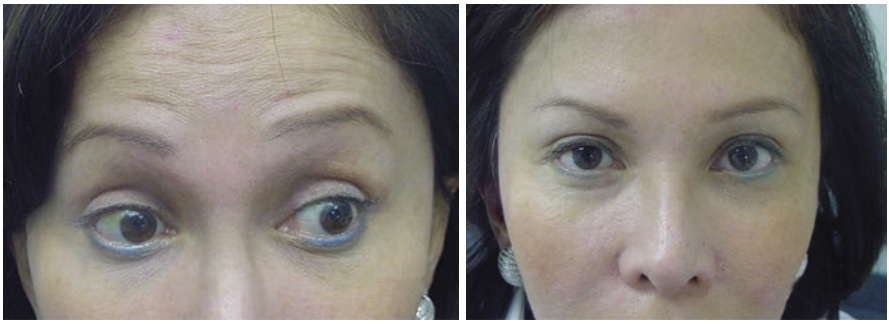

Fig. 5.26 Note the left eyebrow is higher than the right before treatment with onabotulinumtoxinA, but more symmetrical after treatment

Secondary blepharoptosis can be induced when the lower fibers of the frontalis are weakened, producing a drop in the height of the brow. The weight of the ptotic brow then impinges on the upper eyelid and causes it to drop, narrowing the vertical palpebral aperture or fissure. This secondary blepharoptosis seems to occur more frequently in older patients who possess dermatochalasis of the skin of the brow and eyelids. To compensate for a heavy, lax brow, some individuals, regardless of age, involuntarily use the lower fibers of their frontalis to lift the soft tissue of the brow to maintain their upper eyelids in a constantly raised position [49]. When this 'compensatory brow lifting', made possible by the lower fibers of the frontalis, is weakened by injections of BoNT the result is a 'secondary blepharoptosis' (Fig. 5.25).

Asymmetry is a minor adverse sequela that sometimes is unavoidable, particularly when a patient is treated for the first time with a BoNT (Figs. 5.26 and 5.27). When one side of the brow or periorbital area becomes weaker than its contralateral side because of an injection of a BoNT this is known as an iatrogenic asymmetry (Fig. 5.28a). Iatrogenic asymmetry is probably the easiest type of asymmetry to correct with a few additional units of the BoNT appropriately and precisely injected into the affected area (Fig. 5.28b).

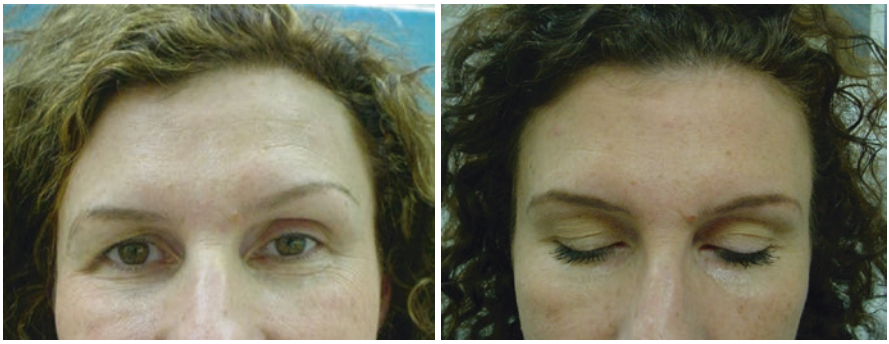

Fig. 5.27 Eyebrow asymmetry corrected with treatment of onabotulinumtoxinA

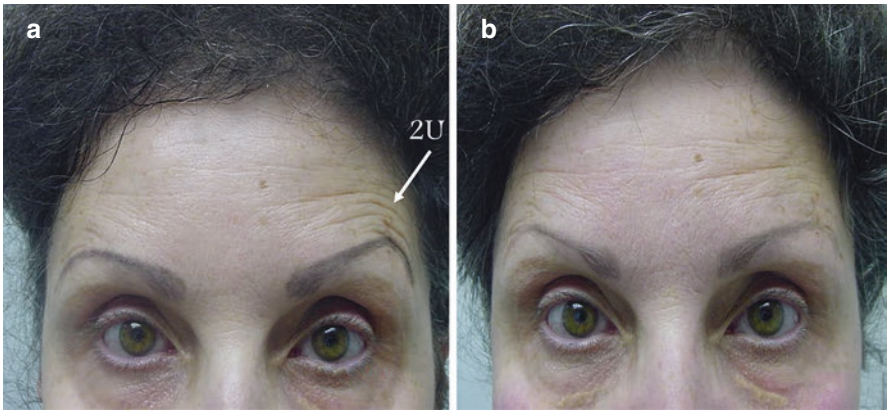

Fig. 5.28 When one side of the brow or periorbital area becomes weaker than its contralateral side because of an injection of a BoNT, this is known as an iatrogenic asymmetry and usually is discovered about 1–2 weeks after a BoNT treatment. (**a**) Iatrogenic asymmetry is probably the easiest type of asymmetry to correct with a few additional units of the BoNT appropriately and precisely injected into the affected area. (**b**) Same patient 3 weeks after an additional 2 U of onabotulinumtoxinA was injected into the hyperkinetic muscle fibers of the frontalis

Other adverse effects caused by injections of BoNT in the periorbital area are the same as those produced by any type of subcutaneous or intramuscular injection. They include pain with injection and erythema, edema and ecchymoses at the injection sites (Fig. 5.29). Rarely, if ever, do any of these side effects last beyond the day of treatment, except for ecchymoses which can last up to 10 days or more afterwards. Injection pain can be partially mitigated with the use of ice before and after the injections, and the application of a topical anesthetic locally. However, the anatomy of the periocular area makes occluding a topical anesthetic to expedite the anesthetic effect somewhat difficult and impractical. Patients also should be reminded to stop for at least 2 weeks prior to treatment any alcoholic beverages, and non-essential, self-administered medications, such as aspirin, nonsteroidal antiinflammatory drugs (NSAIDs), and other over-the counter medications, and food

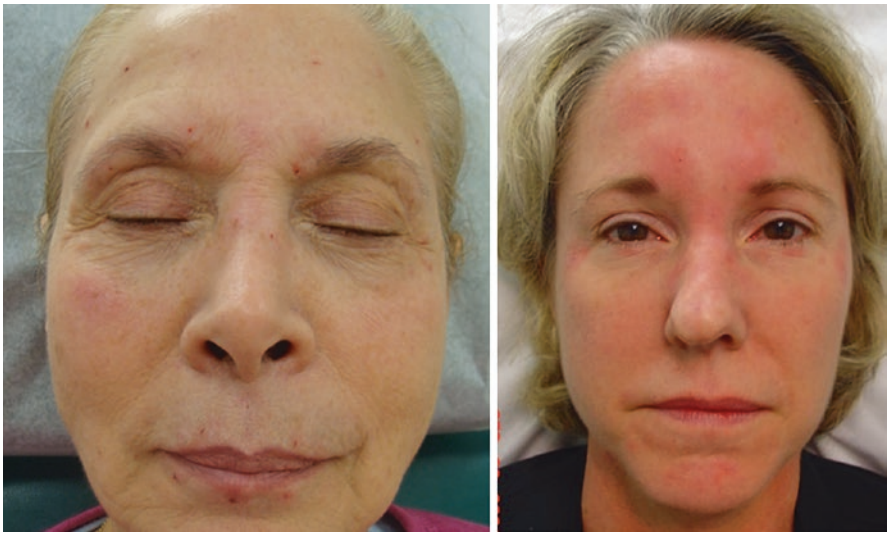

Fig. 5.29 Note the erythema and edema in the pattern of injections following treatment with onabotulinumtoxinA

supplements which increase coagulation time. This will help in reducing injection site ecchymoses.

For some patients, a dull and transient headache with or without general body malaise can occur after injections of a BoNT-A that can last beyond 24–72 h [57]. Headache immediately after a BTX-A injection seems paradoxical since OnaBTX-A injections are now FDA approved for treating tension and migraine headaches [1, 58]. Headaches seem to occur more frequently in patients after their first and subsequent 2 or 3 treatment sessions. They usually cease to occur with subsequent treatments.

Periorbital edema lasting a few hours to days may occur after a periorbital treatment of BTX-A, particularly for a first-time recipient. This is thought to occur because of lymph stasis possibly produced by a reduction of the sphincteric pumping action of the inferior and probably the superior preseptal orbicularis oculi, reducing the efficiency of lymph fluid clearance from the surrounding soft tissue [49]. Also, when there is a substantial reduction in lower eyelid tone, eversion of the punctum and reduced blinking can compromise the action and efficacy of the "lacrimal pump," resulting in transient epiphora, until the normal lower eyelid tone returns (see Fig. 5.10).

When treating the lateral canthal lines with a BoNT-A, if the placement is too low and medial to the lateral canthus, there is a risk of weakening the zygomaticus major and minor, the levators of the lateral aspect of the upper lip and corners of the mouth [52, 55]. This can occur because the zygomaticus major and minor originate at or near the lateral aspect of the superior margin of the zygomatic arch (Fig. 5.30). If either the zygomaticus major or zygomaticus minor is inadvertently exposed to a BoNT-A, the

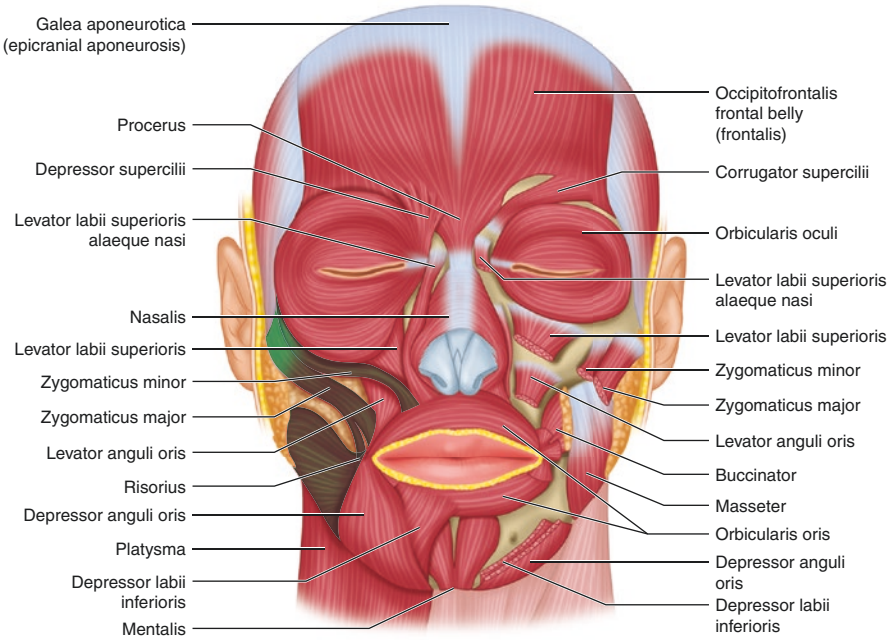

Fig. 5.30 Zygomaticus major assists in lifting the lateral upper lip and oral commissure. Zygomatic minor elevates the upper lip more centrally. Risorius is the muscle of laughter and moves the commissure laterally and slightly upward

lateral one fourth of the ipsilateral upper lip will be weakened, causing a drooping of the upper oral commissure, an asymmetric smile, and possible drooling and dribbling from incontinence of food and liquid. If a BoNT-A is injected or even spreads more medially and inferiorly to the superior margin of the zygomatic arch, then the central and deep upper lip levators (levator labii superioris, levator labii superioris alaeque nasi, and levator anguli oris) can also be affected, causing a more profound interference with upper lip competence and basic sphincteric functions, resulting in dysarthria and dysphagia [55].

Because of their position within the orbit, the lateral and inferior rectus, or inferior oblique are especially disposed to accidental spread of an injected BoNT-A through the orbital septum. This can occur when the injections are too close to the lateral canthus, which is closer than 1.5–2.0 cm from the bony orbital rim. If any of the extraocular muscles are accidently weakened by an improper injection technique of a BoNT-A, diplopia and strabismus will result. Immediate consultation with an ophthalmologist is imperative.

Brow ptosis is caused by the spread of a BoNT-A into the lower fibers of the frontalis when the BoNT-A is injected rapidly and forcefully, or when the area is massaged too vigorously after injection (Figs. 5.31 and 5.32). Patients inadvertently can cause

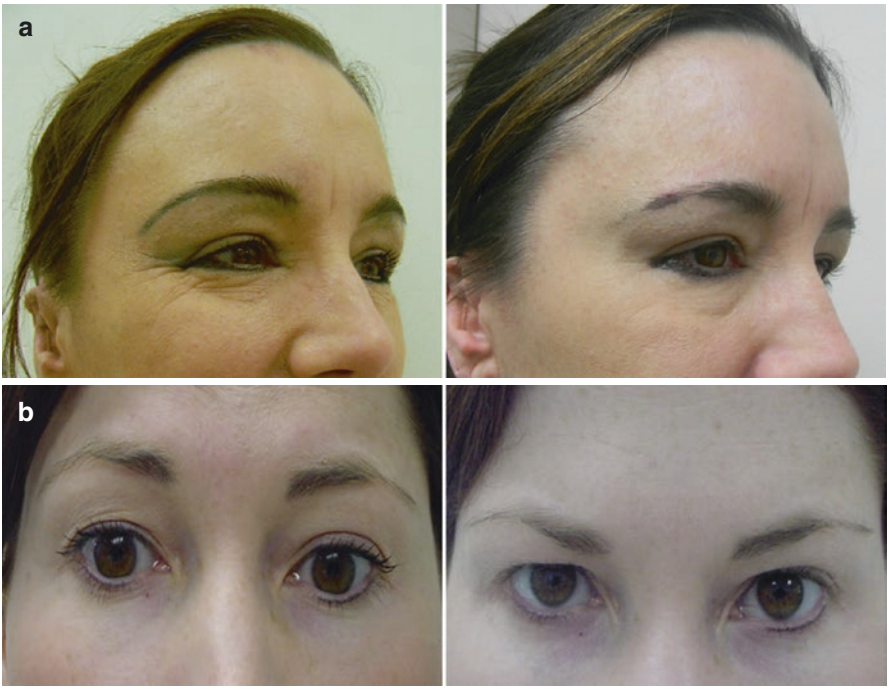

Fig. 5.31 (**a**, **b**) Brow ptosis is caused by the spread of a BoNT-A into the lower fibers of the frontalis when the BoNT-A is injected rapidly and forcefully, or when the area is massaged too vigorously after injection

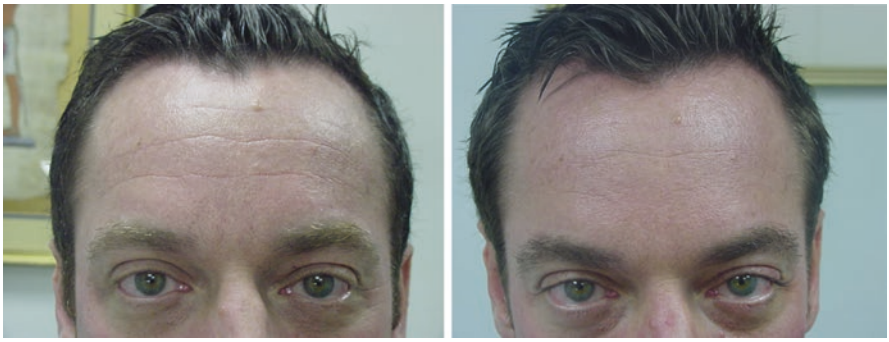

Fig. 5.32 Central brow ptosis. Note the medial brow ptosis after an injection of the glabella and frontalis with onabotulinumtoxinA, causing the medial brow to appear depressed and the lateral eyebrows to appear excessively elevated

brow ptosis if they manipulate and massage the injected area excessively immediately after a treatment session. This is enough to disperse the BoNT-A beyond the targeted area. Injecting large volumes of low concentrations of a BoNT-A, a deviation from the approved method of product reconstitution, also increases the risk of dispersion of product beyond the targeted muscle.

Ectropion occurs when a BoNT-A diffuses into the lower palpebral orbicularis oculi and the muscular sling of the lateral orbicularis is inadvertently weakened by the injections, especially in someone who has had a previous interventional procedure such as a blepharoplasty, deep chemical peeling or laser resurfacing of the eyelids. This is generally seen as lower eyelid retraction appearing as excessive rounding of the contour of the lateral canthus [49].

Proper injection techniques in the approved anatomical locations will avert unintended adverse events that will diminish a patient's confidence in the injector's abilities to inject BoNT-A well. With accumulated experience, a physician injector may want to become creative with their treatments, which will not only enhance the appearance of his or her patients, but will also solidify patients' trust and loyalty (Figs. 5.33, 5.34, 5.35, and 5.36).

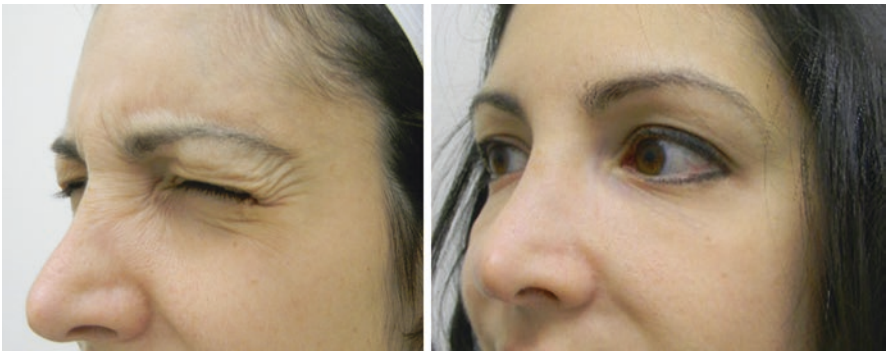

Fig. 5.33 This patient is seen before and 1 month after treatment with onabotulinumtoxinA

Fig. 5.34 This patient is seen before and 2 weeks after treatment with onabotulinumtoxinA

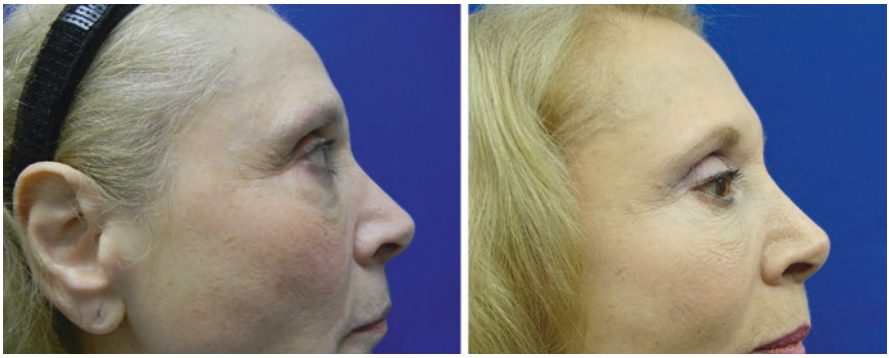

Fig. 5.35 A diminution of periorbital wrinkling and widening of the palpebral fissure enhances the appearance of this 64 year old female

Fig. 5.36 Periorbital wrinkling is eliminated and a naturally appearing widening of the palpebral fissure is accomplished with strategically placed injections of onabotulinumtoxinA

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Chemical Peelings in the Periorbital Region

6

Peter P. Rullan

Introduction

The eye region is the first facial region to show signs of aging, which can make successful Periorbital Rejuvenation (POR) very rewarding to both patient and physician. Periorbital hyperpigmentation (POH) can make a patient look older and more fatigued, and should be taken into consideration with POR [1–3]. POH is a complex condition which is challenging to treat and requires long-term maintenance. These two very common aesthetic conditions can dramatically affect a person's face, whether male or female. Treatment options are as numerous as the anatomic and causative variables involved. The treating physician needs to have a detailed understanding of facial anatomy to properly diagnose the underlying cause and treat accordingly.

Periorbital Rejuvenation

Background

Periorbital aging is variable, based on individual or familial anatomic features involving bone (resorption), fat (pseudo-herniation), muscle (laxity, heaviness, motility) and cutaneous tissue (wrinkles, elastosis). Successful outcomes with chemical peeling depend on understanding these structural variables, since a multimodal approach is commonly needed to rejuvenate this area. Treatment options include surgical blepharoplasty, neuromodulators, dermal fillers, lasers, topical agents and chemical peeling agents of varied strengths (Table 6.1). Peels can tighten the anterior lamella in younger patients with only textural changes or mild fat protrusion [4].

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Table 6.1 Comparison of treatment options for POR

Anatomic feature	Surgical/injectable treatment	Chemical peel
Mild skin laxity/ hooding without fat herniation	Pinch blepharoplasty or micropunch blepharopeeling	Hetter peel 0.1–0.4% CO
Heavy eyelids with pseudo-fat herniation	Upper or lower (transconjunctival) blepharoplasty	Hetter peel (done with or after blepharoplasty)
Hollowed tear trough	Dermal fillers	Superficial peels or low fluence erbium
Crow's feet	Neuromodulators/dermal fillers	Hetter peel (in conjunction with neuromodulators/fillers)

Role of Chemical Peels in Periorbital Rejuvenation

Classification

Chemical peels are classified by the depth of injury produced [4, 5]. Superficial peels will not improve tissue laxity, but can improve skin tones. If skin tightening is desired, then achieving a medium-depth peel is necessary. Peels using 35% trichloroacetic acid (TCA)—alone or preceded by dry ice, Jessner's solution, or 70% unbuffered glycolic acid—are effective for achieving these medium-depth peels and can be repeated in 3 month increments for additive effect [5]. More significant tissue laxity, with or without pseudo-herniation of fat pads, requires surgical (blepharoplasty) or chemical tightening of the anterior lamella. Phenol-croton oil peels are one of the most effective chemical treatment options in this case [6].

History

In 2000, the plastic surgeon Greg Hetter published a landmark set of articles analyzing all known phenol-croton oil peel formulas [7–10]. His quest was to find the active ingredient in these formulas. In these articles, Hetter disproved the common dogma being taught, namely that croton oil was diluting the phenol. Instead, he found the peel solution became stronger as the concentration of croton oil was increased. Furthermore, he devised a progressive croton oil table denoting where low concentrations could be used in thin skin areas like the eyelids and neck, and higher concentrations in thicker skin areas like the upper lip [10].

Segmental Peeling

Segmental phenol-croton oil peels are simpler to learn and perform than full face peels (Figs. 6.1, 6.2, and 6.3) [11, 12]. In skin types I–III, the periorbital skin can be peeled with a very low risk of pigmentary complications like PIH. Patients may experience temporary dyschromia which evens out over several months or at most 2 years [12, 13]. Sun-tanning must be avoided to reduce the severity and longevity of this dyschromia. Skin type IV can be peeled, but the smallest area possible should be treated within the cosmetic unit, such as the upper eyelid skin between the pretarsal skin and the lower margin of the brow. In general, skin types IV and darker will respond better to surgical and dermal filler options [14].

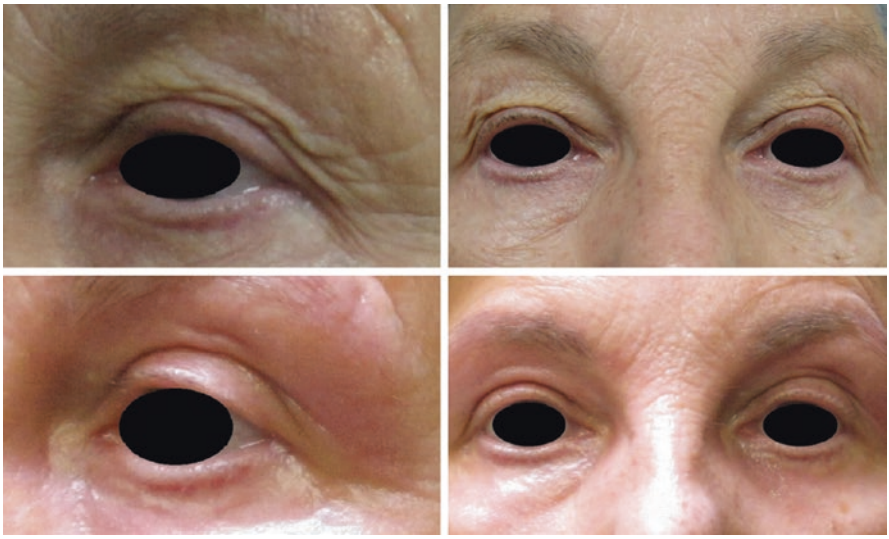

Fig. 6.1 Before treatment and 3 months post-Hetter VL (0.1% croton oil)

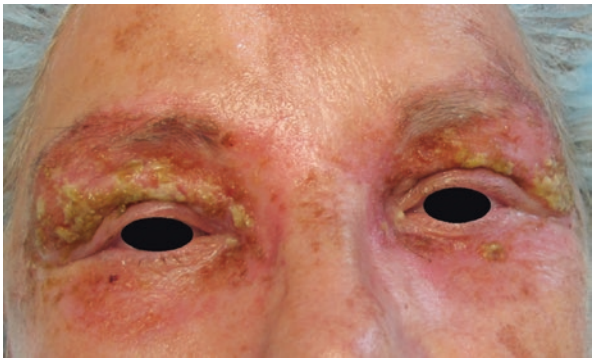

Fig. 6.2 3 days post-Hetter VL (0.1% croton oil)

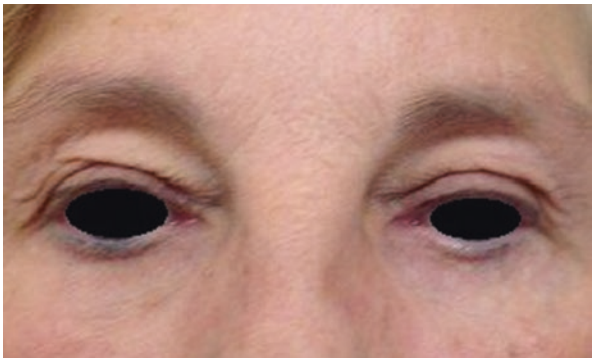

Fig. 6.3 Patient shows lasting results 2 years post-Hetter VL (01.% croton oil)

Technique

Most phenol peel experts agree that variations in application technique can affect the depth of the peel, regardless of croton oil concentration [6]. Therefore, it is essential to identify certain clinical endpoints. The trained physician needs to recognize these key visual indicators: a thin, transparent frost with a pinkish background indicates a peel to the papillary dermis, while a solid, thick, organized frost shows the peel has penetrated to the upper to mid reticular dermis [13]. For peeling the lower lid, the solution should reach the edge of the ciliary margin [12, 13]. Regular or milia Q-tips can be used to apply the solution. Care should be given to the wetness of the applicator and the number of passes being done. Although these are weak concentrations, the thin eyelid skin will frost as expected. The upper eyelids typically respond best to the Very Light 0.1% croton oil solution (Table 6.2). Usually the upper lids are only peeled to the tarsal fold. Most importantly, the success of this peel in correcting laxity depends on treating patients without heavy eyelids and without pseudo-fat herniation (Figs. 6.4 and 6.5).

In darker skin types, the peel should be contained within the borders of the orbital rim. This area of skin responds well to treatment and can easily be camouflaged by makeup or glasses during recovery [13]. The peel is done slowly, under local anesthesia [5]. Recovery typically takes 6–7 days. For a shorter recovery time, a series of lighter peels can be done over time [13].

Table 6.2 Hetter's phenol-croton oil formulas for thin skin areas [10]

Medium Light (0.35% croton oil)	
Phenol 88%	4 cc
Water	6 cc
Septisol[a]	16 gtts
Croton oil	1 gtt
Very light (0.1% croton oil)	
Phenol 88%	2 cc
Water	5 cc
Medium light formula	3 cc

[a]Septisol is a trademark of Steris Corp (Mentor, OH)

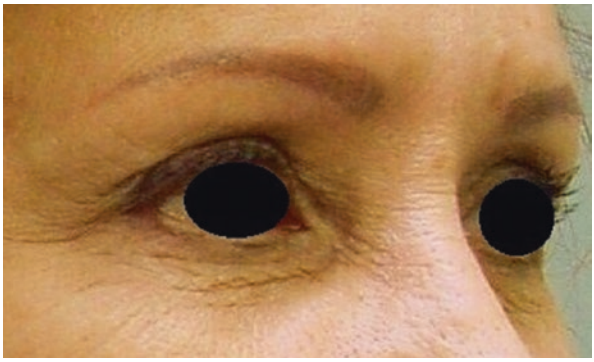

Fig. 6.4 Before upper and lower lid Hetter VL (0.1% croton oil)

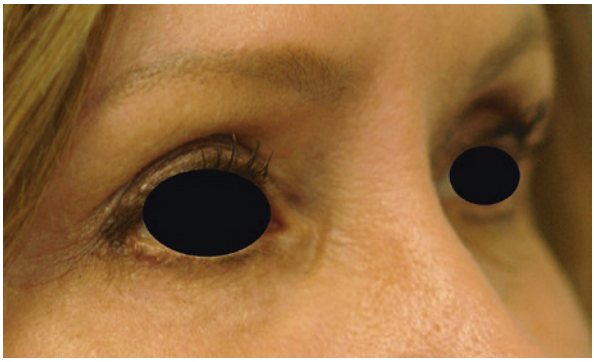

Fig. 6.5 After upper and lower lid Hetter VL

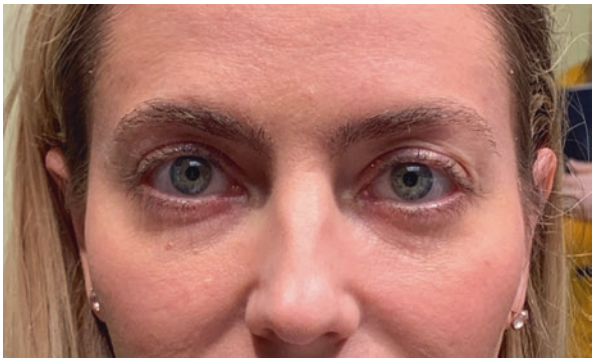

Fig. 6.6 Before micropunch skin removal and Hetter ML (0.35% croton oil)

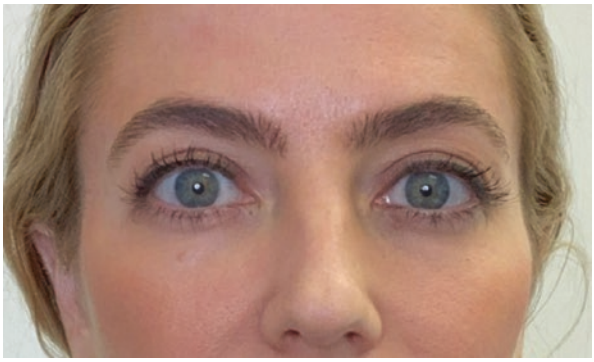

Fig. 6.7 6 months after micropunch skin removal and Hetter ML (0.35% croton oil)

Surgical and Chemical Peel Combined

Micropunch blepharopeeling is a combination surgical and chemical peel procedure recently developed for correcting mild to moderate dermatochalasia (Figs. 6.6, 6.7, and 6.8) [15, 16]. This procedure involves superficially injecting buffered lidocaine with epinephrine into the upper eyelid, then applying very superficial 89% phenol (0.1% Hetter also works well) to the area between the upper eyelid's superior tarsal plate border and the eyebrow's inferior margin, as well as to within 1–2 mm of the

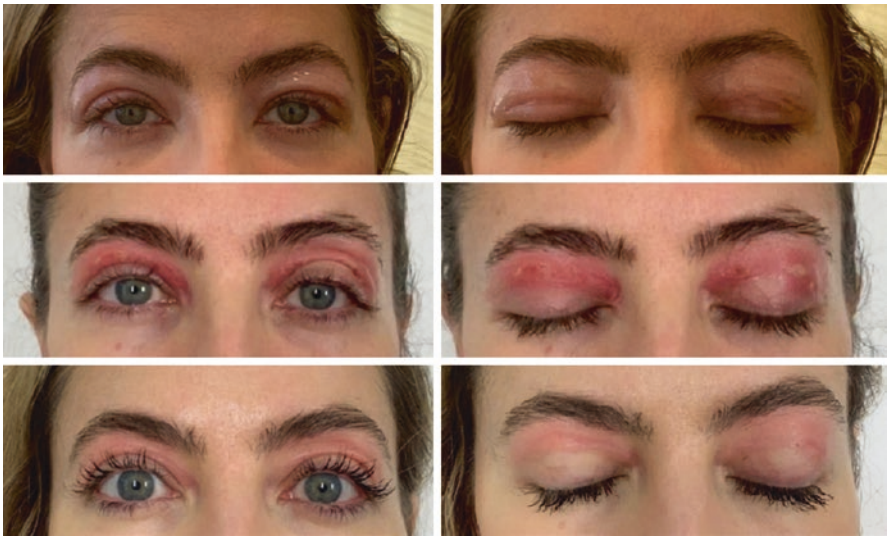

Fig. 6.8 2, 6, and 11 days post-treatment

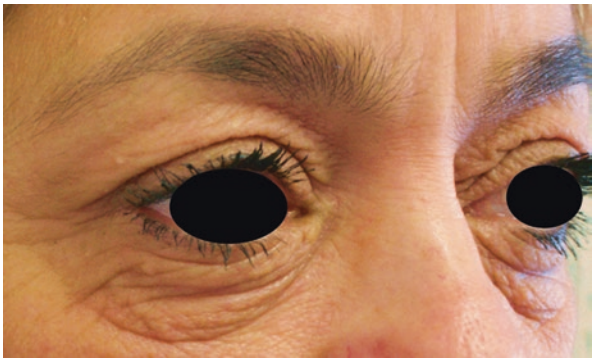

Fig. 6.9 Pre-treatment; combination of surgical and chemical peel treatment proposed

lower eyelid margin [15]. Immediately after frosting, multiple 3–5 mm snips (using iris scissors and Bishop-Harmon forceps) are performed randomly in the centrolateral upper eyelid [4]. Anywhere from 5 to 20 snips may be performed, and these are allowed to heal by secondary intention. Postoperative care includes gentle cleansing and applying Aquaphor™ for 5–6 days [15].

This is a modification of the pinch blepharoplasty, a well-known procedure which involves excising a 2–3 mm strip along the tarsal crease and suturing the myocutaneous flap using 6-0 nylon [11]. Pinch blepharoplasty and phenol-croton oil peels can be combined as well (Figs. 6.9 and 6.10) [6].

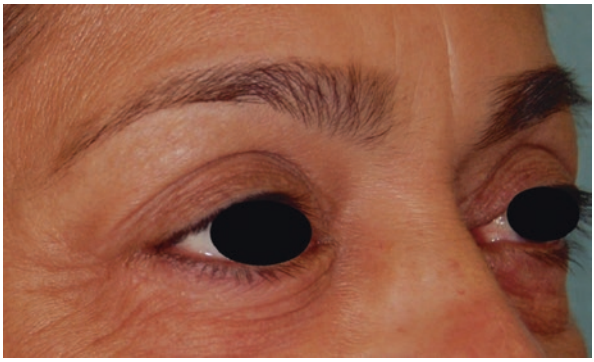

Fig. 6.10 After upper blepharoplasty, lower pinch blepharoplasty and Hetter VL (0.1% croton oil)

Periorbital Hyperpigmentation

Background

POH is easily recognizable, presenting as a bilateral, even-toned, light or dark brown or bluish-black pigmentation around the eyelids (most prominently in the lower lids) [17]. Periorbital dark circles are very troubling cosmetically as they can give the impression of being sad, tired, stressed, or aging. They may also contribute to a diminished sense of self-confidence and well-being [17]. These dark circles can affect patients across every age group, sex and skin type [18]. Possible causative factors of POH include excessive familial melanin pigmentation, hemosiderin deposition from inflammation (irritant contact dermatitis or atopy), and certain medications such as oral contraceptives or ophthalmic prostaglandin [1, 2, 17]. While POH is fairly common, not all dark circles are due to true POH; some dark circles may be caused by translucent lower eyelid skin above the orbicularis oculi muscle. In addition, skin laxity and deep tear troughs may create shadowing which looks similar to POH [1].

Physical Exam

True POH can be distinguished from shadow by stretching the eyelid skin. While the color will clear entirely if it is due to shadow, true POH will only lighten [1, 3]. If the skin coloring becomes more violaceous, this is a sign of thin skin or hypervascularity. Under the light from a Woods lamp, epidermal POH becomes darker whereas dermal tones get lighter [3]. There is often a link between thin skin, a deep shadowy tear trough and a low-set inferior bony orbital rim [1]. However it is unusual to find POH in high-set cheek bones.

Treatment Options for POH

There are many different treatment options for POH, including topical agents like bleaching creams with hydroquinone, kojic or azelaic acid, retinol or retinoic acid, or vitamin C; chemical peels of various strengths; ablative and non-ablative laser therapies; autologous fat transplantation; injectable fillers; and surgery (blepharoplasty) [3, 18]. When performing chemical peels, 2–4 weeks of pretreatment with topical agents is recommended to avoid PIH [3, 14]. Additional physical modalities include camouflage and concealing make-up.

Role of Chemical Peels in Treating POH

Chemical peels can temporarily help correct POH by producing neocollagenesis. This effect camouflages the underlying orbicularis and vasculature which contribute to dark circles. Peeling agents remove melanin from the stratum corneum and epidermis. Deeper peels, which reach the dermis, can remove some of the dermal melanin content [2].

Superficial Peels

The most common peeling agent for POH is 20% glycolic acid (neutralized with sodium bicarbonate) which can result in 73% improvement of melanosis [5, 19]. Lactic acid 15% can result in 56% improvement in periorbital melanosis [19]. 20–30% salicylic acid is also highly effective and low-risk; this can be applied every 2 weeks with little to no downtime (Figs. 6.11 and 6.12). Alternatively, microneedling can be combined with 10% TCA; this has been shown to improve hyperpigmentation in over 90% of patients [20].

Valvouli's study showed that four weekly 3.75% TCA and 15% lactic acid peels (in gel base) resulted in 90% of patients having excellent improvement at 6 months of follow-up [18]. His group reported minimal side effects with 20% of patients experiencing itching, 46.6% experiencing a mild burning sensation, 33.3% experiencing erythema or exfoliation, and 20% experiencing dryness.

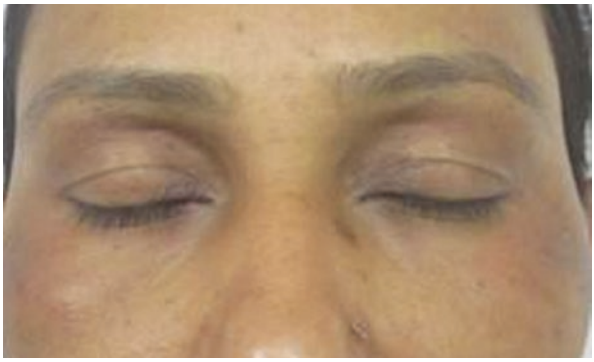

Fig. 6.11 PIH before treatment

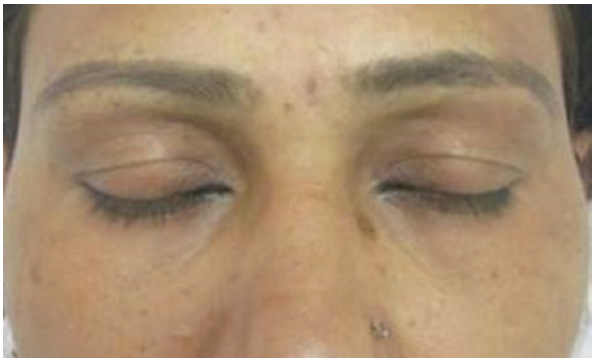

Fig. 6.12 PIH after 6 sessions of 30% salicylic acid peels. Only sunscreen was applied between peels (photos courtesy of Dr. Rashmi Sarkar)

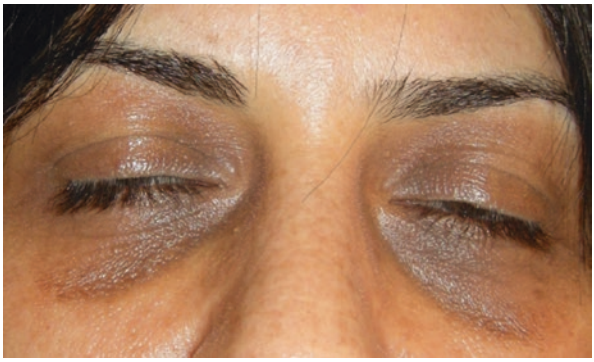

Fig. 6.13 POH before treatment

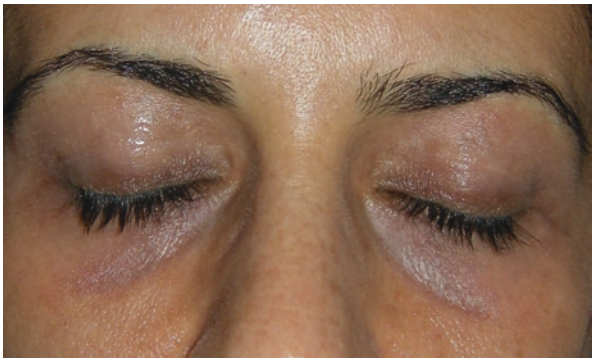

Fig. 6.14 After peeling upper lid with Exoderm™ (photos courtesy of Dr. Marina Landau)

Medium Depth Peels

The most common medium peeling agent is TCA. These peels are available in a variety of concentrations and can be used to achieve deeper treatments with increasing concentration. Some physicians prefer using the phenol-croton oil peels for dermal melanosis seen in POH (Figs. 6.13 and 6.14), as superficial peels may not penetrate deep enough to remove this melanosis (Dr. Marina Landau, personal communication, May 2019). Medium depth phenol-croton oil peels are effective for

resistant POH. Both TCA and phenol-croton oil peels require a 2–4 week preparation with retinoids and bleaching agents, as well as postoperative attention to PIH [5]. Regardless of the croton oil or phenol percentage used, the peeling solution should always be applied with a damp (not wet) Q-tip; application should be stopped as soon as a light white frost with a background erythema is achieved, indicating a medium depth peel down to papillary dermis. Postoperative care includes white vinegar compresses (1 tbsp. in 1 cup of water) and Vaseline/Aquaphor™ ointment for 5–6 days.

Adverse Events

1. Post-inflammatory hyperpigmentation (PIH) is the most common adverse event from peels (Figs. 6.15, 6.16, and 6.17). This is temporary and may be seen weeks after the initial recovery period [13]. PIH responds well to topical retinols/retinoids, mild anti-inflammatory agents and hydroquinone 2–4%. Sun protection is necessary to prevent hyperpigmentation [4].
2. Eyelid ectropion can result from overaggressive peeling of the lower lids. Caution should be taken when performing peels for lid laxity. The preoperative exam should assess this risk and select a milder peel if significant risk factors are present [6, 12].

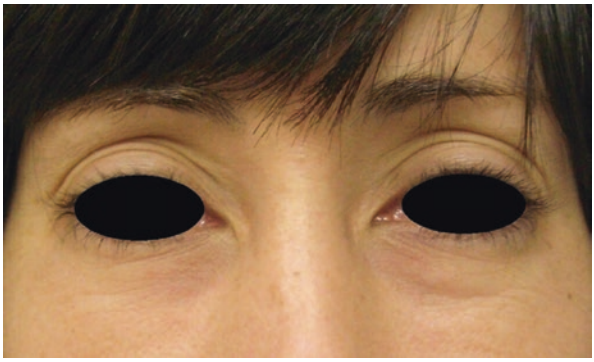

Fig. 6.15 Mild laxity before treatment

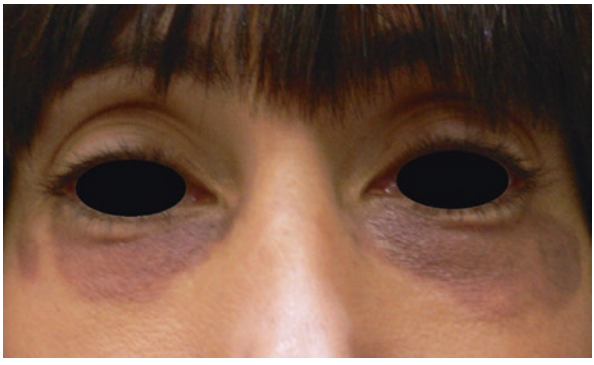

Fig. 6.16 PIH 2 months after lower lid segmental peel

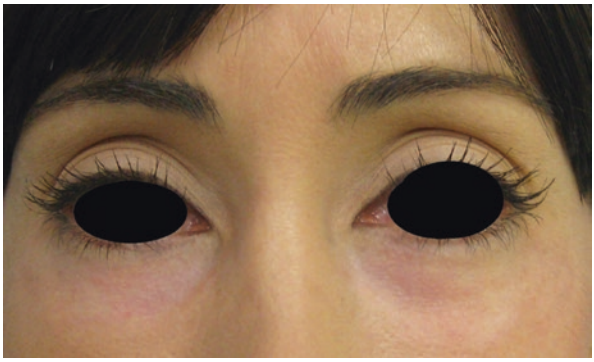

Fig. 6.17 PIH resolved

3. Prolonged erythema (greater than 12 weeks) is a real possibility and requires expert and prompt attention. Overaggressive peeling is usually a factor as well as not preparing the skin with retinoids before-hand [6, 12].
4. Clogged pores or milia may occur early in the healing process, and are linked to overzealous postoperative use of occlusive ointments. Using hyaluronic acid serums or light lotions helps prevent these. Milia can be treated with retinols, or incised and drained with a fine needle or 11-blade [13].

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Lasers and Energy Based Devised Assisted Periorbital Rejuvenation

7

Ashraf Badawi and Shady Mahmoud Ibrahim

Introduction

The periorbital region of the face is an important anatomical area for any surgical and non-surgical rejuvenation procedures which includes different subunits in which the eyes are in the center.

The periorbital area is one of the first regions of the body to show signs of aging, which include static and dynamic rhytids as well as subcutaneous volume loss. The orbital area sends information on general health and impressions regarding individual health, fatigue, emotion and eye-to-eye communication between individuals. Periorbital rejuvenation is one of the most important areas of rejuvenation of the aging face. Typical features of facial aging include changes in skin pigmentation, increased skin laxity, rhytid formation, and volume loss.

There are intrinsic factors and various extrinsic and environmental factors contribute to accelerated signs of aging in this region. Eyelid skin is among the thinnest in the body, at around 0.3–0.5 mm [1].

It lacks underlying subcutaneous fat to alleviate the contour defects and fat prolapse associated with age. The delicate nature of this tissue also readily transmits underlying pigments, including blood products, muscle, and vessels [2].

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Involutional changes of eyebrow and eyelid are divided into static and dynamic components. The static component refers to the global loss of volume due to changes in bone and fat pad that support the eyebrow [3].

On the other side, the dynamic component refers to changes in resting muscle tone and their interactions [4].

Sun damage is an important contributor, leading to the development of deep rhytids, hyperpigmentation, and a skin laxity [5].

Sun exposure as environmental factors of major importance for premature skin wrinkling or facial ageing. This is intensified by the fact that the skin of the eyelids is rarely sufficiently protected even when sunscreen is applied [6].

Frequent intake of alcoholic beverages has also been shown to correlate with appearing older than chronological age. Smoking is another important modifiable factor that contributes to premature and accelerated skin aging through a similar free-radical mediated mechanism [7, 8].

With advances in cosmetic medicine, minimally invasive techniques in aesthetic rejuvenation have become increasingly popular. Topical therapy, chemical peels, laser resurfacing, plasma resurfacing, radiofrequency and surgery, along with neuromodulators and fillers, can be used to enhance the appearance of the periorbital region. The objective of this chapter is to review common applications of lasers and energy-based devices for the treatment of periorbital concerns.

Periorbital Rejuvenation by Laser and EBDs

The periorbital region is a difficult area to treat because of its delicate nature, thinnest part in the body and important function. Careful treatment of the anatomic eyelid structure is crucial in order to avoid any complications. Proper patient selection and assessment of aging severity is important in order to determine the best therapeutic option.

Periorbital Wrinkles

Periorbital rhytids, or crow's feet, are generally one of the first signs of aging and they are the result of chronic ultraviolet-induced photodamage, as well as repetitive muscle contraction of the underlying orbicularis oculi muscle.

Traditional Laser Resurfacing

Ablative laser treatments such as with erbium-doped yttrium aluminum garnet (Er:YAG) or CO_2 allow for single treatment sessions with good and satisfactory results but have 10–14 days downtime during re-epithelialization. Erythema can be prolonged over several months and complication rates can be relatively high for complete resurfacing. Non-ablative laser treatments typically allow for faster recovery but will need multiple treatments.

There is a new technique of resurfacing with ablation of periorbital skin (RAP) performed in a single session using freehand motion and focused technique of the CO_2 laser to induce complete vaporization of the epidermis, covering the entire

treatment area in a homogeneous manner. Vaporized skin was not removed to avoid too superficial or too deep vaporization. The same parameters used for the epidermis were employed to obtain a dermal retraction by using defocused irradiation. The RAP technique seems to be an effective and safe minimally invasive technique for rejuvenation of skin elastosis of the lower eyelid [9].

Another new development was the availability of long pulsed Er:YAG laser which leads to minimal ablation (less than 5 Microns) and variable degree of coagulation. This has been utilized successfully in treating the periocular laxity and wrinkles with minimal down time and side effects.

Fractional Laser Resurfacing

Periorbital traditional laser resurfacing (CO_2 laser or Er:YAG laser) carries a risk that lower lid ectropion may develop that may require surgical correction. These considerations have led to the development of fractional photothermolysis (FP), in which delivery of laser energy to skin produces arrays of microscopic thermal wounds at specified depths without damaging the surrounding tissue. The first FP device was a 1550 nm erbium-doped laser system which considered as a non-ablative fractional lase. Unlike traditional laser devices that produce layers of thermal injury, FP devices produce columns of injury called microscopic treatment zones (MTZs). Since these MTZs are surrounded by normal tissue, keratinocyte migration distance is shorter, healing is faster, and the risk of adverse effects is reduced. The success of FP and the time-honored efficacy of the CO_2 laser device led manufacturers to develop fractional CO_2 laser devices as an ablative fractional laser. Treatment with a fractional CO_2 laser device produces long-lasting improvement in periorbital rhytids and skin laxity and facial rhytids, including crow's feet [10] (Fig. 7.1).

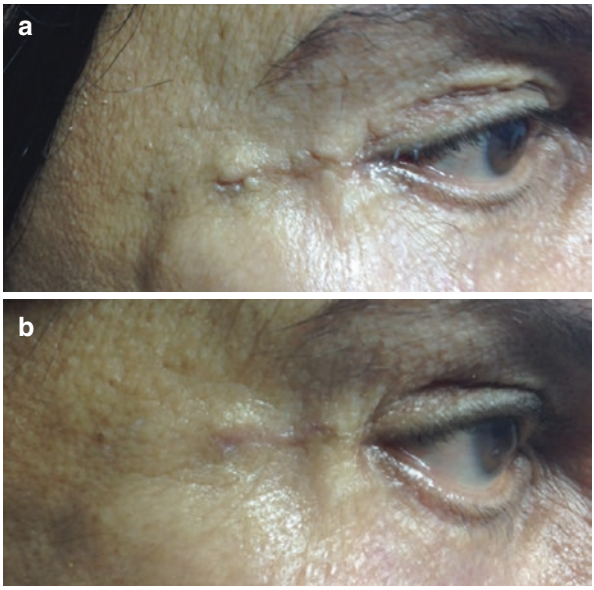

Fig. 7.1 54 years old female patient presenting with (**a**) Post surgical scar before treatment, (**b**) after 3 sessions of fractional CO_2 laser

Radiofrequency

Radiofrequency (RF) devices use energy produced by an electric current (as opposed to a light source as in a laser) to create a thermal effect that results in collagen contraction and neocollagenesis while minimizing collateral damage. The use of RF devices to achieve tightening of the skin in the periorbital region has been reported. These devices produce collagen tightening that many authors describe as mild to moderate and more subtle than the effects seen with ablative or fractionated lasers; however, the inherent low morbidity makes RF a desirable choice if mild effects are desired with a low risk profile.

Several RF electrode configurations are available now in the RF system; monopolar, bipolar, tripolar and multipolar RF, fractional RF and fractional microneedling RF.

Bipolar RF was tried in the treatment of periorbital wrinkles and shows an overall objective improvement in three important clinical signs of aging: solar elastosis, texture, and amount of photodamage surrounding the eyes, with minimal side effects. Fractionated bipolar radiofrequency (RF) is a one of non-ablative energy-based technology used for facial rejuvenation, which is a promising alternative to ablative and non-ablative laser devices [11]. The RF energy generates fractional deep dermal heating that is delivered to the skin via a handheld applicator that consists of multi-electrode pins, which ultimately injures the skin and elicits a wound healing response. Energy is delivered in a pyramid shape with minimal epidermal impact and significant effects being seen in the dermis. Therefore, large volumes of thermal energy can be delivered to the dermis with less than 5% of epidermal destruction [12].

Unlike the non-ablative lasers, RF devices do not rely on the chromophore for efficacy or safety, and thus, are suitable for all skin types. RF devices utilize electrical current to produce heat. Tissue resistance converts the electrical current of RF to thermal energy that induces collagen shrinkage immediately post-RF treatment [13].

Fractional Microneedling RF

Microneedle monopolar RF device has been tried in the treatment of periorbital wrinkles and showed good results due to mechanical effect by needles and thermal effect of monopolar RF [14].

Fractional bipolar radiofrequency microneedle therapy was developed as a minimally invasive and unique system that delivers bipolar RF current through a microneedle electrode assembly. This system efficiently delivers thermal and mechanical effect to the deep dermis and creates a controlled RF thermal zone while sparing the epidermis and key adnexal structures that contribute to rapid wound healing. Microneedle RF could be insulated that generate the thermal effect from only tip of the needle or non-insulated that generate thermal effect from whole length of the needle [15].

Intense Pulsed Light

IPL has been tried in the treatment of periorbital, perioral, and forehead rhytides using a 645-nm filter with a cut-off of 40–50 J/cm^2. Assessment by 2 independent observers showed "some" or "substantial" improvement in 83.3% of patients [16]. The mechanism of action of IPL and nonablative laser application in skin rejuvenation is thought to be dermal remodeling which occurs through increased collagen I and type III deposition and collagen reorganization into parallel arrays of compact fibrils [17].

Plasma

Plasma skin regeneration (PSR) employs the use of plasma, the fourth state of matter. Plasma is a gas-like state of matter composed of ionized atoms. Ionization occurs when sufficient energy is applied to the gas so that electrons can escape from their atoms leaving the atoms positively charged. When the electron is "recaptured" by a positively charged atom, energy is emitted or stored by vibration and rotation of the gas molecules [18].

PSR treatment for non-surgical blepharoplasty requires operator to possess appropriate artistic skills in order to have a good perception of the eyelid faults and a good overview to study the precise points on which to act, to ensure the preservation of the symmetry.

In contrast to ablative treatments such as lasers and traditional radiofrequency, plasma sublimation leaves a layer of intact and desiccated epidermis that acts as a natural biologic dressing, avoiding to damage the deeper layers of the skin and predisposing to a better healing with best aesthetic results. Moreover, the detached spots of sublimation technique leaves spared columns which further aid in healing, with a still more rapid recovery.

Differently from traditional radiofrequency, the Plasma device works without touch and with extreme precision, inducing a sublimation of the superficial skin layers that heat up in a controlled manner [19, 20]. In fact the selected energy can be concentrate in very small tissue areas, acting on the tissues with care and precision, with a layer-by-layer mode, avoiding damaging the deeper layers of the skin.

The technique consists of a modeling of the eyelids that must be sculpted precisely on the excess of skin tissues, with the purpose to reduce and shape it, improving the appearance of eyelids, rejuvenating the eyes, and reducing eyelid heaviness.

Long-wave plasma radiofrequency ablation could be an effective treatment for non-surgical blepharoplasty, and could offer an alternative choice to surgical procedures for aesthetic treatments of eyelids [21].

Plasma ablative device for eyelid laxity shows promising remodeling effects on the collagen of the upper eyelid and seems to improve appearance, without any serious adverse events. So, plasma ablative device could be a valid solution for eyelid dermatochalasis, but further studies are required [20] (Fig. 7.2).

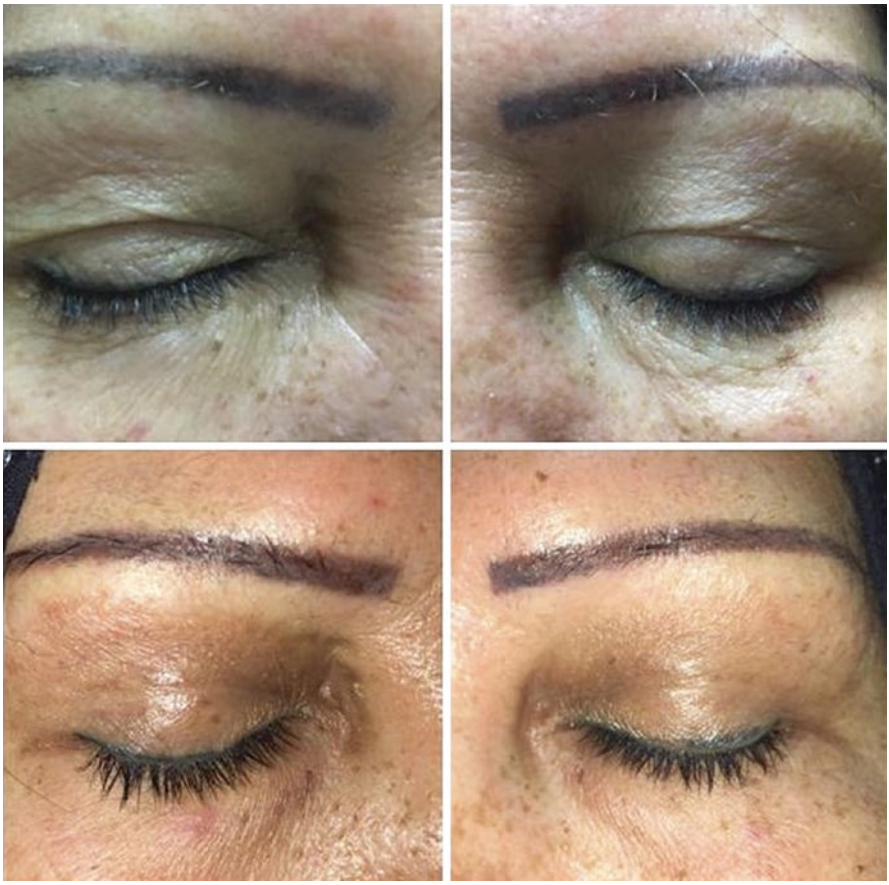

Fig. 7.2 47 years old female patient presenting with bilateral eyelid laxity, she received 3 sessions of plasma skin rejuvenation. Noticable textural improvement but with some residual hyperpigmentation

Skin Microneedling

Skin needling is also called micro-needling therapy or percutaneous collagen induction therapy (PCI). It is a minimally invasive procedure for facial rejuvenation that involves the use of a micro-needling device to create controlled skin injury by roller, automated pen or stamp device.

During the procedure, microscopic wounds created in the papillary dermis by the microneedles being driven into the skin result in the normal chemical cascade that follows trauma. This consists of an inflammatory stage, with its subsequent release of cellular growth factors, followed by the proliferative stage, and ultimately the remodeling stage, with the stimulation of neocollagenesis and formation of a tighter collagen matrix [22].

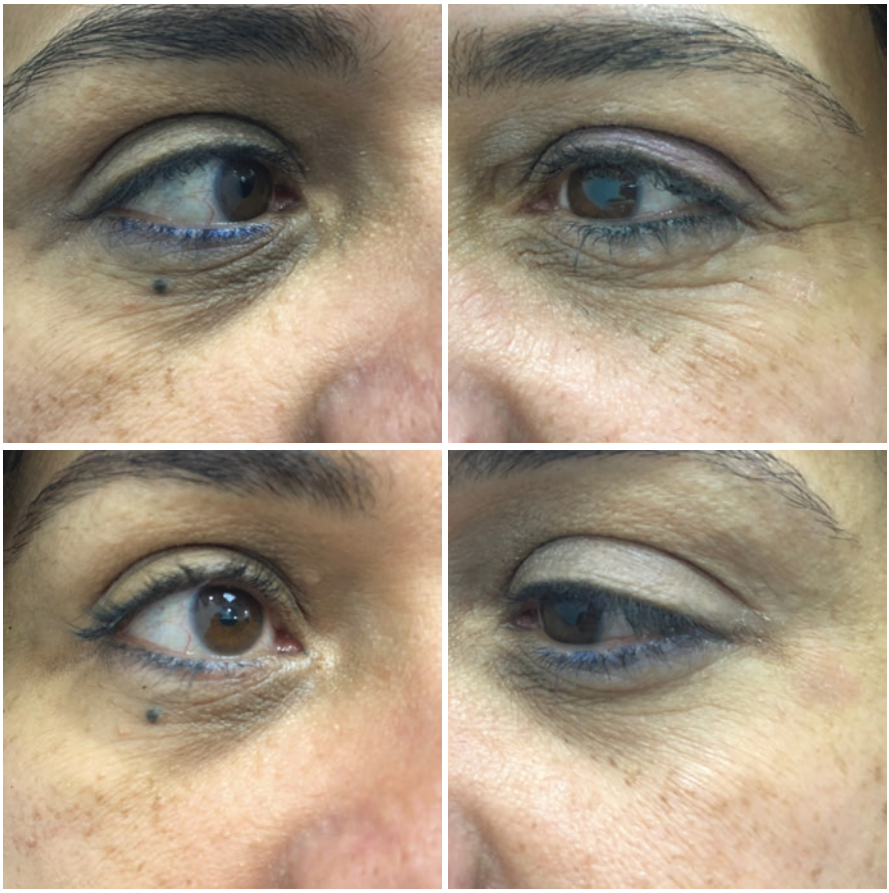

Fig. 7.3 39 years old female patient with infraorbital wrinkles, and she was treated with one session of MFU using 1.5 mm depth transducer (4 months after single session)

MFU/HIFU

The principle of HIFU is to induce cellular damage and volume reduction of the target area selectively by means of coagulation by generating instant microthermal lesions through the accumulation of high-frequency ultrasound beams at the specific tissue site without any damage to the epidermis and adjacent issue [23]. HIFU can generate precise microcoagulation zones named thermal coagulative points (TCPs) at different levels, mainly mid dermis, deep dermis and superficial musculoaponeurotic system (SMAS). These TCPs cause immediate shrinkage of collagen and gradual tightening of the skin through collagen contraction and remodeling [23].

This technique combines direct ultrasound visualization of targeted tissue with the noninvasive delivery of focused ultrasound energy. HIFU with visualization technique treatment has received proper medical attention as a 'high-tech' way to improve wrinkles and skin laxity [24] (Fig. 7.3).

Dark Circles

Periorbital hyperpigmentation (POH), also known as periocular hyperpigmentation, periorbital melanosis, dark circles, infraorbital darkening, infraorbital discoloration, or idiopathic cutaneous hyperchromia of the orbital region and are the result of a variety of factors including deep facial anatomy, soft tissue changes, as well as contributions from the skin [25]. It is an ill-defined entity that presents as bilateral round or semicircular homogenous brown or dark brown pigmented macules in the periocular region [26]. It can affect an individual's emotional well-being and influence quality of life.

Clinically, POH is characterized by light- to dark-colored, surrounding the eyelids. It is important to differentiate the dark eyelid skin with shadowing due to tear trough. Manual stretching of the lower eyelid skin can help to differentiate between true pigmentation and shadowing effect. On skin stretching, the latter improves or resolves entirely. An increase in violaceous discoloration on manual stretching of the lower eyelids is due to thin eyelid skin or hypervascularity of lower eyelid [27]. Wood's lamp examination can be done to differentiate between the epidermal and dermal pigmentation [28]. Ultrasonographic evaluation can help to differentiate the vascular cause from the periorbital puffiness [29].

There are a number of treatment options available for POH. Among the available treatment options for POH include topical depigmenting agents, such as hydroquinone, kojic acid, azelaic acid, topical retinoic acid, vitamin C, chemical peels, and laser therapy.

Q-Switched Lasers

Q-switched lasers are an effective means of treating dark circles that are primarily due to hyperpigmentary changes in the skin. Given the rapid thermal relaxation time of melanosomes, Q-switched lasers with nanosecond pulse technology are ideal for selectively treating melanosomes while causing minimal trauma to the surrounding structures. Q-switched ruby lasers use a 694 nm wavelength resulting in melanosome disruption within melanocytes, melanophages and keratinocytes. This relatively low wavelength is well suited for patients with Fitzpatrick types I and II skin, but the high rate of melanosome disruption is not ideal for patients with more pigmented skin.

Two separate studies have demonstrated a >40% improvement in pigmented dark circles following treatment with ruby Q-switched lasers [30].

A cases of homogenous bilateral pigmented macules and dermal melanocytosis in the periorbital region were treated with the Q switched ruby laser (694 nm); and showed good results [31]. Thus, it was concluded that in treating POH, the Q switched ruby laser should be considered as a treatment modality and it was found

effective in both dermal and epidermal pigmentation [32]. Topical treatment in combined with Q switched Ruby can improve epidermal pigmentation by accelerated discharge of epidermal melanin by tretinoin and suppressing new epidermal melanogenesis by hydroquinone ointment.

Treatment of infraorbital dark circles using low-fluence 1064-nm QSNY laser is safe and effective, particularly in darker skin types. QS Nd: YAG lasers penetrate deep into the skin and have minimal effect on melanosomes, given their high wavelength (1064 nm). This allows for increased safety when treating more pigmented individuals, such as Fitzpatrick type V and VI skin [33].

Intense Pulsed Light

Intense pulsed light (IPL) devices emit light in the visible spectrum and is applied to the skin via a coupling gel. A high-output lamp emits a broad wavelength of light in the 500–1200 nm range using electrical current passed through a xenon-filled chamber. The chromophore of this light is dermal and epidermal pigments in the form of haemoglobin and melanin; which results in selective photothermolysis of pigmented and/or hypervascular areas of skin. The result is improved homogenous tone and hue of the skin. Settings can be adjusted to treat targets of varying degrees of pigment; for example, preferential treatment of haemoglobin over melanin for the treatment of telangiectatic areas. Treatment parameters are individualized and IPL is ideal for patients with Fitzpatrick types I–III [34].

Pulsed Dye Lasers

Pulsed dye lasers are well suited for the treatment of dark circles with a vascular aetiology. Pulsed dye lasers use the principle of selective thermolysis with haemoglobin as the chromophore. These lasers produce visible light at a wavelength of 585–595 nm with pulse durations of 0.45–40 ms. Pulse dye laser is ideal for patients with Fitzpatrick I–III skin types and is typically repeated at intervals of 4–6 weeks and often requires 3 or more sessions to be effective. Investigations in pulsed dye laser in the treatment of other forms of skin hyperpigmentation have been controversial; however, some studies indicate that pulsed dye laser may be useful in the treatment of solar lentigines [29].

Ablative Laser Resurfacing

The mechanism of laser resurfacing to improve periorbital dark circles is controlled tissue injury to the skin with the resultant reparative process resulting in the formation of skin layers with increased collagen, decreased pigment

irregularities and a decrease in rhytids. Laser resurfacing is a powerful means of addressing dark circles in a multi-modal fashion. First, the superficial layers of the skin can be ablated resulting in the regeneration of superficial layers that are less pigmented. In addition, the improved collagen content in the resurfaced skin results in improved camouflage of the underlying orbicularis and associated vasculature that is often responsible for the appearance of dark circles. Fractional CO_2 and erbium-doped yttrium aluminium garnet (Er: YAG) lasers are the most commonly used [35].

Fractionated laser technology utilizes the same technology as full ablative lasers; however, fractionated laser resurfacing reduces the confluent thermal damage of full ablative lasers to a subtotal pixelated pattern of ablation, leaving behind untreated skin which allows for less downtime and a lower complication rate. The results of fractionated CO_2 laser resurfacing have been shown to be comparable to traditional ablative resurfacing; however, with a lower rate of complication and less downtime [36].

Er:YSGG 2790 nm

There are studies showed that 2790 nm erbium:yttrium scandium gallium garnet (Er:YSGG) laser therapy improved wrinkles and pigmentation. The mechanisms of this laser treatment are nonselective ablative resurfacing of the epidermis and nonablative resurfacing of the dermis [37, 38].

Droopy Eyebrow

Eyebrow position plays a considerable role in facial expression and perception; therefore, patients often present to the cosmetic practitioner for treatment of brow ptosis. The effects of age-related atrophy, gravity and movements of the lateral portion of the orbicularis oculi muscle, as well as the patient's genetics, are collectively responsible for the eyebrow descent and the skin and soft tissue alterations in this area. These changes are more pronounced in the lateral than in the medial portion of the eyebrow. There are numerous nonsurgical and surgical options available to lift the brow. Nonsurgical techniques include chemodenervation, fillers, laser resurfacing, radiofrequency, and ultrasound therapy.

Radiofrequency devices have proven to be effective in the decrease of brow ptosis, mentolabial folds and cheek laxity [39].

Micro focused ultrasound (MFU) with visualization appears to be a safe and effective modality for facial skin tightening. A single MFU treatment of the forehead produced on average brow height elevation of 1.7–1.9 mm. Side effects were limited to transient redness and swelling, which are common to all laser, light, and other energy treatments [40].

Infraorbital Veins

Periorbital veins (POVs) are a common cosmetic concern. Anatomically, POVs are formed by superficial facial veins that start from the bridge of the nose, travel as supraorbital and infraorbital veins, and join venous branches from the lateral forehead and scalp. Multiple branches points can be seen, and these can present as not only horizontal but also vertical veins in the thin skin of the upper and lower eyelid. These vascular structures around the eyelids are more visible because of the specific anatomical characteristics of the region with no or limited subcutaneous fat beneath the thin skin. In a patient whose peri-orbital skin is fair and/or thin, POVs can be prominent and often contribute to discoloration making these people appear tired with "dark circles" below around their eyes [41].

Despite all risks and side effects sclerotherapy using sodium tetradecyl sulfate, transection and cautery, extraction (phlebectomy) and electro cauterization remained during a long time the main treatment options. The most effective and safe method for treating these cosmetically unattractive veins in the periocular region is the laser [42].

Long-pulsed 1064-nm Nd:YAG-laser treatment appears effective and safe for the treatment of venous infraorbital dark circles and selectively removes visible prominent veins [43].

The long-pulsed Nd: YAG laser at 1064 nm demonstrated to be a safe, simple, effective and fast treatment in the treatment of superficial vein in the eyelid. There was no relapse demonstrating the efficacy of Nd: YAG laser after the successful treatment of lower lid vein with a follow-up of 8 years in a case report study. Thread-like constriction is the desired treatment endpoint of the vascular laser or achieving blanching without causing a cutaneous burn. This is a consequence of complete vascular occlusion by a thrombus [44]. Protective eye wear was required for these patients especially in upper eyelid.

Expected side effects could be pain, that may require local anesthetic infiltration in some patients. Erythema and mild edema of the overlying skin was found in all patients who were treated. Fine crusting of the skin was reported in several patients, which subsequently cleared. Small purpuric spots were noted in several patients immediately after treatment but resolved within 1 week [45] (Fig. 7.4).

Syringoma

Syringoma is a benign adnexal tumor originating from the intradermal eccrine ducts and predominantly occurs in women at puberty or later in life and commonly develop in periorbital areas. Treatments for syringomas include the following: surgical excision, electrodessication, cryosurgery, chemical peeling, and laser ablation. However, these treatments are frequently unsuccessful for removal and they are often associated with significant scarring and recurrence. Carbon dioxide laser treatment remains a first choice for the treatment of syringomas, particularly when coupled with the pinhole method as a recent trend [46].

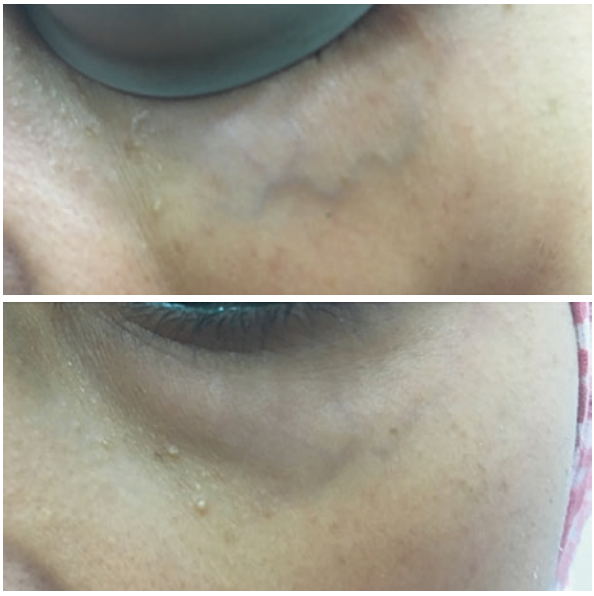

Fig. 7.4 32 years old female patient with infra orbital veins on the left side, and she was treated by 3 sessions of long pulsed Nd:YAG laser using 5 mm spot size, 20 ms and 80 J/cm^2

Periorbital syringomas were treated with topical application of BTXA immediately after CO_2 laser treatment and showed good results [47]. The exact mechanism of BTXA in treating syringomas is unknown. However, it may be explained by BTXA can block cholinergic terminals of autonomic nerve that regulates eccrine sweat gland secretion [48]. BTXA blocks SNAP-25 (synaptosomal-associated protein 25) of SNARE (SNAP receptor) complex and inhibits the release of acetylcholine from vesicle within the cytoplasm of nerve ending [49]. Due to the eccrine origin of syringomas, BTXA was considered as a treatment modality.

Rather than ablating the lesion surface with a CO_2 laser, which is difficult for deeply imbedded lesions, syringomas can also be treated with pinhole and multiple-drilling methods. In the pinhole method, single holes are created for small discrete syringoma lesions, and multiple small holes at intervals of 1–3 mm, similar in arrangement to sweat pores, are created for plaque-type lesions.

Pinhole method by free hand of 10,600-nm carbon dioxide (CO_2) laser refers to a procedure of making several small holes mimicking skin pores in targeted skin lesions. With CO_2 laser treatment via the pinhole method, laser energy can be delivered to the deep dermis to achieve destruction of target dermal tissues, as well as thermal stimulation of surrounding collagen bundles and elastic fibers, resulting in the textural improvement of skin lesions [50]. It was reported that the mean depth for syringoma lesions of 0.70 ± 0.20 mm (ranging from 0.4 to 1.2 mm) [51]. So, the application of the pinhole method utilizing a CO_2 laser in a suitable depth in the dermis may provide a simple and effective treatment modality for treating Asian patients with periorbital syringomas [52].

It was demonstrated that fractional CO_2 lasers offered positive therapeutic effects patients with periorbital syringomas. Because fractional CO_2 laser can induce

regeneration and realignment of collagen bundles and surrounding fibrous tissues of the syringomas, similar to the pinhole and multiple drilling methods, improvements in dermal thickness, wrinkles, and texture on the elevated surface of the syringomas are of additional benefit. Puncturing the targeted lesions with fractional CO_2 laser is convenient, offering shorter procedure time, resulting in less post-treatment bleeding, oozing, and producing shorter recoveries [53].

Nonablative 1550-nm diode-pumped erbium fiber laser was tried in patients with a syringoma but requires several treatment sessions to obtain a satisfactory clinical response [54].

A 1444 nm Nd:YAG laser used subdermally is successful for treating benign eccrine sweat gland cystic tumors, eccrine hydrocystomas, that are not related to fat tissue. Clinically similar to eccrine hydrocystomas, periorbital syringomas are composed of small, cystic lesions. Therefore, it was hypothesized that similar successes would be observed through this approach for destroying periorbital syringomas and it could be an easy, effective, and safe option for periorbital syringoma elimination with minimal side effects, and low recurrence rates [55].

The ideal treatment strategy for syringomas is selective destruction of dermal target lesions with little damage to normal epidermal tissue. As a result, it was tried to treat patients with intralesional insulated needles. Intralesional insulated needles have been used for in the treatment of syringomas and reported good results [56]. Type of the needle that used should had insulation on its base, while its shaft and tip were not insulated. That way, the needle could selectively destroy dermal or subcutaneous tissue without damage to the skin surface [57].

Xanthelasma

Xanthelasma palpebrarum (XP) is the most common type of xanthoma affecting the eyelids. It is characterized by asymptomatic soft yellowish macules, papules, or plaques over the upper and lower eyelids, composed of foamy lipid-laden histiocytes primarily within the upper reticular dermis on histologic examination [58].

Many treatments are available for management of XP, the most commonly used include surgical excision, ablative CO_2 or erbium lasers, non-ablative Q-switched Nd:YAG laser, trichloroacetic acid peeling, and radiofrequency (RF) ablation.

Plasma

The extreme precision of the plasma ablative technique allows to concentrate the selected energy in very small tissue areas (1 mm in diameter) without the involvement of the surrounding skin, acting on the tissues precisely and with extreme care, with a layer by layer mode, avoiding to damage the deeper layers of the skin and predisposing to a better healing with best aesthetic results. Long-wave plasma radiofrequency ablation is an effective option for treatment of xanthelasma

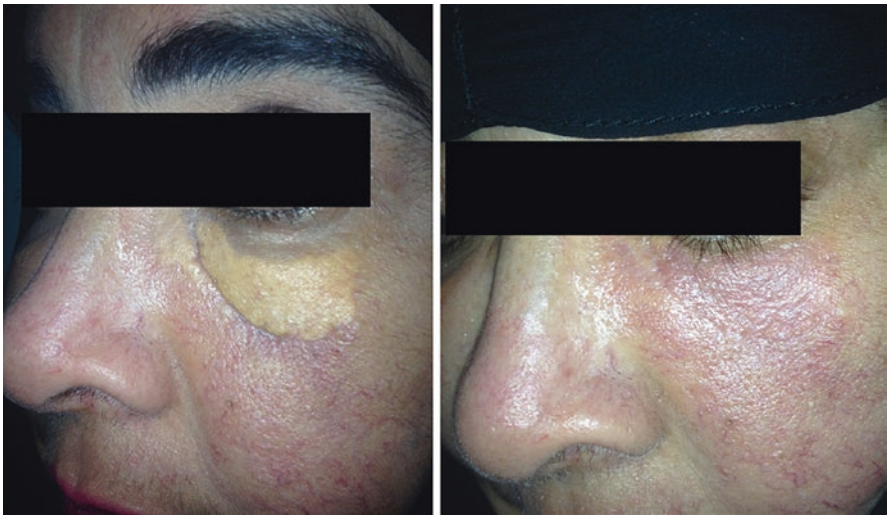

Fig. 7.5 51 years old female patient with xanthelasma, and she was treated by surgical hand piece of CO_2 laser using 1 W and 50 Hz

palpebrarum and adds an additional tool to the increasing list of medical devices for aesthetic treatments [59].

Treatment of xanthelasma with nonablative lasers has also been described. The use of Q-switched neodymium-doped (Nd):YAG laser for the treatment of xanthelasma, showed good-to-excellent results in some studies [60, 61].

Nonablative lasers with specific wavelengths target their respective chromophores and cause selective destruction. Xanthelasmas do not contain melanin and are composed of histiocytes filled with esterified cholesterol. In vitro studies of human fat have shown promising absorption peaks near 1210 and 1720 nm and can be targeted with a 1064-nm laser [62, 63]. It is hypothesized that laser energy is absorbed by water in nearby vessels and stroma and transferred to the surrounding xanthomatous histiocytes causing photoacoustic and thermal destructive effects on xanthelasma. The mechanism of action of the 1064-nm, Q-switched Nd:YAG laser on xanthelasma is likely to be nonspecific bulk heating with some destruction of the epidermis that allows for extrusion of the tissue debris [64] (Fig. 7.5).

Editor's Notes

- When using any laser, light-based devise or energy-based device around the eyes all the related safety measures should be taken into consideration to avoid any possible eye injury.
- Skin type of the patient plays an important role in selecting the appropriate technology to be used.

- Patient education regarding the associated down time, number of sessions required, possible side effects and complications must be discussed with the patient in the process of consultation and deciding the most appropriate treatment plan for each patient.
- The advantage of lasers and EBDs over other modalities is the nature of structural skin improvement happening with those devices compared with other modalities which might lead to temporary cosmetic improvement but without structural improvement.

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Oculoplastic Surgery for Periorbital Rejuvenation

8

R. Chalhoub, N. Kawa, H. Dabbous, and N. Soueidan

The beauty of a woman must be seen from in her eyes, because that is the doorway to her heart, the place where love resides.

Audrey Hepburn

Introduction

The subtleties of facial expressions are among the most important non-verbal cues that guide human communication and relationships. In addition, eye contact is of paramount importance in human interactions, which explains the principal role of periorbital area in the aesthetic domain. The periorbital area mainly encompasses the eyes and eyelids and their intricate relation with neighboring structures such as the brows, temples and midface.

Oculoplastic surgery is particular in that it often has, in addition to the aesthetic goals, functional purposes that are important for the quality of vision and to the general well-being of the ocular structures [1].

The aesthetic standards of the periorbital region vary according to age, gender and ethnicity. These variations mostly involve the eyelid crease, pre-aponeurotic fat, lateral canthus and lid-cheek junction.

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Preoperative Assessment

Evaluation of the periorbital region should always take into consideration physiologic changes related to aging as well as medical functional problems that might exist. These changes include skin, bone, and soft tissue alterations such as lipoatrophy, soft tissue descent, bone resorption, dermatochalasis and eyelid malposition [2, 3].

Obtaining optimal aesthetic surgery outcome begins with a detailed preoperative assessment and thorough knowledge of the anatomy and aesthetic subunits of the face. A detailed assessment of the medical and surgical history is important prior to any surgical intervention. This includes an account of any previous facial injuries, ophthalmic surgery, and cosmetic procedures including skin treatment with energy based devices, chemical peels, neurotoxin or filler injections.

Physical examination should always a thorough ophthalmic examination in addition to the main area of concern. This includes examination of the visual acuity, pupillary function, intraocular pressure, slit lamp examination and fundus examination. The exophthalmometry measurements should always be documented, including an account of any vertical or horizontal globe displacement. Of particular importance in blepharoplasties is the documentation of eye globe proptosis relative to a retracted midface, also known as a negative vector orbit.

Factors that play a role in determining the choice of rejuvenation method include the presenting complaint, the facial anatomy of the patient, the quality and type of skin. These factors should be assessed in every patient regardless of the area of intervention. Special considerations in the areas of the upper face include: ptosis, symmetry, brow shape, rhytids and hairline. A combination of treatments might be needed depending on the needs of the patient.

Finally, documentation using external photography is a critical component of the oculoplastic evaluation. This includes frontal full-face photographs, in addition to lateral or side photos, and worm's eye view to document proptosis and midfacial asymmetry.

Surgical Procedures

Brow Lift

Passot using a simple transverse incision above the brow has described the brow lift as early as 1919. Senescent changes that affect the forehead include soft tissue decent and temporal volume loss, which leads to brow ptosis. To compensate for the ptosis, there is often overaction of the only elevator muscle of the brows, the frontalis muscle [4]. It extends inferiorly to interdigitate with the procerus and corrugator muscle fibers, and its repetitive contraction eventually causes horizontal forehead rhytids.

Preoperative Evaluation

The ideal patient to undergo a brow lift should have brow ptosis with an elongated forehead, as many brow ptosis procedures can shorten the forehead. Important factors that should be taken into account include hairline and hairstyle as incisions can be better placed in hair bearing or other inconspicuous areas such as deep rhytides.

There are a wide variety of approaches to brow lifts including direct brow lift, indirect browpexy, temporal brow lift, endoscopic brow lift, mid-forehead brow lift, peritrichial/trichophytic brow lift, and coronal brow lift. With the advent of minimally invasive techniques, the traditional coronal and direct brow lifts are giving way to endoscopic and other cosmetically hidden incisions.

Coronal approach is the classic and powerful approach for manipulation of the forehead musculature [5]. It is indicated primarily for patients who have a short forehead. The incision is usually made superior to the root of the helix and carried over the crown to the contralateral ear while planning to have to the closed incision 2 cm behind the hairline (Fig. 8.1a). The dissection is carried down to the subgaleal plane and by blunt dissection the fibers of the corrugator are safely divided while preserving the neurovascular bundle. The procerus muscle can then be divided in a similar way. Upon releasing the two muscles the glabellar rhytids will improve and will lead to elevation and separation of the medial brows. The advantage of the coronal approach is basically the well-hidden scar, however; it is a relatively invasive surgery, and can have some serious side effects including alopecia and scalp anesthesia [2].

Endoscopic approach uses five smaller incisions in hear bearing areas which offers a superior scar camouflage and a lower risk of parasthesias [6]. The perfect candidate for the endoscopic brow lift is a middle-aged female with mild to moderate brow ptosis, a short forehead and a small volume retro-orbicularis oculi fat

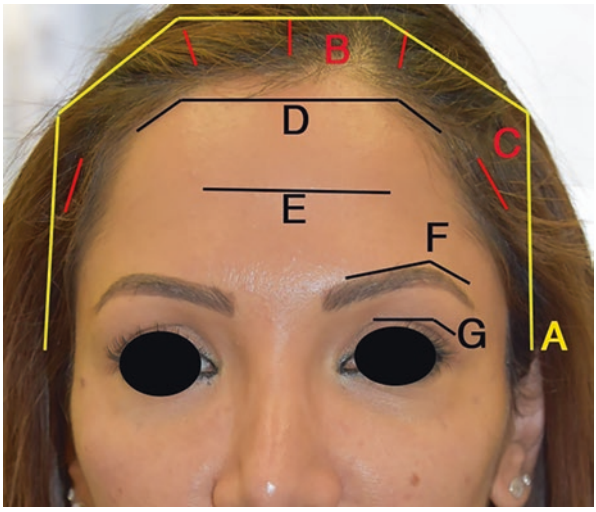

Fig. 8.1 External photograph of a female face demonstrating different incision for brow ptosis repair (**a**) Coronal, (**b**) Endoscopic, (**c**) Temporal, (**d**) Pre-trichial, (**e**) Mid forehead, (**f**) Direct, (**g**) Indirect Browpexy

pad. The incisions are usually two paracentral, two temporal and one central incision that are placed around 1.5–2 cm posterior to the hairline (Fig. 8.1b, c) The plane of dissection of the endoscopic approach is in the sub-periosteal plane medial to the temporal line of fusion, and along the deep temporalis fascia lateral to the temporal line of fusion. Access with the endoscope is achieved via the two parasagittal incisions. Using this approach, the arcus marginalis is released from one lateral canthus to the other which requires dissection through the periosteum at the glabella to access the glabellar muscles. The muscles are divided in layers facilitating the preservation of the supratrochlear and supraorbital neuromuscular bundles. The soft tissues are suspended using either absorbable or non-absorbable screws, bone tunnel with sutures or a fixation device such as Endotine™ or Ultratine™ . The main disadvantages of the endoscopic approach are the steep learning curve, and the need for an endoscope along with its setup and, which is not readily available in all centers.

Temporal brow lift includes only the temporal part of the endoscopic lift (Fig. 8.1c). It can could be performed in isolation or in conjunction with other treatments such as blepharoplasty. It is mainly used to elevate the tail of the eyebrow when there is no medial brow ptosis [2].

Pretrichial/Trichophytic falls in the category of open approaches. The perfect candidates are patients with a large forehead, and patients that wear their hair down (bangs). An non-linear irregular incision is marked few millimeters within the hair bearing area (Fig. 8.1d). Dissection is carried inferiorly in the subgaleal plane until an anterior flap is elevated until there is significant overlap with the hair-bearing scalp. If needed the posterior hair-bearing scalp can be mobilized anteriorly as well. Once the new position of the brow and forehead is achieved the incision is closed in layers. This approach has similar complications to the coronal approach including alopecia and scalp anesthesia [7].

Mid-forehead brow lift is indicated for patients with deep forehead rhytids or facial paralysis. Incisions are strategically placed along a mid-forehead deep rhytid (Fig. 8.1e). Incisions are made bilaterally and don't cross the midline and should follow the contour of the forehead. The dissection is carried in the subcutaneous plane reaching the orbicularis oculi, which is suspended to the periosteum superiorly using braided absorbable sutures. The obvious disadvantage of this method is the visibility of scars.

Direct brow lift employs incisions placed at or within the superior margin of the eyebrow (Fig. 8.1f). Minimal dissection is usually made in the subcutaneous plane. Similar to the mid-forehead lift, the orbicularis muscle can be suspended using braided absorbable sutures. Disadvantages include scar visibility and possibility of recurrence [2] (Fig. 8.2).

Indirect brow lift/Browpexy is the technique used to access the brow fat pad, also called retro-orbicularis oculi fat, through a blepharoplasty incision (Fig. 8.1g) Using a pre-periosteal dissection plane, the fat pad is identified and then sutured to the forehead periosteum around 1–2 cm above the superior orbital rim. This technique is very helpful in cases of mild temporal brow ptosis, that don't require a large elevation of the brow.

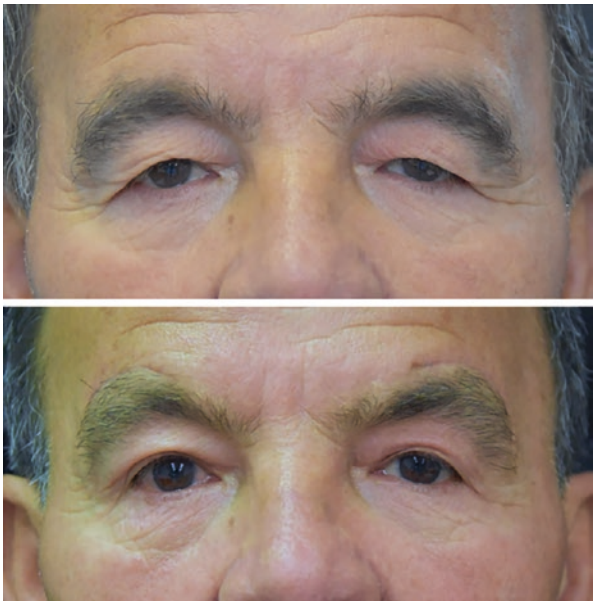

Fig. 8.2 Clinical photograph of eyebrows demonstrating the improvement in brow position following a direct brow ptosis repair

Blepharoplasty

Blepharoplasty remains one of the most common cosmetic procedures performed. Modern blepharoplasty techniques have shifted toward volume enhancement and tissue conservation rather than aggressive excision [8].

Upper eyelid blepharoplasty aims at restoring pre-tarsal space visibility and recreating upper fold volume consistent with a younger age (Fig. 8.3). Lower eyelid blepharoplasty aims to judiciously excise excess fat, treat the tear trough deformity, tightening the skin and create a smooth lid-cheek junction, while keeping an 'almond shaped' eye with sharp canthal angles [9, 10].

Preoperative Evaluation

Preoperative evaluation involves a careful assessment of the eyelid, eye globe, orbital and facial fat pads, and bony anatomy. Physical examination should focus on lateral canthal support, muscle or skin laxity, and lid tone. This can be done using the eyelid distraction and snap back tests to evaluate for laxity. Other factors that should be evaluated include eyelid retraction or ptosis, ectropion or entropion, floppy eyelid, negative vector orbit and lagophthalmos. A full ophthalmologic examination should be done with focus on the lacrimal apparatus, ocular surface and corneal pathologies or previous surgery scars.

There are also many variations outside the scope of this chapter with regards to gender, ethnicity and age that dictates the ideal blepharoplasty outcome.

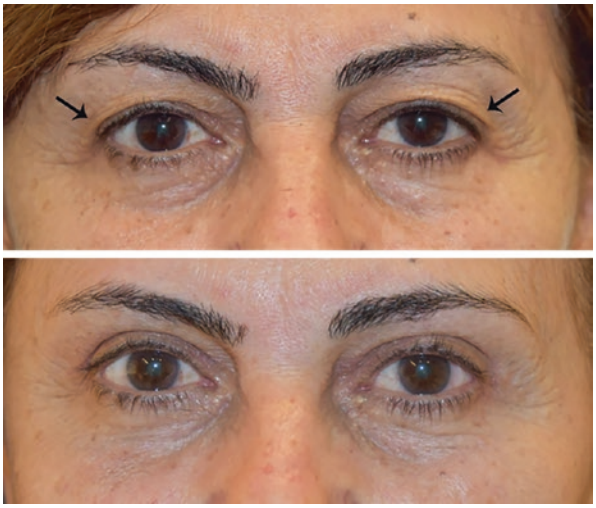

Fig. 8.3 Clinical photograph of eyelids before and after an upper eyelid blepharoplasty, demonstrating improvement in upper eyelid dermatochalasis and tarsal show

Surgical Techniques

Preoperative markings are done with the patient in the upright position with neutral gaze; these markings should be done with the brows manually fixed according to the projected post-operative position. For upper eyelid blepharoplasty, the inferior border of the marking is along the intended eyelid crease, and the superior border of the marking is determined using the skin pinch technique. This technique aims to prevent removal of excess skin and resulting cicatricial lagophthalmos. During surgery, the skin flap is excised, followed by trimming of the nasal fat pad, or laterally translocating it to volumize the central pre-aponeurotic fat pad if need be [11]. The orbicularis oculi muscle is usually preserved, especially in cases of large excision, weak orbicularis oculi tone or pre-existing lagophthalmos.

Lower eyelid blepharoplasty can be performed using the trans-conjunctival or trans-cutaneous methods. The main difference between the two is that the transconjuctival technique does not violate the orbicularis oculi muscle [9].

The transconjunctival technique incision is made in the lower eyelid conjunctiva around 5 mm below the lower eyelid tarsus. The orbital fat is accessed in a pre- or post-septal dissection; and can be re-draped inferiorly to help address the tear trough deformity (Fig. 8.4). The procedure can also be combined with a skin pinch excision of excessive skin, and with a lateral canthoplasty or canthopexy to address mild lower eyelid laxity [12].

The transcutaneous approach involves an incision that is usually infraciliary just below the lower eyelid lashes. The subcutaneous dissection plane is carried inferiorly below the pre-tarsal orbicularis oculi muscle, where dissection is carried through the pre-septal orbicularis to reach the orbital fat pads and inferior orbital rim. The advantage of using the transcutaneous approach is the wide exposure for

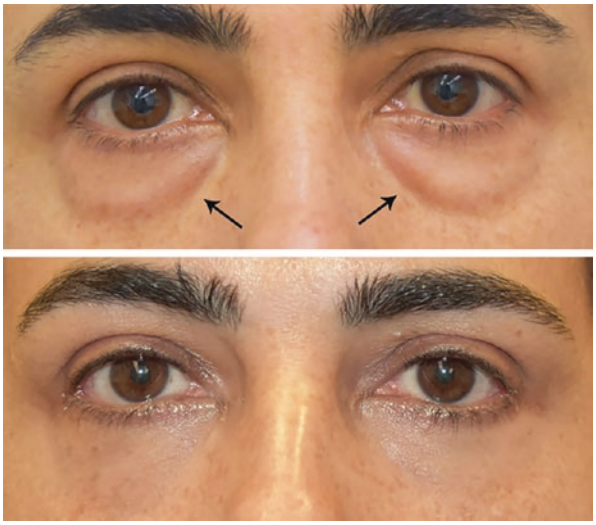

Fig. 8.4 Clinical photograph of eyelids demonstrating the improvement in lower eyelid fat prolapse and tear trough deformity following trans-conjunctival lower eyelid blepharoplasty with fat redraping

fat re-draping, the ability to perform a cheek suborbicularis oculi fat (SOOF) or orbicularis lift, in addition to a more aggressive skin excision. The main disadvantage of this technique is the increased risk of post-surgical lower eyelid retraction and ectropion.

Fat Transfer

Modern concepts in aesthetics and facial rejuvenation have focused on conservation and restoration of volume, in addition to more attention on the relation between different aesthetic units. In the periorbital area, there has been increased interest in preservation of volume in the upper and lower eyelids, and fat redraping to treat the tear trough deformity and improve the lid cheek junction [13, 14].

Lipoatrophy that is associated with aging often affects the upper eyelid preaponeurotic fat pad, brow fat pad, in addition to the different cheek fat compartments. This explains why fat grafting or transfer is increasingly used as a powerful tool to re-volumize and rejuvenate these different aesthetic units [15].

As with any surgical procedures, the preoperative evaluation is essential in elucidating any medical or dietary problem that could affect graft survival. Fat harvest sites must be also evaluated as thin patients with a low total body fat percentage don't have enough subcutaneous fat which makes them poor surgical candidates. Harvest sites include the peri-umbilical area, inner and outer thighs, hips, and buttocks [16].

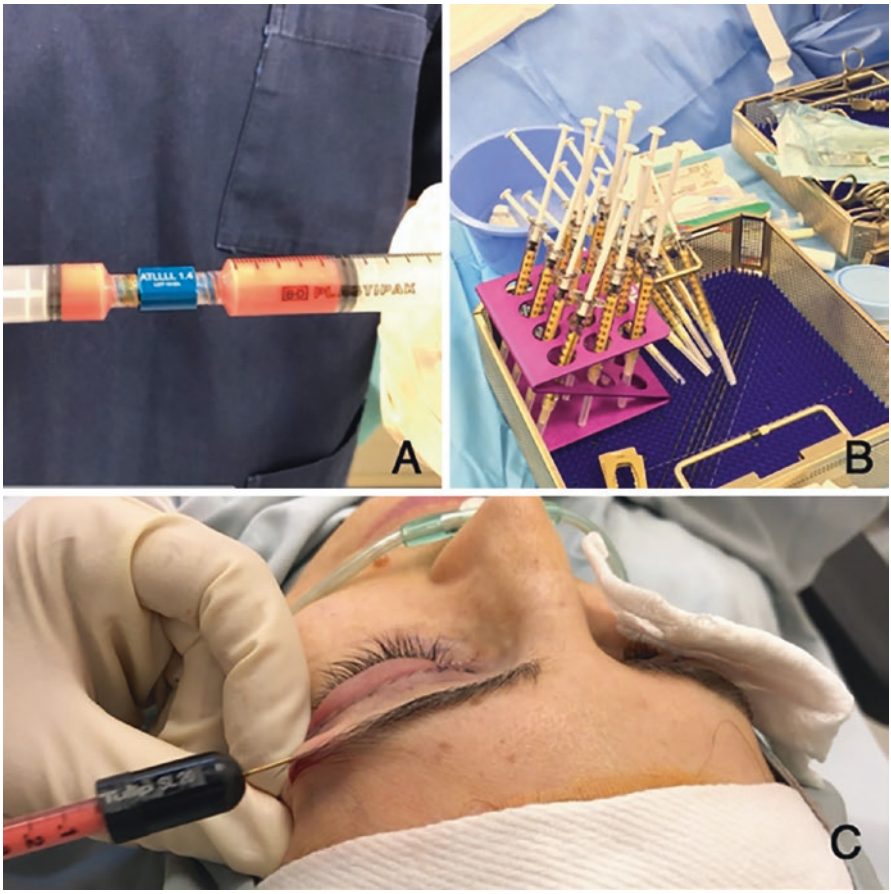

Fig. 8.5 (**a**) Harvested fat is processed into microfat by passing it through a 1.4 mm sieve connecting two syringes, (**b**) Processed fat is transferred into 1 cc syringes to allow small aliquots or strings of fat to be injected, (**c**) Fat is injected into the brow fat pad (retro-orbicularis oculi fat) using a 20 Gauge cannula using multiple passes

During surgery, the harvest area is infiltrated with tumescent anesthesia which is a solution consisting of a mixture of normal saline, lidocaine, sodium bicarbonate, and small amount of epinephrine. A small horizontal incision is created and the suction cannula is inserted, fat is then harvested in a back and forth motion under constant suction [16, 17].

The collected fat can be processed using multiple methods, including centrifugation, irrigation over telfa pads or other closed-system filtering materials to decrease risk of contamination or adipocyte damage [18]. More recent techniques involve passing the harvested fat through sieves of different sizes (Fig. 8.5a) that will yield smaller fat lobules, termed 'microfat', and a fat emulsification termed 'nanofat'. After processing, fat is transferred to 1 cc syringes (Fig. 8.5b), and then injected into the desired areas in multiple passes and by injecting small aliquots during every

pass (Fig. 8.5c). Fat is distributed in several layers and planes to avoid lumping and other irregularities.

Complications arising from fat grafting include scarring, infection, persistent fat nodules, and contour irregularities [17]. The most devastating rare complication is fat embolism and blindness, which can occur in case of iatrogenic intravascular injection. Danger areas are around peri-orbital vascular plexuses, mainly the supra-orbital, supra-trochlear and infraorbital vessels.

Conclusion

Periorbital surgeries require an exceptional interplay of skills and expertise in multiple disciplines including Plastic surgery, Ophthalmology and Dermatology. It is certain that a deep understanding of the intricate peri-orbital anatomy in addition to an increased attention to detail is required to ensure consistent and optimal results.

There remain many more procedures in the armamentarium of an oculoplastic surgeon for the rejuvenation of the periorbital area that are outside the scope of this chapter. We have illustrated different approaches to the most common oculoplastic procedures, and we re-iterate that for the average patient, a combination of different procedures is often required. A thorough pre-operative evaluation and in depth discussion is imperative in every case to set proper patient expectations and avoid undesired outcomes.

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Cosmeceuticals for the Periorbital Region

9

N. Kawa, H. Dabbous, R. Chalhoub, and N. Soueidan

It is often said that the eyes are the windows into the soul, as they convey a form of expression that cannot be put into words. While time passes, and takes its toll on the body and the mind, the eyes remain true to self … ageless.

Similarly to the rest of the body, the periorbital region undergoes the effects of chronological aging and cellular senescence. This is associated with progressive failure of the highly regulated cellular mechanisms responsible for tissue health and renewal. Chronic sun exposure also leads to concomitant photo-aging, due to ultraviolet exposure from the sun [1, 2]. Although these processes affect the face as a whole, the thin nature of the peri-orbital skin makes this region even more prone to early signs of aging. The presence of superficial periorbital vessels and paucity of soft tissue also contribute to the potentially aged appearance.

A variety of treatment modalities can be used to address periorbital rejuvenation, ranging from minimally invasive and device based procedures, to surgical interventions [3]. Irrespective of the selected interventions, prevention, early treatment and long term maintenance with topical therapies is essential for optimal outcomes [4]. While topical therapies play an important role in treatment of pigment and texture, it is important that patients understand the extent of expected outcomes. Over time, skin laxity, fat loss and bone resorption may require more aggressive treatments.

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Skincare regimens also provide a synergistic effect to procedural interventions when paired correctly.

While skin may be the main target of topical interventions, the nearby eye lashes and eyebrows should also be treated as part of the aesthetic unit.

Products known as "eye creams" have oversaturated the market and are advertised as treatments for "dark circles", "puffiness" and wrinkles among others. In this chapter we will focus on the various substances and ingredients found in cosmeceuticals, which are known to provide actual benefit alone or in combination with other treatments. To be considered effective, these products must be able to penetrate the skin barrier, act locally, and provide effective and visible outcomes [5, 6].

Primary Assessment

Before initiating any treatment, be it topical or otherwise, a thorough survey of the patient's skin and general health are essential in guiding treatment (Box 9.1). This will allow treating physicians to better decide whether or not topical treatments will suffice or whether cosmeceuticals must be combined with other therapies.

Cutaneous and extra-cutaneous medical illnesses may present as altered pigment or texture of periorbital skin. Allergic shiners are one such example associated with atopic disease or asthma. Similarly, patients with dry eyes may tend to rub surrounding skin more frequently or vigorously, contributing to local skin irritation. Allergic history should also be noted as periorbital skin is sensitive and even mild topical treatments may not be tolerated. Knowledge of the underlying conditions can thus guide treatment but also set expectations.

Ask the patient about their main concern, previous treatments received, and their therapeutic expectations. Patients who understand their prescribed regimen are more likely to follow through with treatment plan and be satisfied with outcomes. Furthermore, patients' chief complaint can result from previous treatments. For example, superficial injection of under-eye fillers can result in bluish discoloration due to Tyndall effect.

Box 9.1 Primary Evaluation of the Periorbital Area Prior to Topical Treatment Initiation

General skin overview:

- Fitzpatrick skin phototype
- Presence of sun damage

Periorbital skin assessment:

- Skin texture
- Presence of swelling or puffiness
- Presence of dark circles
- Presence of wrinkles

Deep structure assessment:
1. Vascular show
2. Extent of volume loss
3. Extent of bone resorption

Other:
1. Hair distribution of lashes
2. Hair distribution of eyebrows

Box 9.2 Ingredients Commonly Found in Sunscreen

Common in chemical sunscreen:
- Zinc oxide∗
- Titanium dioxide∗
- Iron oxide
- Kaolin
- Ichthamol

Common in physical sunscreen:
- Oxybenzone
- Avobenzone
- Benzophenone
- Homosalate
- Octisalate
- Octocrylene
- Homosalate
- Octinoxate
- Methyl anthranilate
- Octyl methoxycinnamate

∗*Currently labeled in FDA's latest revision as "Generally Regarded As Safe and Effective"*

Other ingredients with insufficient safety data to date.

Sun Protection

Sun exposure contributed to extrinsic aging associated with wrinkling, collagen degradation, dryness and pigmentary changes. Ultraviolet A and B are the main culprits in this process. Daily and repeated application of sunblock helps mitigate sun damage (Table 9.1). Recent studies indicated that eyelids and the periorbital region are disproportionately missed during sunscreen application [7]. Further emphasis on overall skin coverage should be addressed by treating physician.

Chemical and physical sunscreens are both effective as long as they exceed a sun protective factor of 30 and are reapplied every few hours. The latter tend to be less irritant in nature, and may be better suited for sensitive periorbital skin (Box 9.2) [8].

Many makeup lines have created products that include sun protective ingredients however they may lack adequate efficacy. Alternately, tinted sunscreens may be a better option.

Table 9.1 Sunscreens and their properties

Product	Effect	Mechanism of action
Sunscreen		
Chemical sunscreen	• Prevention of photodamage • Prevention of post inflammatory pigmentary changes associated with energy-based treatments	Turn UV radiation into heat
Physical sunscreen		Disperse incoming radiation by means of reflection and absorption

Retinoids

These vitamin A derivatives have long been regarded as the mainstay treatment for maintenance of healthy youthful skin, acting both on intrinsic and extrinsic aging processes. Retinoids have proven clinical efficacy in treatment of irregularly pigmented skin as well as diminishing fine lines and wrinkles. Correction of skin dyschromia results from tyrosinase activity, the enzyme responsible for conversion of dopamine to melanin, with downstream effects on melanosome transfer. The textural effects are a result of simultaneous increased type I pro-collagen expression, and decreased collagenase activity, leading to dermal collagen synthesis [9]. There is also an observed hyaluronic acid deposition and compaction of the stratum corneum as well as increased epidermal mucin [10].

They are available in both prescription strength formulations such as tazarotene and tretinoin (retinoic acid), as well as over the counter products like retinol and retinaldehyde. While the former are more potent and lead to higher cutaneous concentrations, the latter are milder all while retaining clinical efficacy.

In spite of the excellent clinical efficacy of such products, they are notorious for producing dry, flaky and erythematous skin [11]. This is a particular concern when considering the sensitive periorbital area. Conjunctival irritation can also occur in case of direct contact with the eye. It is therefore preferable to use formulations that are less potent, or those containing emollients when treating the periorbital region. Progressively increasing the quantity and frequency of application can also be helpful to avoid skin irritation. Sun protection during treatment is crucial.

Antioxidants

Healthy skin has intrinsic capacity to repair damaged cells by means of an antioxidant defense system [12]. This includes scavenging and enzymatic processes that result in elimination of accumulated reactive oxygen species (ROS). ROS induce irregularities in skin cell DNA, lipids and proteins, leaving skin lax, discolored and with potential for cancerous growths. Antioxidants have the ability to increasing the minimal dose of UVB required to induce erythema of the skin, known as the Minimal Erythemal Dose (MED). By doing so, antioxidants reduce cellular damage, prevent sunburns, pigmentary irregularities and wrinkle formation (Table 9.2).

Table 9.2 Antioxidant properties

Antioxidants		
Vitamin C (L—ascorbic acid)	• Decreased sunburn potential • Decreased in wrinkles formation • Lightening of skin	• Electron donor • Neutralizer of free radicals • Suppression of NF-κβ • Inhibition of tyrosinase • Inhibition of enzymatic collagen degradation
Vitamin E (Tocopherols, Tocotrienols)	• Decreased sunburn potential • Decreased wrinkles formation • Decreased skin cancer potential	• Inhibition of elastin degradation by metalloproteinases
Ferulic acid	• Enhancement of photoprotection of vitamin C and E • Lengthening of skin	• Prevention of thymine dimer production • Prevention of keratinocyte apoptosis
Phloretin		• Prevention of lipid peroxidation • Prevention of metalloproteinases and elastase • Inhibit tyrosinase
Vitamin B3 (Niacinamide)	• Reduction in hyperpigmentation • Decreased wrinkle formation • Enhances skin barrier properties	• Enzyme cofactor • Inhibition of melanosome transfer from melanocyte to keratinocyte • Enhances lipid and protein in stratum corneum

Vitamin C is a water-soluble antioxidant with clinical proven efficacy. It also has anti-inflammatory and lightening benefits in addition to its role in collagen synthesis [13, 14]. Due to its hydrophilic nature, higher concentrations are necessary for adequate results. Lipid soluble formulations such as tetrahexyldecyl ascorbate have improved penetration capacity.

Vitamin E is a lipid soluble antioxidant with similar abilities in reduction of MED and wrinkle formation [15]. The main site of action is stratum corneum lipid bilayer and cell membrane. It has also been found to reduce development of skin cancers. α-tocopherol is the main active isomer. This product may be slightly irritating to some.

Ferulic acid and **Phloretin** are plant-based antioxidants with photoprotective effects [16]. When combined with vitamins C and E, they provide a stabilizing effect, enhancing photoprotection and vitamin penetration. Given that vitamins C and E are easily oxidized upon exposure to air, these combinations may be more suitable.

Vitamin B3 is a potent enzymatic cofactor with antioxidant properties and easy skin penetration capacity. Its stable nature allows it to easily be incorporated into topical therapies. In addition to wrinkle prevention and unification of pigment, this substance also enhances the skin's barrier capacity by reducing transepidermal water loss.

Alpha Hydroxy Acids (AHA)

This group of carboxylic acids includes lactic acid, glycolic acid, mandelic acid, citric acid, tartaric acid, malic acid and benzilic acid. They are commonly referred to as fruit acids. AHAs are incorporated into a number of skincare products

including exfoliants and chemical peels. By promoting separation of corneocytes at the junction between the stratum corneum and granulosum, treatment with AHAs leads to markedly increased epidermal thickness as well as enhanced glycosaminoglycan and collagen synthesis [6, 10]. This keratolytics effect is useful in photoaged skin with accumulated corneocytes.

Collagen Enhancing Products

In young skin, collagen production is able to keep up with normal breakdown, allowing the skin scaffold to remain firm. Over time, this process slows down, leading to increased skin laxity and wrinkle formation.

Up-regulated synthesis and down-regulated degradation of collagen by means of topical therapies can help enhance rejuvenation.

Topical **peptides** have been included in the armamentarium of anti-aging treatments. These are thought to act by multiple mechanisms including signaling cascades, carrier peptide action, enzyme inhibition, and neurotransmitter inhibition [17]. Collagen fragments and precursors have been studies both ex-vivo and in-vivo, showing potential anti-aging benefits. Inhibition of metalloproteinases has also been described. Pro-collagen products have lead to increased extracellular matrix protein production in fibroblast cultures. These effects allow adequate dermal remodeling to ensue. Neurotransmitter inhibiting peptides such as **argireline** may also diminish the appearance of wrinkles in a manner similar to that of injected neuromodulators. Clinical trials pertaining to the periorbital area specifically have been initiated and showed positive outcomes, however repeated and long-term application is necessary [18].

Cytokines and growth factors allow similar dermal fibroblast proliferation and tissue repair. Their role in stabilizing the dermo-epidermal junction, increasing dermal thickness and collagen production is well documented. As a result, products containing growth factors may potentially improve texture, pigment and wrinkle appearance. This includes Transforming Growth Factor (TGF), Vascular Endothelial Growth Factor (VEGF), hepatocyte growth factor, granulocyte colony stimulating factor, interleukins, epidermal growth factor, Platelet Derived Growth Factor (PDGF), Fibroblast Growth Factor (FGF), and insulin-like growth factor. These can be derived from human, animal or plant sources. In spite of the larger molecular structure, clinical studies showed positive outcomes in facial skin, with particularly superior results in the periorbital area [19, 20]. Histological data corroborates clinical findings associated with daily long-term topical treatment. Theoretical increased potential for growth or development of skin cancers, particularly with VEGF, warrants careful periodic revision of the literature.

Skin Lightening Agents

A common complain pertaining to the periorbital area includes hyperpigmentation. While the etiologies associated with this concern are out of the scope of this chapter, we will review some of the topical depigmenting options available [21].

It is noteworthy that the main etiology of hyperpigmentation should be established and treated. The mechanism of action of these agents mainly relies on inhibition of tyrosinase. **Hydroquinone** is a very effective and popular bleaching agent, which may be used in the periocular region. This is a potent treatment that can cause skin irritation acutely, and more serious dispigmentation with chronic use such as post-inflammatory hyperpigmentation, exogenous ochronosis, or leukomelanoderma en confetti. **Arbutin** is a plant extract with similar dose dependent tyrosinase action. It has been used in melisma treatments at a 3% concentration and may serve as an option for periocular hyperpigmentation. **Kojic acid** is a fungal derivative, which was shown to potentiate the action of hydroquinone when combined for treatment for hyperpigmentation. Further studies are needed to assess its efficacy in the periocular area. **Azaleic acid** is an alternative that has a better long-term safety profile [22]. This drug works by means of cytotoxic effect on melanocytes by interfering with DNA synthesis. It is more commonly used for general facial hyperpigmentation however may be a promising option in the periocular area.

Hydrating Products

Hyaluronic acid (HA) is a glycosaminoglycan with humectant properties, making it a popular component of over the counter anti-aging products. Although it plays an important water-binding role in the skin, the ability of hyaluronic acid to do so applied topically in unsure. The large molecular weight of HA would preclude it from penetrating the skin barrier. Nevertheless, some evidence of decreased wrinkle depth with topical application of low molecular weight HA was noted in the literature [23]. Similarly, **ceramides** serve as a lipid interface within the stratum corneum, allowing decreased transepidermal water loss. They are therefore often incorporated into eye creams for hydration purposes.

Hair Growth Products

Although the main focus of periocular rejuvenation remains skin health, long and full lashes provide a youthful and aesthetically pleasing appearance. **Bimatoprost** is a synthetic prostaglandin analog that was initially intended for treatment of glaucoma. Once daily topical application to the lash line was found to significantly thicken and lengthen eyelashes. This product comes in a 3% concentration form and is the only FDA approved lash enhancing treatment [24]. While the exact mechanism of action is unknown, bimatoprost is thought to increase the proportion of lash follicles in anagen as well as the duration of this phase. Off label use for eyebrows is common, as many clinical studies have found it to be an effective and safe treatment option in eyebrow hypotrichosis [25]. This product is generally regarded as safe with few irritant side effects to the eye. Due to reports of iris pigmentary changes, it is important to inform patients of the potentially permanent brown iris pigmentation.

Herbal, Plant Derived and Other Compounds

A variety of compounds are commonly found in commercially available products for periocular rejuvenation. While many of these are recurrent ingredients, their clinical efficacy is not well studied. We will briefly discuss them for completion however a recommendation for these products is unclear. Components of green tea have been described as potent antioxidants with photoprotective effects. Epicatechin-3-gallate and epigallocatechin-3-gallate in particular have demonstrated UV protection, down-regulation of deleterious NF-κβ expression and enzymatic degradation of collagen [26]. α-bisabolol, a compound found in chamomile as well as soy have exhibited some anti-oxidant and anti-inflammatory activity. Licorice root extracts have been described to provide lightening properties in addition to some anti-oxidant activity. Further clinical studies are needed for all these compounds before they can be recommended [6]. Similarly, caffeine has exhibited some anti-inflammatory effects. Nevertheless, it has been found to decrease collagen synthesis in cultured fibroblasts making it a potentially unfavorable ingredient for rejuvenation therapies. Peptides of palmitic acid (Palmitoyl tetrapeptide-7, Palmitoyl oligopeptide, Palmitoyl tripeptide-5) have been implicated in some dermal cellular mechanisms that may improve repair functions of the skin. They are incorportated into some products but their role for periorbital rejuvenation is unclear [5].

Role of Combination Treatments

While topical therapy may be an excellent cornerstone periorbital rejuvenation, a myriad of effective treatment options exist. When paired successfully, a baseline topical regime can prepare the skin for more invasive procedures, allowing optimal results [27]. While clinical studies are lacking, anecdotal findings have demonstrated that combining retinoids with certain non-ablative laser procedures results in earlier healing and re-epithelialization as well as superior and more lasting outcomes [28]. This consists of a pre-treatment phase with intensive treatment with topicals, and a post treatment phase with less abrasive products. Chemical peels are a common facial rejuvenation procedure. Adjunctive pre-treatments with AHAs and retinoids can begin thinning the stratum corneum prior to the procedure, allowing the peel to reach deeper in the skin. When combined with topical bleaching agents such as hydroquinone, the chemical peel may also allow deeper penetration of the topical agents, improving lightening capacity. Following procedures, topical humectants, such as HA and ceramides mentioned above, are commonly recommended to help with wound care.

Concluding Remarks

With the vast array of products and treatments available, physicians are able to provide their patients with many treatment options. While many of them have excellent clinical efficacy, it is important to know that not all products are suited for all

patients, and not all products are created equal, and even the best of products may not be sufficient to achieve desired results. Clinical judgment and a holistic approach should to be guide physicians to always offer what is best to each individual patient.

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Editor's Tips

10

Ashraf Badawi

- Periocular region rejuvenation is gaining more popularity due to the fact that eye contact occurs in more than 80% of the human interactions hence the periocular area is responsible for many impressions people are getting about people they deal with.
- No physician should touch a patient with a syringe in his hand before being familiar with the anatomy of the region to be treated.
- The structure of the orbit and periorbital tissue and skin changes with aging and this is to be considered while working on the periorbital area.
- Rejuvenation means restoration of the structure and function; this should be the ultimate goal and not only a quick fix or temporary cosmetic improvement with no structural improvement.
- As long as ageing is a dynamic process, rejuvenation also needs to be dynamic and an ongoing plan.
- Lopidine (Apraclonidine 0.5%) eye drops (an alpha2 adrenergic agonist, which causes Muller muscles to contract quickly elevating the upper eye lid 1–3 mm) is the only known treatment for upper eye lid ptosis after Botulinum Toxin injection. If it did not work, reassure, it will improve gradually over few months.
- Malar edema is not uncommon complication of using the fillers in the tear trough area and is most probably due to too superficial injection or too much filler injection and is caused by lymphatic obstruction in an area with poor lymphatic drainage to start with. Dissolving the injected filler might be the best option.

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A. Badawi (ed.), *Periorbital Rejuvenation*,
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- Dark circles around the eyes is not caused by hyperpigmentation only. In many cases dark circles are caused by other issues than hyperpigmentation as skin laxity and wrinkles which affect the light reflection as well as veins in the infraorbital area. In addition, systemic causes as anemia, chronic fatigue, insomnia, poor diet, atopy or hormonal disturbances should be explored before initiating any local treatments.
- Oculoplastic surgery leads to immediate improvement of the skin tone but have minimal impact on the skin structure contrary to energy-based devices and lasers which might need more time and multiple sessions to show the result however it improves the structure of the skin significantly.
- With the current dynamic life people are demanding no or minimal down time which is an advantage offered by using the injectables which might be the most popular non-surgical aesthetic procedures performed all over the world however more recently people are also became concerned about the natural look which needs experience, talent, proper understanding of the anatomy and physiology as well as being familiar with the different technologies offered by the lasers and energy based devices which can offer good rejuvenation to the skin with minimal down time and very natural look.
- Combination therapy is always going to be the best. Improving the skin structure and function should be a priority then using materials from outside the body should be the next step if required.
- If retinol containing skin care products are to be used by the patients, it should be used gradually starting with short application time which should be gradually increased on weekly interval to avoid the skin irritation and peeling. Caution should be taken so that it does not go into the eye when applied in the periocular area.

Index

A. Badawi (ed.), *Periorbital Rejuvenation*,
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