CHAPTER 80
Minimally Invasive Treatments and Procedures for Ageing Skin

N.J. Lowe
Cranley Clinic, London, UK and UCLA School of Medicine, Los Angeles, CA, USA

Introduction
Over the last century there has been a dramatic increase in the ageing population in most developed countries. For example, it is expected that one in five Americans will be aged 65 years or older by the year 2030 (source 2000 USA census), a trend similar to that in most developed countries. Increased social pressure to look younger has led to great demand for effective cosmetic treatments for skin and facial rejuvenation. In particular, there has been an increase in what have been termed non-invasive and minimally-invasive cosmetic treatments, that is treatments that avoid surgery and involve surface skin treatment such as lasers or peels, or a variety of injections [1].

Currently, most of those seeking these treatments are women, but an increasing number of men are considering rejuvenation treatments, and it is important for the practising dermatologist to be aware of the treatment options.

Types of skin ageing
Skin ageing has historically been divided into intrinsic ageing [2], which will occur in all skin, whether or not exposed to external ageing factors, and extrinsic ageing, which is accelerated skin ageing due to external influences such as smoking and sun exposure [3].

Intrinsic ageing
There are numerous factors that contribute to intrinsic ageing, including oxidative phosphorylation that generates destructive ‘superoxides’, which are thought to damage mitochondrial DNA and lead to progressive cell and tissue senescence [2]. Other factors that can prematurely age skin intrinsically are inflammatory skin diseases, for example inflammatory acne which can lead to dermal injury and subsequent scarring.

Collagen comprises up to 80% of the dry weight of ageing skin, and it is type 1 collagen, which comprises 70% of the total collagen content, whose larger diameter fibres provide the mechanical and stretch integrity of the skin. Type 3 collagen, which has narrow fibres, is also important. The quality and functionality of collagen substantially decreases with time [4].

The dermis is a connective tissue matrix of collagen housed in an elastin network. As part of the intrinsic ageing process there is a reduction of fibroblast activity in the dermis, and a decline in the ability of these cells to synthesize collagen and elastin contributes to loss of elasticity and wrinkles. In combination with the decline in collagen synthesis there is altered expression of matrix metalloproteinases (MMP), which mediate collagen breakdown. As a result, intrinsic ageing and dermal thinning occurs; dermal collagen, elastin and glycosaminoglycans are all altered during the ageing process [5].

Skin collagen fibres do not appear to shrink with age, but the balance of their intermolecular cross-links changes, with an increase in cross-linking resulting in a stiffening of the skin. Ageing is also associated with a decrease in proteoglycan content, resulting in a reduction of the tensile strength of the skin. The elastic fibres show a progressive change, and there is evidence that elastin gene expression declines with age [5].

Accompanying these changes is a reduction of skin microvasculature, a reduction in activity but not in numbers of sebaceous glands, and a reduction of subdermal fat leading to skin laxity and change of facial profile (Fig. 80.1).

Hyaluronic acid and other glycosaminoglycans decline during the intrinsic ageing process; a 50-year-old is estimated to have half the hyaluronic acid level of a youth. As an accompaniment to the dermal changes of intrinsic ageing, the epidermis becomes thinner, with a reduction in thickness of 10 to 50% between the ages of 30
and 80. Mitotic activity of keratinocytes is reduced, and the epidermal transit time is increased. The orderly maturation of the epidermis becomes irregular. The corneocytes become less adherent and this produces a clinical appearance of roughness and scale. There is a flattening of the dermal–epidermal interface by as much as 35%, with increased skin fragility [4].

Table 80.1 summarizes some of the changes of intrinsic ageing.

### Table 80.1 Some features of intrinsic skin ageing.

<table>
<thead>
<tr>
<th>Component</th>
<th>Function</th>
<th>Change with age</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fibroblasts</strong></td>
<td>Synthesis and degradation of extracellular matrix (ECM)</td>
<td>Decrease in number. Decline in growth factor response.</td>
</tr>
<tr>
<td><strong>Collagen</strong></td>
<td>ECM component, Dermal support</td>
<td>Reduced synthesis of ‘new’ and decreased degradation of existing collagen.</td>
</tr>
<tr>
<td><strong>Elastin</strong></td>
<td>ECM component, Elasticity of skin</td>
<td>Reduced microfibril content, Elastin fragmentation.</td>
</tr>
<tr>
<td><strong>Keratinocytes</strong></td>
<td>UV protection—barrier and mechanical protection, Cell signalling, Melanin carrier</td>
<td>Less proliferation and differentiation, Reduced barrier function.</td>
</tr>
<tr>
<td><strong>Melanocytes</strong></td>
<td>Melanogenesis for UV radiation protection, Endogenous free radical ‘quencher’</td>
<td>Decline in melanocyte number and life span.</td>
</tr>
<tr>
<td><strong>Langerhans’ cells</strong></td>
<td>Antigen presentation</td>
<td>Reduction in number and morphological abnormalities.</td>
</tr>
</tbody>
</table>

Extrinsic ageing

Extrinsic ageing, whose principal cause is ultraviolet radiation, results in changes in areas exposed to the environment such as the face, neck and dorsal hands. UVB (290–320 nm) penetrates to the lower epidermis, whereas UVA (320–400 nm) penetrates into the dermis and may be more responsible for some of the clinical changes associated with photoageing. Other factors that contribute to facial and skin ageing include repetitive facial expressions, leading to dynamic lines and rhytides. Gravity accelerates facial skin ageing, and this factor becomes more evident in the 30s when skin elasticity starts to decline [1].

Cigarette smoking also contributes to some of the characteristic changes of skin ‘coarseness’ and colour, or sallowness, which can be recognized in many who smoke 10 cigarettes or more daily for 10 years [6].

Signs of extrinsically aged skin include fine and coarse rhytides, macular and diffuse pigmentation, solar lentigines, increase in surface roughness, telangiectasias, sallowness, loss of skin tone and solar keratoses, basal and squamous cell carcinomas, and melanoma—particularly superficial variants such as lentigo maligna.

Structural changes that occur during extrinsic ageing include deficiency of collagen types 1, 3 and 7, which include the anchoring fibres and fibrillin in the papillary dermis. Fibrillin is thought to be one of the key structural support components. There is usually a decline in connective tissue support for dermal blood vessels, leading to vascular dilatation and the clinical appearance of telangiectasia [6].

A primary cause of UVA skin damage is oxidative damage mediated by a variety of reactive oxygen species [7]. It has been estimated that 50% of UV-induced damage results from the generation of these reactive oxygen species. Unlike intrinsic skin ageing, where collagen production declines, collagen synthesis is increased during UV radiation. There is a decrease in pro-collagen, which is absent 24 hours after exposure to sunlight. Increased production of matrix metalloproteinases, such as collagenase and gelatinase, results in collagen and dermal extracellular matrix degradation. The total collagen content of chronically sun-damaged skin is reported to be 20% less than non-solar exposed skin.

Ultraviolet exposure also leads to changes in the structural organization and function of elastic tissues. Photodamage results in abnormally thickened, tangled and disintegrated elastic fibres, which form an amorphous mass [6].

It has been shown that small fluences of repetitive UVA radiation can produce abnormal pigment and vascular damage after 12 weeks of twice-weekly radiation [8]. UV radiation creates a favourable environment for angiogenesis and dermal blood vessel fragility. UVA radiation also damages DNA, cell membranes and proteins, leading to cell ageing and an increased risk of skin cancer.

The changes of facial ageing are summarized in Table 80.2 and shown in Figs 80.1 & 80.2.

---

**Fig. 80.1** Signs of intrinsic ageing—the patient shows brow ptosis, loss of cheek volume and malar ptosis, hollowness in the lower face, atrophic lips and marionette lines.
Table 80.2 Some clinical effects of intrinsic and extrinsic facial ageing (see also Figs 80.1 and 80.2).

<table>
<thead>
<tr>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater visibility of bony landmarks</td>
</tr>
<tr>
<td>Increased rhytides</td>
</tr>
<tr>
<td>Hollowing of the cheek and perioral area</td>
</tr>
<tr>
<td>Deepening nasolabial folds</td>
</tr>
<tr>
<td>Descent of facial fat pads</td>
</tr>
<tr>
<td>Brow ptosis</td>
</tr>
<tr>
<td>Upper eyelid laxity</td>
</tr>
<tr>
<td>Infraorbital laxity and fat herniation</td>
</tr>
<tr>
<td>Atrophy of lips</td>
</tr>
<tr>
<td>Descent of the corners of the mouth</td>
</tr>
<tr>
<td>Ptosis of the nasal tip</td>
</tr>
<tr>
<td>Lower face and neck sagging and laxity</td>
</tr>
<tr>
<td>Surface photodamage—lentigo, telangiectasia, solar comedones, rhytides</td>
</tr>
<tr>
<td>Solar keratoses and skin cancers</td>
</tr>
</tbody>
</table>

Fig. 80.2 Signs of extrinsic ageing—surface photodamage, loss of volume, lentigo, sagging, dynamic rhytids, atrophy of lips and solar elastosis.

References

Prevention of skin and facial ageing

Topical protection is the primary means of prevention of photodamage and should be a part of routine skin care. The first sunscreen was developed in 1928, and combined benzylsalicylate and benzylcinnamate [1]. Details of sunscreens and photoprotection are discussed in Chapter 29. In order to be effective a sunscreen must be both a UVB and UVA filter or reflector. The concept of sun protection factor (SPF) as an assay for protection is well established [2,3].

The methods of evaluating protection by sunscreens against UVA continue to be debated, but guidelines have been established in the UK using an in vitro UVA assay [4].

Topical treatments

Photoprotection and topical treatments should be a key part of any antiageing programme. Tretinoin has been shown to be effective for improvement of both photodamaged and intrinsically aged skin [5]. It is a non-selective retinoic acid that increases epidermal thickness, promotes dermal collagen production and reduces its degradation, and inhibits UV-induced matrix metalloproteinases [6]. Other retinoids shown to produce objective clinical and histological changes include retinal, retinaldehyde and retinyl esters [7]. An important part of any topical retinoid treatment protocol is to control retinoid-induced skin irritancy while maintaining retinoid-induced skin rejuvenation. Choice of frequency of treatment and adequate skin moisturization are key variables. A range of non-prescription topical products have been claimed to possess some activity against skin ageing changes. These agents have been called cosmeceuticals, as they are not regulated as medicines by the Food and Drug Administration (FDA) in the USA, or the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK. Accurate assessment of their efficacy is often difficult because of limited available data.

A recent study of the effects of retinol on intrinsically aged forearm skin has been presented as further evidence of the rejuvenation potential of topical retinoids for ageing skin, increased dermal matrix protein synthesis and glycosaminoglycan induction being noted in this study [8].

A variety of antioxidants have been incorporated in the formulation of some topical products. There is evidence that they are capable of reducing some photodamage, with a reduction of erythema and other markers of UV damage such as sunburn cell accumulation. Some topical vitamin C analogues have been shown to regulate collagen and tissue inhibitors of matrix metalloproteinase [9]. Other antioxidants employed include botanical agents, such as extracts of grape seed, pomegranate, green tea and raspberry [10]. It appears that polyphenol and isoflavone are also ingredients that may be effective for photoprotection. Coenzyme Q-10, which is a component of a mitochondrial electron transport chain acting as an antioxidant in the skin, has also been used as a protective antioxidant in cosmeceutical topical products [11].

A variety of synthetic plant derivatives such as N6-furfuryladenine, and ferulic acid have also been employed in some cosmetic preparations because of their in vitro cell protective properties [12]. Further research is required to confirm the degree of in vivo human activity of these agents in different formulations for photoprotection and repair of ageing skin.

Oestrogen

Oral oestrogen use in females is associated with a statistically significant decline in the risk of skin wrinkling, but interestingly...
not in atrophy [13]. These clinical changes are due to an increase in skin collagen content. Topical progesterone is associated with increased skin elasticity in pre- and postmenopausal women, suggesting a possible value for improving some aspects of ageing skin in women [14].

References

Skin rejuvenation procedures

There are now many non-invasive or minimally invasive treatments for skin rejuvenation. The remainder of this chapter will discuss some of the more commonly accepted options (Table 80.3).

Volume replacement by fillers

Volume replacement using a variety of dermal fillers is designed to address the subcutaneous atrophy and facial hollows that often accompany ageing. A number of soft-tissue fillers are now employed, ranging from non-biodegradable, which may be permanent, to more transient, biodegradable fillers [1]. It is important to know that these fillers have different risks of adverse events [2], which are related to the skill of the injector and the intrinsic properties of the filler [2–4].

Categories of dermal fillers

Fillers can be categorized according to their source:
• Autogeneic, e.g. fat, autologous plasma, autologous collagen
• Allogeneic, e.g. human cadaver tissue, human fibroblast cell culture

Table 80.3 Some treatment options for facial rejuvenation.

<table>
<thead>
<tr>
<th>Objective</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial rejuvenation</td>
<td>Topical antiageing creams, Superficial peels, Microdermabrasion</td>
</tr>
<tr>
<td>Dermal remodelling</td>
<td>Intense pulsed light, Non-ablative facial, Rejuvenation (lasers), Laser and fractional resurfacing</td>
</tr>
<tr>
<td>Muscle relaxation</td>
<td>Botulinum toxin type A injections</td>
</tr>
<tr>
<td>Soft tissue augmentation</td>
<td>Fillers</td>
</tr>
<tr>
<td>Volume replacement</td>
<td>Fractional resurfacing—carbon dioxide fraxel</td>
</tr>
<tr>
<td>Deeper rejuvenation</td>
<td>Carbon dioxide lasers, Medium peels, Deep peels</td>
</tr>
</tbody>
</table>

• Xenogeneic, e.g. collagen, usually derived from bovine or porcine sources; hyaluronic acid products derived from animal sources or the results of bacterial fermentation
• Synthetic products, e.g. silicone, polymethyl methacrylate, hydroxyapatite, carboxy cellulose, poly-L-lactic acid, polyacrylamide.

Specific dermal fillers

Xenogeneic bovine collagen has been used for over 20 years, and results can last from 3 to 12 months, depending on the choice of bovine collagen [5]. The duration depends on the site and type of injection selected. Because of a risk of delayed cutaneous allergic reactions with bovine collagen it is advised that double skin testing is carried out, as it has been estimated that approximately 3% of injected patients will develop delayed nodular reactions [2,6], including necrotic reactions [7].

Products developed over the last 10 years include a variety of hyaluronic acid derivatives. In some parts of the world there is little regulatory requirement for testing of these new fillers before they are used on patients. The original hyaluronic acid filler was derived from rooster combs [7], but this has now been largely superseded by materials produced by bacterial fermentation and stabilization using proprietary processes [8].

The duration of benefits from hyaluronic acids fillers for correction of nasolabial folds is usually between 6 and 12 months, but it is less when used for lip augmentation [9] (Figs 80.3 & 80.4). The duration of benefit in an individual will depend on several factors, including formulation of the hyaluronic acid filler, depth of injection and laxity of skin injected.

Side effects include immediate oedema, haematoma, delayed allergic reactions, nodules, vascular occlusion and infections, including, rarely, atypical mycobacteria [2,3].

There are still occasional delayed reactions to these fillers, leading to inflammatory nodule formation, although their frequency has declined significantly over the past 5 years [2,10]. Other volume replacements that give immediate filling include calcium hydroxyapatite, which is useful as deep injections for...
volume replacement of cheeks and deep nasolabial folds [11]. Another group of injectables that increase the collagen matrix, ground substance and dermal elastic formation by stimulating dermal fibroblast activity include poly-l-lactic acid (PLLA). This is injected as a dilute suspension which dissolves within the dermis and subcutaneous levels, inducing fibroplasia and increasing dermal and subcutaneous thickness. Originally, PLLA was used to improve the facial lipodystrophy often associated with earlier types of antiretroviral therapy [12]. It was subsequently shown to be effective for correcting facial volume loss in the ageing face and for atrophic scars. The main side effect is nodule formation, most commonly in perioral and periorbital areas, and these are therefore areas which should be avoided with PLLA [12]. It is most useful for nasolabial folds and mid-cheek sites [13]. PLLA has also been used for atrophic scar improvement [14].

Another recent approach has been to use allogeneic human-derived fibroblasts from a single source of neonatal tissue; this procedure is in the early stages of research and development [15]. Safety phase studies have shown increased dermal and epidermal thickness, and no toxicity. Further studies are proceeding.

An autologous filler that has been used for many years is fat, harvested from the patient and processed with filtration plus cleansing, or simply reinjected. A debate as to the efficacy of these different methods of fat replacement injections continues. One problem is variable duration of benefit, and it has been suggested that this is site specific, with the cheek area having the best retention of injectable fat [16]. Post-injection oedema and bruising is temporary but can last several weeks [16]. One study suggested that fresh autologous fat transfer has good viability compared with refrigerated or frozen fat storage and later injection [17].
Fat is best used for deeper volume replacement of the face or localized areas of fat atrophy [16].

**Adverse reactions (Table 80.4)**

Adverse reactions to fillers can be described in terms of:

- Clinical seriousness
- Aesthetic relevance
- Immediate versus delayed onset
- Causality: expected procedure related events; events related to improper technique; reactions to the product.

Reactions can be attributed to the procedure itself, procedural technique and the agent injected. Some of these reactions are preventable, whereas others are inevitable; most are mild and transient. Improving product formulations, altering the concentration of product injected or changing injection technique can dramatically reduce the incidence of adverse reactions. Since its reformulation in mid-1999, the biologically engineered hyaluronic acid filler, Restylane, elicits less than one allergic reaction in 1600 treatments. There are over 85 different hyaluronic acid fillers currently available in Europe. Skin reactions with PLLA (New-Fill) to treatment with Zyderm and Zyplaso collagen implant. J Am Acad Dermatol 1991; 25: 319–26.


References


Table 80.5 Available botulinum neurotoxins.

<table>
<thead>
<tr>
<th>Product</th>
<th>Toxin type</th>
<th>Toxin mol wt (kDa)</th>
<th>pH</th>
<th>Approved in Europe and USA for cosmetic use</th>
<th>Approved for hyperhidrosis in UK, Europe, USA</th>
<th>Approved for medical indications (dystonia, blepharospasm etc.) in Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botox</td>
<td>A</td>
<td>900</td>
<td>~7</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Dysport</td>
<td>A</td>
<td>500–900</td>
<td>~7</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Xeomin</td>
<td>A</td>
<td>150</td>
<td>~7</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Neuronox</td>
<td>A</td>
<td>Unknown</td>
<td>6.8</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Myobloc/Neurobloc</td>
<td>B</td>
<td>300–500</td>
<td>~5.6</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Botulinum toxins—their use in controlling facial lines

The first medical use of botulinum neurotoxin was described by Dr Alan Scott during the 1970s when he used a botulinum toxin type A (BTX-A) for reducing over-activity of selected periocular muscles in patients with strabismus [1–3]. Following this observation botulinum neurotoxins have been increasingly studied for a wide variety of therapeutic and aesthetic uses. Double-blind controlled studies of BTX-A for reduction of upper facial lines in the USA have shown benefit of approximately 4 months’ duration [4,5]. These initial observations were followed by double-blind, placebo-controlled studies of several hundred patients performed in the USA, which demonstrated that BTX-A was safe and effective for reducing the severity of glabellar lines (lower forehead vertical frown lines) [6,7]. Significant improvement was observed as early as a few days after treatment, and the mean duration of improvement was in excess of 4 months using appropriate doses of BTX-A, which were initially 20 units for lower forehead frown lines. Several other studies confirm that BTX-A is also effective for lateral periorbital lines, often known as ‘crow’s feet’ [8] and also rhytides of the infraorbital area [9].

There are two main serotypes of botulinum toxins used clinically—the most commonly used being botulinum toxin type A (BTX-A) (Table 80.5). Type B botulinum toxin (BTX-B) has a much shorter duration of effect than BTX-A, but is occasionally used if therapeutic resistance is observed to BTX-A.

Other clinical studies have confirmed that both type A and type B botulinum toxins are effective at reducing facial lines [10], as well as excessive sweating in areas such as the axillae [11,12]. BTX-A treatment for axillary hyperhidrosis has been approved by the MHRA in the UK, and regulatory agencies in numerous other countries including the FDA in the USA.

The mode of action of BTX-A is by rapid inhibition of acetylcholine release at the neuromuscular junction. As a result, BTX-A causes localized, reversible muscle relaxation [1], and because some facial lines result from repetitive contraction of underlying muscles this produces a reduction of facial lines [4,5,7,8]. The mode of action against hyperhidrosis (which is covered in more detail in Chapter 44) is again the result of inhibition of release of acetylcholine, which is one of the neurotransmitters for emotional, non-thermoregulatory sweating [11,12].

The sites of injection used to improve facial lines, and therefore some signs of facial ageing, are most commonly: upper face—horizontal forehead lines, vertical forehead lines, supraorbital lines, periorbital (crow’s feet) lines, infraorbital lines, paranasal lines; lower face—perioral lines, vertical rhytides above the upper lip and turning down of the angles of the mouth (melomental folds) [13]. Vertical neck bands produced by platysmal muscle activity can also be reduced by the use of BTX-A [14].

Two different clinical types of BTX-A have been available in Europe since the 1990s. They are produced by different bacteria, with differing fermentation and purification processes, and have different potency and diffusion. Dilution and dosing have been investigated, and estimated conversion ratios of one type of BTX-A to the other have been proposed [15,16].

Side effects from BTX-A are local at doses used for aesthetic indications, for example bruising and brow and/or eyelid ptosis. They are usually the result of inexpert injection of BTX-A—for example, injection of too high a dose of BTX-A into the lower lateral forehead may result in both brow and upper eyelid ptosis. Injection too low in the infraorbital area may result in upper lip and lower facial weakness. Facial asymmetry may occur. These side effects are usually temporary, but can be of understandable concern to patients [17]. The physician injecting BTX-A should be trained to try to avoid these problems.

Other side effects are extremely uncommon. A rare problem is that of resistance to BTX-A, the mechanism of which is unknown, but may involve antibodies blocking the uptake or action of BTX-A.

Combination treatments with BTX-A

Combination treatments are selected for appropriate patients to rejuvenate the ageing face [17]. An example of a combination treatment is administration of BTX-A prior to use of either resurfacing lasers [18] (Fig. 80.5) or fractionated rejuvenation lasers (p. 80.11). The BTX-A is ideally delivered at least 1 week prior to the laser; this enables the hyperactive muscle action to be diminished thereby reducing the facial lines. In addition, as one theory of skin rejuvenation with these laser systems is the stimulation of neocollagenesis, it is likely that a less folded skin following BTX-A leads to more uniform neocollagenesis.

The effects of combined BTX-A injections and lasers have been confirmed as being superior to placebo injections and laser alone [18].

Another situation where combination treatments are useful is the use of BTX-A and dermal fillers in problems such as deep vertical lower forehead lines. Here, BTX-A alone will improve, but not clear, the deep furrows that are present in some patients. The
use of BTX-A plus temporary filler can give a more prolonged effect than using the filler alone [19]. In a similar mechanism, the use of BTX-A to the upper lip area together with filler in the upper lip can provide adjunctive benefit in the correction of upper lip lines. Dermal fillers and BTX-A can also be combined in lower facial areas, where the BTX-A is injected into areas such as depressor angulae oris and mentalis muscles and the filler is injected into melolental folds.

Figure 80.6 shows the effect of BTX-A injected in the periorbital area, thereby reducing the intensity of the periorbital rhytides.

References
Chemical peels for improvement of facial ageing

Chemical peels have been used for many years for skin surface rejuvenation, and treating irregular pigmentation and superficial scars [1].

A limiting factor is the depth of penetration of the different chemicals used for skin peeling. Another important factor is the toxicity of the chemical, for example phenol or 50% trichloroacetic acid are considerably more toxic to the skin than 50% buffered glycolic acid peels [2,3]. Even in expert hands there are some patients who will have undesirable results from chemical peels. These may include changes in pigmentation, for example hypopigmentation, which can be permanent, and hyperpigmentation, which can be long-lasting, and may be permanent and scarring.

More superficial peels, for example glycolic acid, lactic acid [3] and Jessner’s peels, will accelerate epidermal shedding, but other more aggressive peels can chemically destroy epidermis and progressive layers of the dermis by protein coagulation and cell lysis. The main classification of peels is usually based on the expected depth and severity of the peel—a commonly used classification being superficial peels, medium-depth peels and deep peels [2–4]. Examples of the peeling agents leading to different severities of peel are listed in Table 80.6.

The nature of the chemical influences the depth of peel; for example, lactic acid is usually a very superficial peeling agent and 50% trichloroacetic acid (TCA) is a much deeper peeling agent [2,3]. Another factor that affects the peel is skin preparation with topical retinoids, which is felt to increase the uniformity of the peel. It alters the stratum corneum barrier, and enhances the penetration of some peeling agents by altering epidermal and stratum corneum morphology. It is possible to change a superficial-depth glycolic acid peel into a medium-depth peel by altering the degree of hyperpigmentation [4] (Fig. 80.7).

Superficial peels include a combination of resorcinol, lactic acid and salicylic acid, known as Jessner’s peel. This is useful for abnormal superficial pigment, fine rhytides and very superficial scars. It can be reapplied numerous times over the treatment session [7].

Table 80.6 Different depths of chemical peels.

<table>
<thead>
<tr>
<th>Level</th>
<th>Histology</th>
<th>Peel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial</td>
<td>Destruction of epidermis alone</td>
<td>10–25% TCA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glycolic acid 50–70% Jessner’s solution</td>
</tr>
<tr>
<td>Medium</td>
<td>Destruction of epidermis plus papillary</td>
<td>TCA 35% Jessner’s solution</td>
</tr>
<tr>
<td></td>
<td>dermis</td>
<td>Glycolic acid + 35% TCA Baker’s phenol/TCA 50%</td>
</tr>
<tr>
<td>Deep</td>
<td>Destruction of reticular dermis</td>
<td></td>
</tr>
</tbody>
</table>

TCA, trichloroacetic acid.

Every practitioner using peels in their practice should become trained and familiar with the particular peel they will be using.

Site dependence

The density of appendageal structures, such as pilosebaceous glands, will also govern the safety and healing of the skin following deeper chemical peels. An area such as the face, which has a much higher density of pilosebaceous structures, generally responds in a more predictable way to chemical peels than the neck, chest and limbs. Superficial peels should only be used in areas where there are minimal sebaceous appendages, that is most areas other than the face. Medium-depth peels can be used on the face, but care should be exercised in using them on other parts of the body. Because of the relatively low density of skin appendageal structures, impaired healing can occur in these non-facial areas, resulting in an increased risk of scarring and pigmented changes.

Skin phototype and chemical peels

Skin phototype (Table 80.7) is of key importance in chemical peel selection. Because of the risks of facial pigmentation disorders following the peels it is important that skin phototypes III and above are treated with peels that are not likely to result in hypopigmentation [7]. Patients with skin phototype III and above will always have some hyperpigmentation following peels. This is usually transient, but often requires pre- and post-treatment therapy with tretinoin 0.25% or 0.5% creams for 6 weeks prior to the peel, often together with skin lightening preparations such as hydroquinone. Post-peel treatment with these agents is usually begun after complete re-epithelialization and stabilized erythema, several weeks after the peel. This post-peel treatment may reduce the degree of hyperpigmentation [4] (Fig. 80.7).

The superficial chemical peels remain valuable for treating milder skin ageing problems and as adjunctive treatments in diseases such as acne. The medium-depth and deeper chemical peels have now largely been replaced by laser skin rejuvenation, as described below in this chapter. There is some agreement that lasers lead to a more controlled impact on the skin and are not dependent on the vagaries of chemical peeling, for example variations of percutaneous penetration and toxicity that can lead to variable results. These problems are much less with modern lasers such as fractionated lasers (Lowe, N.J. personal observations).

Table 80.7 Fitzpatrick’s classification of skin phototypes.

<table>
<thead>
<tr>
<th>Skin type</th>
<th>Colour</th>
<th>Reaction to sun</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Very white or freckled</td>
<td>Always burns</td>
</tr>
<tr>
<td>II</td>
<td>White</td>
<td>Usually burns</td>
</tr>
<tr>
<td>III</td>
<td>White to olive</td>
<td>Sometimes burns</td>
</tr>
<tr>
<td>IV</td>
<td>Brown</td>
<td>Rarely burns</td>
</tr>
<tr>
<td>V</td>
<td>Dark brown</td>
<td>Very rarely burns</td>
</tr>
<tr>
<td>VI</td>
<td>Black</td>
<td>Never burns</td>
</tr>
</tbody>
</table>
References

**Intense pulsed light and laser treatment—selection for cosmetic indications**
Selection of intense pulsed light (IPL) and lasers will depend on the nature of the clinical lesion to be treated. Table 80.8 summarizes some of the more frequent clinical lesions to be treated and the selection of the type of laser and light source to be used. The reader is also referred to Chapter 78 for further information on lasers and light sources.

**Intense pulsed light system**
Intense pulsed light (IPL) sources give a non-coherent emission rather than the coherent specific single wavelength of a laser [1]. Most IPL systems emit a spectrum between 500 and 1200 nm, with a variety of cut-off filters designed to reduce selectively lower visible wavelengths, for example below 515 nm or below 560 nm. This lower wavelength selectivity allows for selection of different treatment indications. For vascular problems, for example telangiectasia and haemangiomas [1], wavelengths down to 500 nm are used, whereas skin pigmenatry problems such as lentigo will best respond to wavelengths down to 560 nm. Poikiloderma of Civatte has also been treated with IPL. Care has to be taken to obtain a uniform improvement [2].

**Skin surface cooling for cosmetic IPL and laser procedures**
Surface skin cooling has provided significant safety advantages for some laser and IPL systems. The concept is that by cooling the skin surface it is possible to reduce undesirable thermal injury to the epidermis by the IPL or laser, thus diminishing the risk of hypopigmentation and scarring (see Chapter 78).

There are three main types of tissue cooling:
1. Cold air convection, which is directed on to the area prior to and during treatment
2. Contact cooling, where the laser or light tip itself is cooled and thereby cools the skin surface
3. Cryogen spray cooling, where a frozen gas is sprayed on to the skin just prior to, and with some lasers during, the delivery of the laser light [3].

### Table 80.8 IPL and laser treatment of clinical problems.

<table>
<thead>
<tr>
<th>Clinical problem</th>
<th>Type of laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular lesions</td>
<td>Pulsed-dye usually 585–595 nm</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>Copper bromide</td>
</tr>
<tr>
<td>Haemangiomas/port-wine stains</td>
<td>KTP</td>
</tr>
<tr>
<td>Cambell de Morgan angiomas</td>
<td>IPL</td>
</tr>
<tr>
<td>Benign pigmented lesions</td>
<td>Q-switched, ruby, alexandrite, neodynium:YAG, IPL</td>
</tr>
<tr>
<td>Lentigo, melanosis, melasma</td>
<td>Q-switched</td>
</tr>
<tr>
<td>Tattoos</td>
<td>Ruby, alexandrite</td>
</tr>
<tr>
<td>Neodynium : YAG</td>
<td></td>
</tr>
<tr>
<td>Ageing skin, rhytides, laxity</td>
<td>Carbon dioxide lasers</td>
</tr>
<tr>
<td>Seborrhoeic keratosis</td>
<td>Erbium YAG lasers</td>
</tr>
<tr>
<td>Hirsutes (pigmented hair)</td>
<td>Fractional lasers</td>
</tr>
</tbody>
</table>

Fig. 80.7 (a) Pre-treatment and (b) post-treatment with a combined tretinoin, hydroquinone and hydrocortisone skin ‘lightening cream’, four glycolic peels and broad-spectrum daily sunscreen.
Another benefit of the use of cooling is that higher laser and IPL fluences can be used, enabling otherwise more resistant lesions, for example high blood-flow telangiectasia or vascular haemangiomas, to respond. Cooling also has another important effect of reducing the discomfort associated with treatment. It is important, however, to avoid cold injury from the cooling device. Cryogen freeze injury has been seen (Lowe, N.J., personal observations), particularly in skin phototypes III and darker from cryogen-cooled hair removal lasers.

Lasers for skin ageing problems
These may be grouped into treatment of vascular, pigmented or skin surface irregularities, that is superficial rhytides, and deeper problems of skin laxity, deeper rhytides and scars.

Vascular changes associated with skin ageing
Telangiectasiae on the cheeks, nose and other light-exposed areas are vascular abnormalities commonly associated with skin ageing. In addition, poikiloderma of Civatte, particularly affecting the lateral face and neck, is a superficial abnormality that is probably the result of repetitive ultraviolet injury together with, in some patients, phototoxic or photoallergic reactions to fragrances.

Choice of lasers for these vascular problems includes vascular pulsed dye lasers are (usually between 585 and 595 nm), alexandrite (755 nm), Nd:YAG lasers (1064 nm), copper bromide lasers and potassium titanyl phosphate (KTP) lasers. The initial development of these lasers resulted from knowledge of the action spectrum responsible for laser vascular injury [4].

Electrocautery is sometimes used for solitary telangiectasia. One of the problems with electrocautery is a higher risk of recurrence of the lesion and/or atrophic scarring compared with pulsed-dye lasers. However, electrocautery does not give the transient purpura associated with pulsed-dye lasers.

An important guideline when treating a large area with any of these laser or light systems is to perform a test treatment on a small, preferably non-visible part of the skin, to ensure the correct choice of laser and laser parameters. This is particularly important before treating large areas of skin, for example poikiloderma on the neck or extensive telangiectasiae on the cheek. It is possible to get irregular ‘patchy’ improvement that requires numerous further treatment sessions to become more uniform and acceptable.

Some darker skin phototypes, for example phenotype III and darker, may elicit long-term and occasionally permanent hyperpigmentation following light and laser therapy. If too aggressive an IPL or laser treatment is selected, skin blistering with subsequent scarring and hypopigmentation is possible [5].

Benign pigmented skin lesions associated with ageing
The most common type of benign pigmented skin lesion associated with photoageing is the solar lentigo. These usually respond well to a variety of lasers and pulsed light sources. The original observations on laser treatment by Goldman used a ruby laser for tattoos and pigmented lesions [6].

Naevus of Ota persists into old age and responds well to a variety of Q-switched pigment lasers [7]. Melasma shows an extremely variable response to all lights and laser treatments—indeed to most treatment intervention [7]. The reasons remain to be determined, but possibly involve continued endogenous or exogenous hormonal stimulation of melanogenesis [8].

Lasers for benign pigmented lesions include Q-switched ruby (605 nm), alexandrite (755 nm), Nd:YAG lasers (532 and 1064 nm) and Q-switched KTP (532 nm) [7–9].

Frequently, patients with photodamage will exhibit a combination of facial telangiectasia, plus lentigo and diffuse facial melano-sis which can be treated with IPL sources. One advantage of an IPL system is that because of its broad spectrum of visible wavelengths both these types of photodamage may respond to the IPL [5,10].

Pigmented and non-pigmented seborrhoeic keratoses will respond well to laser ablation with either carbon dioxide or Er:YAG lasers. These can give a more accurate lesion vaporization than cryotherapy, and in some patients may be less likely to result in hypopigmented areas.

Lasers for surface skin changes
The first laser to be used successfully for photodamage treatment by ‘skin resurfacing’ was a pulsed carbon dioxide laser [11]. The carbon dioxide laser emits a wavelength of 10600 nm and is absorbed by tissue water content. It penetrates up to 30 μm into previously non-treated skin; once absorbed, further penetration is limited by the reduced tissue water content.

Various other types of carbon dioxide laser have been developed, including scanned devices. The concept of ultrapulsing [12,13] is to give a uniform treatment area from the laser that produces skin surface vaporization but rapid re-epithelialization from undamaged hair follicles and other adnexal structures. There is a rejuvenation of the damaged skin surface. In addition, it has been shown that with ultrapulse carbon dioxide lasers there is a degree of dermal tightening which may continue for up to 1 year after treatment [14]. This tissue tightening may be the result of either a delayed wound healing response following the laser or neocollagenesis resulting from release of cytokines and other dermal growth factor stimuli [15–17]. Other carbon dioxide devices have used scanning systems rather than ultrapulsed systems to control skin injury [18].

Another skin resurfacing laser, which has greater affinity for water absorption compared to the carbon dioxide device, is the Er:YAG laser, emitting a wavelength of 2940 nm [19,20]. It is highly absorbed by skin water, but has a relatively low penetration of 3 to 5 μm. Ultrapulse carbon dioxide lasers are more effective than conventional Er:YAG lasers [21]. In addition, because they do not produce as much haemostasis as the carbon dioxide laser there tends to be a greater degree of bleeding during treatment [21].

Some newer Er:YAG lasers have variable pulse duration so that they act in a manner similar to the carbon dioxide laser (Lowe, N.J. unpublished observations).

Fractional laser skin rejuvenation
Newer developments in skin rejuvenation by lasers have been the use of the fractional laser delivery systems [22]. Fractional
photothermolysis (FP) is a relatively new technology that creates microscopic zones or columns of thermal damage surrounded by healthy tissue, in contrast to layers of thermal vaporization from the ultrapulse carbon dioxide and Erbium:YAG lasers. The first FP laser device was introduced in 2003, as an erbium-doped fibre laser emitting at 1550 nm [22,23].

The microscopic thermal treatment zones vary in depth depending on the energy settings of the laser. As they are surrounded by an area of untreated skin this acts as a reservoir of keratinocytes for rapid repair of the treated areas of skin. Success has been reported with facial rhytides, photodamaged skin and scarring [23–25].

Initially, this system used a surface-applied blue dye to act as an optical activator of the laser [23]. The latest Fraxel laser system employs a motion detector whereby the laser is triggered by motion across the skin. This can be described as a ‘rolling’ FP laser system. The efficacy of FP with the 1550 nm laser, mentioned above, has been reported in a number of studies [23–25]. Results are encouraging for the improvement of surface photodamage, solar lentigo, diffuse facial melanosis, fine rhytides and atrophic facial scars (Figs 80.8–80.10). Another advantage of this laser is that it can be used (at appropriate settings) on areas other than the face, for example the neck, chest and limbs (Fig. 80.11). With previous lasers, for example ultrapulse carbon dioxide and Erbium:YAG, there was complete epidermal and dermal photothermolysis and a significant risk in non-facial areas of compromised, delayed healing with scarring risk due to the relative paucity of adnexal structures. A very recent development is a fractionated delivery carbon dioxide laser.

A variety of other ‘pseudo-fractionated’ and ‘stamp’ fractionated systems have been developed including systems using several wavelengths between 532 and 10600 nm. These all have their own proponents, but as yet there is a lack of data to enable comparison with the rolling FP system.

**Skin preparation and post-treatment care for laser rejuvenation**

Pre-treatment preparation and post-treatment care of the skin are important, particularly in the management of pigmented and photodamaged skin. Pre-treatment with topical retinoids and, where pigmentation is a problem, additional depigmenting agents such as hydroquinone or combinations thereof, may help to enhance healing and reduce post-laser hyperpigmentation [14]. In addition, it is important to enquire about the occurrence of herpes simplex on the area to be treated, and prophylactic oral aciclovir 400 mg b.d. 1 day prior to and 7 days following laser treatment may be employed [26]. Post-laser care involves the use of topical emollients, as well as treatment of any possible post-laser acne relapses and folliculitis.
After initial healing—usually 1–2 weeks—the patient should be encouraged to use daily photoprotection with a sunscreen, topical antioxidants and, if necessary, depigmenting agents. Maintenance treatment can include topical retinoids, for example tretinoin 0.025% cream may be used nightly as tolerated.

**Non-laser skin surface rejuvenation**

A recent development is a ‘plasma’ skin rejuvenation system, using high surface energy generated with nitrogen gas released at high velocity. This ‘plasma’ system is currently being evaluated as an alternative to laser skin rejuvenation [27].

**References**


**Radiofrequency**

Radiofrequency has been developed as a treatment to promote skin and facial tightening. The results to date are mixed. Appropriate patient selection is critical, with early facial laxity subjects more likely to respond than older patients.

Monopolar radiofrequency skin tightening was first approved by the US FDA in 2002 as a facial treatment. More recently, it has gained approval for treatment of selected body areas [1,2]. The concept is that a controlled radiofrequency pulse selectively heats
zones of the dermis and deeper tissue, while a proprietary cooling surface system protects against injury to the epidermis and upper dermis.

Initial investigations showed some degree of improvement in selected patients, but in general the first treatment algorithms were unpredictable. Subsequently, this monopolar radiofrequency system has become more consistent and the algorithm is now to use multiple passes over the same area, with moderate energy settings, to give greater consistency.

A recent retrospective study showed that 54% of patients observed skin tightening 6 months after treatment, and 26% showed an immediate tightening. This was with the original treatment algorithm. However, with the multiple pass moderate energy treatment algorithm 87% were reported as observing immediate tightening and 92% noted skin tightening 6 months after treatment [2].

In the author’s opinion one of the most important factors in the use of monopolar radiofrequency is patient selection. Patients who are candidates for facelift surgery are clearly not candidates for radiofrequency facial skin tightening. Conversely, patients who have early laxity of forehead, as well as lower facial and neck skin, may be improved using these treatments.

Other forms of radiofrequency treatment include bipolar radiofrequency, which is sometimes combined in some instruments with intense pulsed light. One of the problems with these other systems is that there has been little consistent research.

Combination minimally invasive treatment
The idea of combining several different non- or minimally invasive treatments is a relatively recent concept for facial rejuvenation. See Figure 80.11 for an example of a combination of minimally invasive treatment. Examples of such combinations include:
1. Topical agents, e.g. sunscreens, tretinoin cream, glycolic acid peels and BTX-A
2. BTX-A to forehead and crow’s feet; filler to mid and lower face; Fraxel laser to face and neck
3. Fraxel laser to neck plus BTX-A to platysmal band.

These combinations are selected for appropriate indications and patterns of ageing [3,4].

References