

## INTRODUCTION

Since ancient people, physical attractiveness has been socially advantageous and resulted in perceptions of “goodness” and success as well as a sense of well-being (Ενγασερ ανδ Μαιβαχη, 1999).

There are many dysmorphic dermatoses such as acne vulgaris, pitted scars, unsightly pigmentations and signs of aging that have a significant impact on a patient's quality of life, namely the relationship to others, self-image, self-esteem and economic opportunities (Βοηνηγκε ετ αλ., 2002; Ραππ ετ αλ.,2004 & Βαλκρισηναν ετ αλ., 2005). Hence, there is increased demand for aesthetic information and treatments, not only for patients suffering from these dysmorphic disorders but also for those who want their appearance to match their inward perception of youth and vitality(Ωιλσον ανδ Αρπεψ,2004 & Γορδον, 2005).

Corresponding to this trend, there is an ever-increasing number of products and procedures available that claim to aid in this pursuit(Ηιρσχη ετ αλ., 2004).These resurfacing techniques include the use of laser resurfacing, dermabrasion, microdermabrasion, jet peel and chemical peels (Γολαν ανδ Ηαι ,2005; Καριμιπουρ ετ αλ., 2005& Ροψ,2005).

Chemical peeling is one of the facial rejuvenation procedures that have many cosmetic clinical applications such as reversal of photoaging, dyschromias, freckles, lentigens, melasma, nevi, seborrhoeic keratosis, postinflammatory hyperpigmentation and improvement of acne scars. Chemical peels may be superficial, medium depth, or deep. The

indication determines to great extent the type and depth of peel necessary (Ροβερτσ, 2004).

A variety of peeling agents can be used including trichloroacetic acid (TCA), Jessner's solution, alpha hydroxy acids, alpha keto acids, azelaic acid, retinoic acid, salicylic acid, and phenol. Now, Amino acid filaggrin based antioxidants are used (Κλειν, 2000; Βριδεν, 2004 & Σηαρθυιε ετ αλ., 2005).

## AIM OF THE WORK

**T**he aim of this work is to compare the efficacy of trichloroacetic acid (TCA), glycolic acid and amino acid filaggrin based antioxidants (AFA) in the treatment of melasma, acne vulgaris, and fine wrinkles.

## MELASMA

Melasma is defined as a symmetric progressive hyperpigmentation of facial skin that occurs in all races but has a predilection for darker skin phenotypes. It is one of the three common forms of hyperpigmentation (melasma, lentigines, and post-inflammatory hyperpigmentation) with significant negative psychological consequences. Many therapeutic options exist, though, treatment is often difficult requiring lengthy therapy (Χαψγε et al., 2004 & Περεζ ,2005).

### **Etiopathogenesis:**

The pathogenesis of melasma is unknown. Many etiologic factors have been implicated, but sunlight is certainly the major factor that selectively increases the functional state of melanocytes (ζιχτορ et al., 2004). Melasma can be associated with many other factors like, *a*) Hormonal imbalances (pregnancy, ovarian tumors, long use of contraceptive pills and thyroid abnormality). *b*) Deficiency states (hypoproteinemia, hypovitaminosis and gastrointestinal disturbances as hepatic dysfunction and parasitic infestations). *c*) Drugs (diphenylhydantoin and 5-ethyl-methyl-5-phenylhydantion). *d*) cosmetics. *e*) Genetic predisposition (Σανχηεζ et al., 1981; Νιεπομνισζχζε ανδ Αμαδ ,2001 & Περεζ ,2005).

### **Clinical picture:**

Clinically, melasma can be divided into three patterns according to the pigment distribution on the skin; *a*) Centrofacial (involved the cheeks, forehead, upper lip, nose and chin). *b*) Malar (involved the

cheeks and nose). *c*) Mandibular (involved the ramus of the mandible). According to visible light and Wood's light examination, four types of melasma exist; *i*) Epidermal type, with usually light brown hyperpigmentation and enhancement of the color contrast by Wood's light, compared to day night. *ii*) Dermal type, displaying ashen or bluish grey pigmentation, with no accentuation of contrasts under Wood's light. *iii*) Mixed type, often dark brown in color, and contrast of hyperpigmentation irregularly enhanced by Wood's light. *iv*) Skin types V-VI: lesions are visible at daylight, but not evident under Wood's light (Λοριντζ, 1985 & Περεζ, 2005). Many other methods and scores can be used for melasma evaluation maxemeter, colorimeters by narrow – band reflectance spectrophotometer taken from an area of normal coloration and area of hyperpigmentation at base line, Melasma Area Severity Index (MASI) and Melasma Area and Melanin Index (Λεενυταπηονγ ετ αλ., 1999; Μαρψ ετ αλ., 2002 & Σηαρθυιε ετ αλ., 2005)

### **Treatment:**

Its pathogenesis remains largely unknown whatever, there are many differences between melasma and normal skin, melasma skin contains increased melanin, melanocytes, and melanosomes, as well as increased synthesis of tyrosinase. So, *principles and aims of therapy* should include *a*) Protection from sunlight. *b*) Inhibition of activity of melanocytes. *c*) Inhibition of the synthesis of melanin. *d*) Removal of melanin. *e*) Disruption of melanin granules (Πιαμπηονγσαντ, 1998 & ςιχτορ ετ αλ., 2004).

*a) Protection from sunlight:*

Either topically by sunscreens or by systemic drugs such as Chloroquine, Indomethacin, Vitamin C and E, Beta- carotene, Fish oils and Green tea which can be used as protective agents from both ultraviolet rays A and B (Ρηοδεσ, 1998).

*b) Inhibition of activity of melanocytes:*

By avoidance of sunlight, contraceptive pills, scented cosmetics and phototoxic drugs (Πιαμπηονγσαντ, 1998).

*c) Inhibition of the synthesis of melanin*

[Table 1] (Πιαμπηονγσαντ, 1998):

<b>Action</b>	<b>Agent</b>
Tyrosinaseinhibitor(Ρενδον, 2004 & Τοροκ ετ αλ., 2005)	-Hydroquinone -Kojic acid -Azelaic acid -LicoriceP-T -Arbutin -Melawhite
Inhibition of melanin production (Φιτζπατριγκ ετ αλ., 1993 & Καμεψομα ετ αλ., 1996).	-Ascorbic acid, magnesium-l-ascorbyl-2-phosphate -Glutathione
Selective melanocyte toxicity (θιμβωω ετ αλ., 1995 & Νφοο ετ αλ., 1997)	-Ammoniated mercury -Isopropylcatechol -N-Acetyl-4-S-cysteaminyphenol -N-2,4-Acetoxyphenylthioethylacetamide -N-Acetylcysteine
Nonselective suppression of melanogenesis (Μεντερ,2004)	-Indomethacin -Corticosteroids

d) *Removal of melanin:*

-In the stratum corneum by: chemical peeling. Single- or combination-agent chemical peels are shown to be efficacious and safe (Ροβερτσ, 2004). Many agents can be used for this purpose as AHAs, Jessner's solution and TCA(Ηυρλεψετ αλ., 2002; Υσυκι ετ αλ., 2003 & Λυγο-θανερ ετ αλ., 2003).

-In the upper dermis by: dermabrasion and chemodermabrasion which may be performed in recalcitrant cases but post inflammatory hyperpigmentation may be noted in Asian and dark skin people. This side effect may be avoided by the use of microdermabrasion technique. (Πιαμπηονγσαντ, 1998)

e) *Disruption of melanin granule* (Ταννουσ ανδ Αστνερ, 2005):

\* Dye and alexandrite lasers.

\*Q-switched Nd: YAG laser.

\* Q-switched ruby laser.

\*carbon dioxide silk touch laser.

Melanin granules in the upper dermis are disrupted by these lasers and the tiny granules are subsequently engulfed by macrophages (Γριμεσ, 1995 & Ανγσυωαρανγσεε ανδ Πολνικον ,2003)

**Combination therapy, the marriage of device and drug**

(Νεστορ, 2004):

The pigmentary disorders including melasma, are usually resistant to all treatment modalities, and are therefore very frustrating to the patient and clinician, so combination therapies can be more effective and safe. Exampels include: a) Chemical peeling and laser. b) 4%

hydroquinone, 10% buffered glycolic acid, vitamins C and E, and sunscreen (Λεε ετ αλ., 2002 & Γυεωαρα ανδ Πανδψα ,2003).

**New agents designed as skin lighteners** (Μασυδα ετ αλ., 1996)

Oral intake of proanthocyanidin (powerful antioxidant) -rich extract from grape seeds (GSE), is effective in reducing the hyperpigmentation of women with cloasma. The beneficial effect of GSE is maximally achieved after 6 months of regular intake(Ψαμακοσηι ετ αλ., 2004).

Miconazole, a regional antifungal agent, has been used worldwide in the treatment of superficial mycosis. However, the effect of Miconazole on skin pigmentation is not known, the depigmenting effect of Miconazole might be due to the inhibition of tyrosinase activity and tyrosinase expression, which eventually slows melanin biosynthesis. So, it may have beneficial effects in the treatment of hyperpigmentation disorders such as ephelis and melasma (Μυν ετ αλ., 2004).

Topical application of 2% Lenoleic acid (LA) in combination wit 0.05% betamethasone valerate (BV) on the face every night has a beneficial effect in the treatment of melasma patients, as, it activates protein kinase C and inhibits melanogenesis (Λεε ετ αλ., 2002).

## ACNE VULGARIS

Acne vulgaris is defined as a chronic, self limited, inflammatory disease of the pilosebaceous units which exhibits a series of diverse lesions; comedones, papules, pustules, nodules, cysts and scars (Χυνλιφφε ανδ Σιμπσον, 1998), seen primarily in more or less exacerbated form in approximately 85% of adolescent population (Βιαλεχκα ετ αλ., 2004). If left untreated, it can leave physical and emotional scars that can be devastating (Δαλε ανδ Ροναλδ, 1998 & Μοηρενσχηλαγερ ετ αλ., 2005).

### **Etiopathogenesis:**

Acne vulgaris is a multifactorial disease affecting the pilosebaceous follicles that arises from the interplay of 4 pathogenic factors: *a)* Increased sebum production. *b)* Follicular hyperkeratinization. *c)* Microbial colonization of the pilosebaceous unit by *Propionibacterium acnes*. *d)* Release of inflammatory mediators into the follicle and surrounding dermis (Σονψα ανδ Αλαν, 1998). Increased sebum production and follicular hyperkeratosis result in the development of microcomedones, and growth of *P. acnes* which secretes several proinflammatory products, playing an important role in the development of inflammation. Immune response to *P. acnes* includes humoral and cell-mediated immunity as well as complement activation. Keratinocytes and sebocytes, as major components of pilosebaceous unit, act as immune cells and may be activated by *P. acnes* and recognize altered lipid content in sebum, followed by the production of inflammatory cytokines leading to more proliferation of both cell types. Further

inflammatory responses lead to the development of increasing degrees of severity in inflammatory forms of acne (Γολλνιχκ, 2003 & Κνορ, 2005).

### **Clinical picture:**

Acne vulgaris can be manifested in a wide variety of clinical presentations inflammatory versus noninflammatory (Σηαλιτα, 2004). The face, back, shoulders and chest are the sites of predilection (Ηερανε ανδ Ανδο, 2003).

#### ***Noninflammatory lesions:-***

- Ωηιτεηεαδσ (χλοσεδ χομεδονε): Whiteheads result when a pore is completely blocked, trapping sebum (oil), bacteria, and dead skin cells, causing a white appearance on the surface(Εβλινγ ανδ Χυνλιφφε, 1992).
- Βλακκηεαδσ (Οπενεδ χομεδονε): Blackheads result when a pore is only partially blocked, allowing some of the trapped sebum (oil), bacteria, and dead skin cells to slowly drain to the surface. The black color is caused by reaction of the skin's own pigment, melanin, with the oxygen in the air (Πλεωινγ, 1980).

#### ***Inflammatory lesions*** (Αρνολδ ετ αλ., 1990):

- Παπυλεσ: Papules are small, red, tender bumps with no heads.
- Πυστυλεσ: Pustules are similar to whiteheads, but are inflamed, and appear as a red circle with a white or yellow center.

*Severe acne vulgaris is characterized by* (Αρνολδ ετ αλ., 1990 & Ποχηι, 1990):

- **Νοδυλεσ:** As opposed to the lesions mentioned above, but are much larger, can be quite painful, and can sometimes last for months. Scarring is common.
- **Χηστω:** Cysts can appear similar to nodules, but are pus-filled, and have been described as having a diameter of 5mm. or more across. They can be painful. Again, scarring is common.
- **Αχνε χονγλοβατα:** This is the most severe form of acne vulgaris and is more common in males. It is characterized by numerous large lesions, which are sometimes interconnected, along with widespread blackheads. It can cause severe, irrevocable damage to the skin, and disfiguring scarring. It is found on the face, chest, back, buttocks, upper arms, and thighs.
- **Αχνε φυλμινωνσ:** This is an abrupt onset of acne conglobata which normally afflicts young men. As with acne conglobata, extreme disfiguring scarring is common, but it also includes a fever and aching of the joints.
- **Πψοδερμα φαχιαλε:** This type of severe acne affects only females, usually between the ages of 20 to 40 years old, and is characterized by painful large nodules, pustules and sores which may leave scarring.

## STRATEGIES FOR SUCCESSFUL ACNE MANAGEMENT

Although acne is not a life-threatening disease, it has significant physical and psychological ramifications including depression, suicidal ideation, anxiety, psychosomatic symptoms, including pain and discomfort, embarrassment and social inhibition. Effective treatment of acne was accompanied by improvement in self-esteem, affect, obsessive-compulsiveness, shame, embarrassment, body image, social assertiveness and self-confidence. Effective treatment should be directed at a combination of the 4 pathogenic factors (Tαν, 2004).

The treatment of acne is based on local and systemic treatments which must be adapted to the type of acne and take some prognostic factors into account. Because of the possibility of drug resistance, combined treatments are preferred (Δρεvo, 2005).

### **I-Topical therapy:**

Available **topical antiacne agents** and factors reported are, the topical retinoid class, which includes tretinoin, adapalene and tazarotene (Ωαυγη ετ αλ.,2004 & Σηαλιτα ετ αλ.,2005), and the topical antibacterials, clindamycin, erythromycin and azithromycin(ΜχΗυγη ετ αλ.,2004). Another prescription drugs, 20% azelaic acid, benzoyl peroxide, salicylic acid, sulfur, and sodium sulfacetamide are available in over-the-counter acne treatments (Ακηαωαν ανδ Βερσηαδ, 2003).

## II-Systemic therapy:

### *A-Antibiotics:-*

- Τετρακυκλινε and its lipophylic derivatives, Doxycycline, and Minocycline. The most recent developed derivative is glycylcycline which is a derivative of minocycline, otherwise known as tigecycline, that exhibit antibacterial activities typical of earlier tetracyclines, but with more potent activity against tetracycline-resistant organisms (Ζηανελ et al., 2004 & Ταν ανδ Ταν , 2005).
- Ερπητρομυκιν: Oral erythromycin is comparable to tetracycline in its therapeutic effect on acne ,but resistance of P. acnes to erythromycin seems to be more common than that produced by tetracyclines (Τηβουτοτ, 1996 & Ταν ανδ Ταν, 2005).

A newer macrolide, azithromycin, offers superior tissue distribution and cellular concentration and is an effective oral anti-acne agent (Καπαδια ανδ Ταλιβ, 2004 & Κυς et al., 2005).

- Ρεχεντ αντιαχνε θυινολονε, Ναδιφλοξακιν, which is a fluorinated quinolone, has potent antimicrobial activities against Gram-negative and -positive microbes and is used to treat multiple inflamed acne lesions (Κυωαηαρα et al., 2005).

### *B-Systemic Isotretinoin*

Isotretinoin (13-cis retinoic acid) is the most effective agent available for severe inflammatory acne or nodulocystic acne (Σψκεσ ανδ Ωεβστερ, 1994). It is the only drug that affects all 4 pathogenic factors of acne (Χυνλιφε ανδ Γολλνιχκ, 1996 & Αλχαλαψ, 2004). Doses of 0.5 to 1.0 mg/kg per day are typical and treatment duration is usually 20 weeks.

It has many side effects but the most dangerous one is teratogenicity so negative pregnancy test must be obtained from female patients of childbearing potential prior to and throughout therapy (Χηλια et al., 2005 & Γιαννουλιδου et al., 2005).

### ***C-Hormonal therapy***

#### **Οραλ Εστρογεν/Προγεστιν**

Acne is related to androgenic skin disorders which affect a high proportion of women after menarche. Androgens play an important role in the pathogenesis of acne through the stimulation of sebum secretion, increasing sebaceous gland size and possibly through follicular hyperkeratinization. Conversely, estrogens decrease sebum production by suppressing gonadotropin release and androgen production and increasing sex hormone binding globulin production. One of the treatment options for acne is hormonal therapy, especially for women who require contraception. The effect of combined oral contraceptives in androgenic skin disorders depends on their estrogen:progestogen balance and on the antiestrogenic activity of the progestogen component (δελ Μαρμολ et al., 2004). So, numerous combination oral contraceptive pills have been evaluated in the treatment of acne vulgaris and have been found to be effective (Harper et al., 2005).

**Αντιανδρογενιχσ:**— There are several types of antiandrogenic drugs which have been tried for the control of acne such as; i) spironolactone (usually 50 to 100 mg/d), ii) cyproterone acetate plus ethinylestradiol (Diane), iii) flutamide (250 mg daily), iv) Finasteride (5mg daily) and others. These antiandrogenic drugs may be used for women with the history of new-onset or worsening acne in their adult

years, for patients who report premenstrual flare-ups, and for women whose conditions have not responded to standard systemic antiacne treatments (Ψεμισχι et al., 2005).

### **III- Other measures:**

**Πηοτοτηεραπψ:** Phototherapy is emerging as an alternative option to treat acne vulgaris which has many pictures; *a)* Visible light, specifically blue light, has a marked effect on inflammatory acne lesions and seems sufficient for the treatment of acne. In addition, the combination of blue-red light radiation seems to be superior to blue light alone, with minimal adverse effects. *b)* Photodynamic therapy has also been used, even in nodular and cystic acne, and had excellent therapeutic outcomes, although with significant adverse effects. *c)* Recently, low energy pulsed dye laser therapy has been used, and seems to be a promising alternative that would allow the simultaneous treatment of active acne and acne scarring (Χηαρακιδα et al.,2004; Βηαρδωαφ et al., 2005 & Ζακηαρψ, Ελλισ,2005).

**Συβχισιον:** Subcision is a technique that has been anecdotally reported to be of value in treating so-called "rolling scars". The side effects of swelling, bruising and pain are transient, but patients may have persistent firm bumps at the treatment site (Αλαμ et al., 2005).

**Μιχροδερμαβρασιον:** It is a simple, safe, office cosmetic procedure in which aluminum oxide crystals or other abrasive substances are blown onto the face, and then vacuumed off, using a single handpiece. This procedure has rapidly become widely utilized for a variety of cosmetic objectives, including the improvement of

photoaging, hyperpigmentation, acne, scars and stretch marks (Σπενχερ, 2005).

Χημικαλ πeeλινγ: Several types of peeling procedures can be used, superficial, medium depth and deep peels. Superficial peel is considered to be the most accepted one as it's considered suitable for both inflammatory and non inflammatory. The most common used peeling agents are Jessner's solution, TCA and AHAs(Ροβερτσ, 2004 & Πολι ετ αλ., 2005).

## FACIAL WRINKLES

Wrinkles are defined as modifications of the skin associated with cutaneous ageing and develop preferentially on sun-exposed skin, it represents the most common place of all the signs of aging and most of patients complain of looking older (Κοχη ετ αλ., 1997 & Βοσσετ ετ αλ., 2003). Also, individuals with these wrinkles may be misinterpreted as hostile, depressed, fatigued and anxious (Κεεν ανδ Κηοση, 1995).

### **Pathogenesis:**

Wrinkles are a natural process of aging which result from the combination of three factors: aging, muscular action, and gravity (Ματαρασσο, 1998 & Σαριφακιογλυ ετ αλ, 2004).

Wrinkles can be classified into three morphological types  
*a)* Crinkles, or very fine wrinkles that occur in aged skin, even in areas protected from sunlight. They disappear when the skin is slightly stretched. *b)* Glyphic wrinkles that represent an accentuation of the normal skin markings in the form of criss-cross pattern. They occur on the prematurely aged skin, due to elastotic degeneration caused by sunlight. *c)* Linear furrows are long, straight or slightly curved grooves, which are usually seen in the faces of old people. They include the horizontal frown lines along the forehead, the glabellar lines, and the “crow's feet” radiating from the lateral canthus of the eye (Τσυφι ετ αλ., 1986).

Glogau developed the traditional rhytide/photoaging classification scheme that is used most often today (Γλογαυ, 1994):

- Mild (age 28-35 years):- Few wrinkles, no keratosis, requires little or no makeup for coverage.
- Moderate (age 35-50 years):- Early wrinkling, shallow complexion with early actinic keratosis, requires little makeup.
- Advanced (age 50-60 years):- Persistent wrinkling, discoloration of the skin with telangiectasias and actinic keratosis, always wears makeup.
- Severe (age 65-70 years):- Severe wrinkling, photoaging, gravitational and dynamic forces affecting skin, actinic keratosis with or without cancer, wears makeup with poor coverage.

Fitzpatrick (1996) reported an alternative classification system that is useful in assessing the degree of perioral and periorbital rhytidosis:

- **Class I** - Fine wrinkles.
- **Class II** - Fine-to-moderately deep wrinkles and moderate number of wrinkle lines.
- **Class III** - Fine-to-deep wrinkles, numerous wrinkle lines, and redundant folds possibly present.

Fitzpatrick also correlated these 3 classes with the following scoring system and degree of elastosis:

- **Class I** (score 1-3) - Mild elastosis.
- **Class II** (score 4-6) - Moderate elastosis.
- **Class III** (score 7-9) - Severe elastosis.

Mild elastosis is defined as fine textural changes with minimal skin lines. Moderate denotes a yellow discoloration of individual papules (papular elastosis). Severe describes marked confluent elastosis with thickened, multipapular, and yellowed skin (Φιτζπατριχκ, 1996).

**TREATMENT MEASURES**(ΛεΡοψ, 1998; Φαγιεν, 2000; Ελ-Δομψατι ετ αλ.,2003 & Κανε, 2003).

The most common procedures are; sunscreens, topical tretinoin, chemical peeling, dermabrasion, face lift, soft tissue augmentation, **botulinum** toxin-A (BTX-A) injection and laser resurfacing. Now, fucose-rich oligo- and polysaccharide (FROP-3) in a base-cream can be used to improve fine wrinkles after about four weeks of topical application (Ροβερτ ετ αλ., 2005).

-All these have been associated with definite drawbacks for example *face-lift operations as rhytidectomy* carry the risk of facial, or sensory nerve injury, hematoma formation, infection, abnormal facial motion, and scarring. In addition, it is not a simple office procedure (Κεεν ανδ Κηοση, 1995).Moreover, it removes the heavy folds, but does not affect the fine wrinkles and the results are not permanent. Face-lift can be repeated, perhaps three or four times however, the skin becomes thin, shiny and atrophic (Ωολφε ετ αλ., 1980).

-*Soft tissue augmentation*, either by collagen, silicone, fat injection, or implants, is an effort to balloon out skin and flatten the folds (Φαγιεν, 2000 & Μυρραψ ετ αλ., 2005). They are only effective for variable periods according to the nature of the filler used. Also, it is technique-sensitive and has a tendency to appear lumpy in the periorbital area (Κεεν ανδ Κηοση, 1995 & Χορρυτηερσ ετ αλ., 1996).

*Botulinum toxin-A (BTX-A) injection* seems to be more effective in the treatment of hyperkinetic facial wrinkles leading to flaccid paralysis of those hyperkinetic muscles but it is technique sensitive and carry the possibility of occurrence of hazardous complications. it also, can't improve superficial wrinkles (Bovι et al., 2000 & Ψαμαυχηι et al., 2004).

*Resurfacing measures* such as chemical peels, as well as dermabrasion and laser resurfacing remove the outer layers of the skin with more collagen synthesis. Upon healing, the wrinkles are reduced and the skin is tightened. However, they are only effective in treating superficial skin wrinkles, but do not adequately address the hyperkinetic facial wrinkles. Although they make the skin smoother, hypopigmentation, hyperpigmentation, or small scars can occur. While laser skin resurfacing is considered less adventitious than chemical peeling as laser resurfacing may lead to erythema, pigmentary alterations, milia, scarring and infections (Ηερδ ανδ Ψαρβουουγη, 1999).

According to the previous considerations, there is no single ideal line of wrinkle treatment. So, effect can be maximized by combining lines of treatment that approach the different causative factors such as the combination of botulinum toxin injection and laser resurfacing or facelift operation and superficial chemical peeling (Γυερριτσι, 2000 & Αλστερ et al., 2004).

## CHEMICAL PEELING

Chemical peeling is an in-office procedure that involves the application of a chemical agent to the skin to induce controlled destruction or exfoliation of old skin and stimulation of new epidermal growth with more evenly distributed melanin. When peeling agents reach the dermal layer, important wound-healing activities occur by way of an organized repair process that cause skin remodeling and skin smoothing, with antiaging benefits (Βριδεν, 2004). In addition, it is considered one of the three most common modalities used in facial resurfacing which are chemical peels, dermabrasion, and laser resurfacing (Ροψ, 2005).

Moreover, chemical peeling is safe and effective in the management of many dysmorphic dermatoses like photo aging, scarring, pigmentary dyschromias (postinflammatory hyperpigmentation and melasma), and in the destruction of superficial skin lesions (acne vulgaris and pseudofolliculitis barbae) (Μονηειτ ανδ Χηασταιν, 2001 & Ροβερτσ, 2004).

### **Historical review of chemical peelings:**

Chemical peeling for skin arose in ancient Egypt, Mesopotamia, and other ancient cultures in and around Africa (Ροβερτσ, 2004). As previously mentioned, the ancient Egyptians used salt, animal oils and alabaster to improve skin appearance. Sulphur, mustard and limestone were also used in olden days (Βοκκερ ανδ Γορδον, 1987). Early in the 1900's, MacKee used phenol for treatment of acne scars. Gross practiced phenol peeling in Los Angeles occurred in the 1930's. In 1941, Eller and

Wolff reviewed various exfoliation regimens which included the use of pumice on the skin as well as sulphur and resorcinol pastes (Γλογαυ ανδ Ματαρασσο, 1991).

In 1966, Urkov described methods using phenol. In the 1960's, Ayres compared his results with those of Morash, citing histologies of trichloroacetic acid (TCA) and phenol. Brown et al., (1960) reported phenol formula, the histological changes it produced and its potential toxicity. In 1962, Litton and Baker published their respective nonsaponized and saponized formulas (Ρεσνικ ετ αλ., 1976). The 1970's and 1980's saw further advancements in full-face phenol application or TCA peels in combination with dermabrasion (Σταγνονε, 1977) Stegman's work in 1980s on both the animal and the human model compared the histological depth of both chemical wounding agents and dermabrasion, paving the way for chemical peeling in a controlled and scientific fashion (Στεγμαν, 1982). These excellent histologic concepts influenced authors to combine two superficial agents to produce medium depth peel (Βροδψ ανδ Ηαιλεψ, 1986).

Authors began investigating  $\alpha$  – hydroxy acids in the late 1970s but their experimentation as superficial peeling agents came to fruition in 1980s (ζαν Σχοττ ανδ. Ψυ, 1984). As the 1990s, the  $\alpha$  – hydroxy acids have become an addition to the peel spectrum especially glycolic acid formulations and they have been combined with TCA for medium depth peeling (Χολεμαν ανδ Φυτρελλ., 1994 & Βριδεν, 2004).

## **Types of chemical peelings:**

Chemical peels are classified according to depth of peeling into:-  
*a) Very superficial* (exfoliation). *b) Superficial* (epidermal) e.g. Glycolic acid formulations and amino acid filaggrin based antioxidants (AFAs)  
*c) Medium* (papillary dermal) e.g.combination medium depth peeling [CO<sub>2</sub> +35% trichloroactic acid], [Jessner's solution+35% TCA] and [70% glycolic acid+35% TCA]. *d)Deep* (reticular dermal) e.g. the Gordon-Baker phenol peel which is formed by combination of 3cc of 80%phenol, 2cc distilled water, 2drops of croton oil and 8 drops of sptisol (Κλειν, 2000; Μονηειτ, 2004 & Ωιεστ, 2004).

## **Histological changes of chemical peel:**

Chemical peeling involves the application of a chemical exfoliant to wound the epidermis and dermis for removal of superficial lesions and improve the texture of skin. Various acidic and basic chemical agents are used to produce the varying effects of light to medium-to-deep chemical peels through differences in their ability to destroy skin. The level of penetration, destruction and inflammation determines the level of peeling (Στεγμαν, 1982 & Ωιεστ, 2004):-

- \* Light superficial peel exfoliation: It is the removal of stratum corneum without necrosis leading to epidermal thickening with qualitative regenerative changes.
- \* Full superficial chemical peel: It is the destruction of the epidermis inducing epidermal regeneration.
- \* Medium-depth peel: It is the further destruction of the epidermis and induction of inflammation within the papillary dermis.

- \* Deep chemical peel: It indicates the further inflammatory response in the deep reticular dermis inducing new collagen production and ground substances.

As one ages, there is loss of subepidermal collagen(as the relatively inelastic epidermis loses volume beneath it), fine wrinkles form, irregular formation of connective tissue (elastosis), melanocytes can form local irregularities, and epidermis tends to become thin and atrophic. Chemical peeling has been shown to improve the dermis with formation of dense homogenous parallel collagen fibers. These changes persist histologically for at least twenty years. Histological sections will show a new layer of connective tissue above the older elastotic tissue, reverse epidermal atypia, uniform dispersion of melanin granules and reverse epidermal atrophy. Increased angiogenesis occurs which is thought to aid the appearance of skin by adding a warm glow(Αλφορδ ανδ Πορτερ, 1999).

### **Indications of chemical peeling:**

There are many indications for chemical peeling which differs according to the depth of the lesion (Μονηειτ ανδ Χηασταιν, 2001 & Ροβερτσ, 2004):

**Upper epidermal skin lesion as :** Ephelides(freckles)-basal layer and superficial Melasma.

**Epidermal and dermal skin lesion as:** Lentigines, combined Melasma, postinflammatory hyperpigmentation, actinic keratosis with mucinous dermis, superficial wrinkles, acne, and radiation dermatitis

**Dermal skin lesion as:** Deep wrinkles and Scarring .

**Table (2): Indications and peel depth** (Γριμεσ, 1995)

<b>INDICATION</b>	<b>Peel Depth For Best Response</b>
<b>*Actinic keratosis</b>	Medium or deep
<b>*Actinic rhytides,</b> -Very mild -Mild -Moderate -Severe	Superficial or medium Medium Medium or deep deep
<b>*Pigmentary dyschromia</b> -Superficial melasma -Mixed melasma -Postinflammatory hyperpigmentation -Ephelides(freckles)-basal layer -Lentigines-basal layer and upper dermis	Superficial or medium Superficial ,medium or deep Superficial ,medium or deep Superficial or medium Superficial or medium
<b>Scarring</b>	Medium or other resurfacing modality
<b>Acne</b>	Superficial when active ; medium after clear
<b>Radiation dermatitis</b>	Medium or deep

## **Strategies of patient evaluation for chemical peeling**

(Βροδψ ετ αλ, 1995):

There are many measures according to which patients can be evaluated to be suitable or non suitable for chemical peeling procedure.

A discussion between the physician and patient is necessary prior to a chemical peel, especially a deep peel, in which a detailed history is

obtained. Examples of “before and after” results should be shown, and the possibility of complications must be explained to the patient.

Some habits of patients can affect the peeling procedure outcome like philosophy of sun exposure, cosmetic usage and smoking. Hence, the dynamic action of puffing can worsen perioral rhytides, and the chemicals in the smoke can cause enzymatic reactions that weaken the skin and cause further wrinkling around the mouth and eyes (Τινγερ αλ., 2003).

Certain medications may have an effect on peeling strategy. Oral contraceptive pills can cause melasma, further worsening the skin discoloration that the chemical peel was intended to eradicate. Patients taking blood thinners, such as warfarin, should avoid deep peels because of the possibility of blood oozing from the peel site. Patients taking aspirin usually do not have complications, but, if the medication is not necessary, it is advised to stop taking it 1 week prior to a deep peel.

Also, pregnancy must be excluded as it raises level of estrogen and progesterone and causes skin pigmentation. Also chemical peeling shouldn't be done during pregnancy for fear of teratogenicity.

General state of patient physical health is important particularly with phenol peels since phenols can cause arrhythmias so, ECG monitoring is necessary during the peeling process. Good kidney and liver function are necessary for adequate excretion and detoxification.

Also peeling outcome is affected by accurate evaluation of skin according to its pigmentary responsiveness to ultraviolet light (Fitzpatrick classification), actinic damage and degree of photoaging (Glogau Classification) and sebaceous gland density.

According to Fitzpatrick skin type classification (Φιτζπατριγκ, 1988) patient with fair complexion were found to be better candidates than those with olivetoned skin. Darker individuals tend to show more obvious line of demarcation between peeled and unpeeled skin. So regional peeling can be done in fair complexions but when peeling darker ones we must do complete face peeling (Γλογαυ ανδ Ματαρασσο, 1995).

**Table (3): Fitzpatrick classification of sun reactive skin types**

Skin Type	Color	Reaction To First Summer Exposure
I	White	Always burn never tan
II	White	Usually burn, tan with difficulty
III	White	Sometimes mild burn, tan average.
IV	Moderate brown	Rarely burn, tan with ease
V	Dark Brown	Very rarely burn, tan very easily
VI	Black	No burn, tan very easily

According to degree of photoaging (Glogau Classification), patients with photoaging type I are not good candidates for deep peeling because the peel may be more damaging than beneficial, while a superficial peel would be more efficacious. Patients with type IV may benefit from deep peeling, while a superficial peel may hardly make a difference on this type of skin. Patients with skin types II and III ordinarily benefit from superficial or medium depth peels depending on the exact circumstances concerning the patient (Γλογαυ, 1994 & Ραψμονδ, 2001).

Previous isotretinoin, radiation or cosmetic surgery affect hair follicle unit density. Since these follicle units are where the reepithelialization occurs, patients should wait until 6 months after to reduce the risk of scarring.

### **Factors affecting efficacy of peeling:**

Many different agents have been used in chemical peeling. It has been shown that the effect of peeling is dependant on good selection of patient, preoperative preparation and depth of injury (Δετηαρδ ανδ Χαληαυν, 2000).

*(i) Rejuvenation regimen of the skin before and after peeling* with a bleaching agent may prevent hyperpigmentation on susceptible individuals:

- 1- Immediately after evaluating patient, he should be informed that strict sun avoidance and daily morning use of sunscreen with sun protection factor of 15 or greater as moisturizer and after shave is imperative on an indefinite basis (Φυνκ ετ αλ., 1995).
- 2- Hydroquinone, an isomer of resorcinol and phenol, is commonly used. In peeling Fitzpatrick V and VI skin or recalcitrant I- IV skin, hydroquinone concentration 6:8% of Bleach Eaze Formula (Hydroquinone 6-10%, Ascorbic acid 0.05%, Retinoic acid 0.1% dissolve the three crystals in Propylene glycol 4% and mix with hytone cream 2.5%) should be used beginning with 6%. This may be increased if pigmentation returns after peeling. If this occurs or anticipated, the concentration may be increased to 10:15%. This may be tried for a week before peeling and if successful can be applied only for one week after peeling to stabilize pigment resolution and to avoid pigment return. Creams with high HQ concentration should be

discontinued as soon as appropriate amount of pigment loss is achieved (Γλένν ετ αλ., 1991).

- 3- Kojic acid and Azelaic acid are also used as bleaching agents(Νογυψν ανδ Βυι, 1995 & Γαρχιχα ανδ Φυλτον, 1996).
- 4- Topical Tretinoin is an important factor in pretreatment regimen. In addition to its role in collagen improvement and thinning of stratum corneum,it allows for better and more even penetration(Ηυμπηρεψσ ετ αλ., 1996).

**(ii) Skin defatting technique:** The skin degreaser should be a solvent or detergent with high lipid solubility and it should be non toxic, noninflammable, easily usable and residue free. The skin should be cleaned and excess fat removed with such agents as acetone, rubbing alcohol, or septisol, or a combination of these agents for proper penetration of the peeling agent since most agents are not lipid soluble (Πεικερτ ετ αλ., 1994 & Ραψμονδ, 2001).

**(iii) Mode of application and choice of applicator:** The peeling agent can be applied with 4X4 gauze, cotton swabs, fan shaped brush, or the foam applicator that comes with the peel kit. Apply the peeling agent, beginning with the forehead and finishing with the chin. Feather the peeling agent into the hairline and the shadow of the mandible. Reapplication of the peeling agent may be necessary if the frost is uneven or is not white enough. The acid should not form pools in the facial folds nor drip from the face. The more acid that the clinician applies, the deeper the peel (Στεγμαν, 1982 & Ραψμονδ, 2001).

**(iv) Monitoring depth and clinical observations (Obagi's classification):** It depends on the appearance of frosting which is

defined as the visible response of skin to peeling agents and indicates keratocoagulation or protein denaturation of keratin and at this point the reaction is complete and the following three parameters should be encountered [Color, Firmness and Epidermal sliding] (Ρυβιν, 1995 & Οβραγ, 1996).

- ✎ *Exfoliation only*: No frost, misty or cloudy appearance and healing time one to three days.
- ✎ *Superficial peel*: Light pink frost, epidermal sliding, defrosting time ten to twenty minutes and healing period five to ten days.
- ✎ *Medium peel*: Solid white frost, no epidermal sliding, defrosting time twenty to thirty minutes and healing period of ten to fourteen days.
- ✎ *Deep peel*: Solid grey frost, firm skin to feel, defrosting time < forty minutes and healing period twelve to twenty days.

**(v) Occlusion:** Clinically the results may be the same with or without occlusion. In conclusion, it was found that occlusion in peeling are of no value, as it is terms that has misconstructured over the decades (Βροδψ, 1989).

**(vi) Contact time:** After the appropriate time has passed, neutralization is performed. Some chemical peels, such as salicylic acid and trichloroacetic acid, do not require a neutralization step since the skin neutralizes the acid. Glycolic acid peels must be neutralized. Always wash the patient's face with water following the peel.

**(vii) Peeling agent concentration:** Peeling agent concentration can vary, even, weight-to-volume method, and grams of acid crystal mixed to 100 cc of water can be used.

**(viii) Free acid availability:** The pH of the agent, or free acid available pKa, is another measurement. The pKa of the solution is the pH at

which half is in acid form; therefore, a lower pKa means that more free acid is available. Many products advertise the acid percentage; however, pKa is a more accurate determinant of strength.

**(ix) Density of adnexal structures:** Recent radiation treatment can affect the density of adnexal structures. The reepithelialization process partially occurs from the adnexal structures; therefore, some clinicians advise that a punch biopsy be performed to verify their existence.

**(x) Frequency that patient receives a peel:** Most patients can tolerate a monthly superficial peel, while medium depth peels can be performed at 6-month intervals if necessary.

**(xi) Neutralization:** is an important step once the clinician has achieved the proper depth of the peel, which is determined either by the frost, the burning sensation or erythema how much time has elapsed. Neutralization can be achieved by cold water or wet cool towels applied to the face following the frost. This soothes the sharp tingling discomfort caused by the peeling agent. Other neutralizing agents that can be used include bicarbonate spray or soapless cleanser. Peels for which this neutralization step is less important include salicylic acid, Jessner's, TCA and phenol.

**(xii) Ointments:** Petroleum jelly and other occlusive ointments may act as an occlusive barrier to a minor degree if applied after peeling (Ραψμονδ, 2001).

### **Application concepts:**

Mode of application: It is advised to begin with the most sensitive lower eyelash area first because the patient is unsedated and alert. Moving in rapid succession to the upper eyelids, nose, cheeks, perioral

area, and the least sensitive forehead area offers greatest ease for the physician to safely peel the periorbital area, and best tolerance of the patient. Peeling doesn't affect hair follicles or hair growth. Careful feathering of the solution into the hair line and around angle of mandible conceals the line of demarcation between the peeled and unpeeled skin. Ear lobes should be peeled to maximize visual results. The reverse order is described with the eyes being peeled last but the patient is usually sedated (Λοωε ετ αλ., 1995).

Obtaining informed consent from every patient before peeling should be insisted on (Βροδψ, 1997).

Peeling technique and agent selection: The selection of proper wounding agent or wounding technique is based on the experience of the physician and the depth and location of the problem to be corrected in each cosmetic unit of the face (Βροδψ, 1997).

Procedural sheet taking: It should be done for each selected patient prior to peeling to evaluate a patients skin, determine the defects to be treated and the most suitable methods of peeling for this patient, to detect any susceptibility of postoperative complications in order to be avoided and for further follow up of the patient after peeling(Βροδψ, 1989).

## SUPERFICIAL CHEMICAL PEELING

Superficial chemical peeling is defined as the application of wounding agents sufficient to wound the epidermis and the papillary dermis in whole or in part and these peels are called freshening peels or light peels which offer great flexibility over a range of skin types and conditions with minimal to no "downtime" and can be combined with other cosmetic procedures in the office to maximize benefits (Στεγμων ετ αλ., 1990 & Ροβερτσ, 2004).

Superficial peeling agents include trichloroacetic acid TCA (10-35%), Alpha hydroxy acid peels (AHAs), Amino acid Filaggrin based antioxidant (AFA), Salicylic acid, Carbon dioxide (CO<sub>2</sub>), Retinoic acid, Jessner's peel, and Modified Unna's Resorcinol Paste (Χολλινσ, 1987; Βροδψ, 1992 & Δεχηαρδ ανδ Χαληουν, 2000).

### **Trichloroacetic acid TCA (10-35%):**

Trichloroacetic acid (TCA) is a member of the family of compounds known as chloroacetic acids, which includes mono-, di- and trichloroacetic acid (Λεωισ ετ αλ., 2004). Since the beginning of the twentieth century, trichloroacetic acid solutions of various concentrations have been used for chemical exfoliation. In 1926, *Roberts* described TCA as one of the prototypes of chemical peeling and this work was completed by Monash in 1945 as it showed good results in the treatment of acne scarring then it was used by Ayres 1960 in the treatment of actinic damage (ζοσσεν ετ αλ., 2000).

Trichloroacetic acid as a chemical substance has many **uses** in dermatology other than its use as chemical peeling agent treating; *benign pigmented lesions*, including [seborrheic keratosis, solar lentigines, melasma, and freckles], *photodamaged skin* [lentigines, actinic keratoses, wrinkles, and textural alteration]and in the treatment of *acne scars*(Ηυμπηρεψ ετ αλ.,1996; Λεε ετ αλ.,2002 & Χηυν ετ αλ.,2004) but it can be used in the treatment of *genital warts* ,and in the treatment of *apocrine hydrocystomas* (Δαιλεψ ετ αλ.,2005 & Οεμαηονψ,2005).

**Preparation and stability of TCA:** because alcoholic solutions of TCA don't penetrate skin, aqueous solutions must be prepared for dermatologic use. Solutions should be pharmaceutically prepared by one of the following methods; Weight-to-volume solution in which water may be added to desired grams of trichloroacetic acid crystals until 100 ml of solution is obtained; Weight-to-weight solution in which desired grams of water may be added to desired grams of trichloroacetic acid crystals; Weight-plus-volume solution in which desired grams of trichloroacetic acid crystals may be solved in 100 ml of water; or Dilution method where trichloroacetic acid solution may be diluted by desired volume of water(Ρεσνικ,1884 & ζοσσεν ετ αλ., 2000).

It was found that weight-to-volume (wt/vol) method is preferred to avoid complications caused by concentration variation(Βριδενεστεν ανδ Δολεζαλ, 1994 & ζοσσεν ετ αλ., 2000).

The crystals are hygroscopic and deliquescent but in solutions they don't gather further moisture, and they are stable for at least 6 months unless contaminated (Σπινοωιτζ ανδ Ρυμσφιελδ, 1989).

The solution is stable both at room temperature and when refrigerated because there is no evidence that TCA is light sensitive. It can be stored in clear or amber glass bottle as TCA destroys plastic containers. The solution should be poured in a small container or a shot glass or directly onto gauze sponge for use (Δολεζαλ, 1990).

### **Concentrations of TCA:**

TCA itself has the advantage of having no systemic toxicity but it has the disadvantage of penetrating irregularly and is more likely to be fraught with complications especially scarring in strengths of 50% or higher, so, it has fallen out of favor as single agent chemical peel (Φυλτον, 1994).

For this reason, the favorite TCA formulations are between 20% and 35% concentrations. Increased depth from these light TCA peel formulations can be achieved by preconditioning the skin before TCA peel with the application of anyone of the followings; Jessner's solution, hard block CO<sub>2</sub> freezing, liquid nitrogen freezing or glycolic acid 70% (Φυλτον, 1994 & Μονηιερ, 2004).

### **Preparation for peel procedure** (ζαν Σχοττ ετ αλ., 1996):

- ✎ Makeup and any contact lenses must be removed.
- ✎ Scalp is protected with a plastic cap or shower bonnet.
- ✎ A paper drape can be applied around the neck and placed up over the ears.
- ✎ Lateral and medial canthi, nasolabial creases and nasal alae, lateral comissures of the lips and the lips themselves can be protected with petrolatum, this helps to avoid accidental eye affection.

- ⊗ Eyes are protected by antibiotic ointment, gauze pads, and hypo allergic tape or goggles.
- ⊗ Antiviral should be used in patients with history of fever blisters or as some believes in all patients.

**Equipments and method**(Φυλτων, 1994; Ρυβιν, 1995; Οβαγι, 1996 & Δεχηαρδ ανδ Χαληουιν, 2000):

**Preparation:** The skin is degreased by scrubbing with cotton gauze soaked in one part acetone to three parts alcohol promoting more uniform penetration of peeling agent.

**Equipments:** Bottles containing appropriate concentration of TCA(15%,25%,35%), cotton tipped applicators, square cotton gauze, small glass cup to hold small quantities of TCA, a readily accessible container of sterile water and an electric fan.

**Procedure:** Cotton –tipped applicator is moistened with TCA and rolled against the wall of glass cup to remove excess fluid. Then applied to an area of skin not more than 2 by 3 cm by firmly rubbing the moistened applicator in circular fashion. It is distributed as the following; forehead at first then cheeks followed by the nose then upper lip and chin.

The TCA solutions are coat dependant, each application yields deeper penetration. The physician should achieve a level II to level III frosting, which usually appears complete in the treated area within 30 seconds to 2 minutes. Even applications eliminate the need to go over area for the second or the third time. Area of poor frosting should be retreated. Careless overlapping in the center of the forehead or over cheek bones can result in ulceration.

*Feathering techniques* are used at the jaw line extending onto the neck and behind the ear to prevent sharp demarcation lines. TCA application also extends to the hairline without post peel hair loss. The entire procedure takes approximately twenty minutes per patient.

The cotton tipped applicator is disposable and used only once and discarded. A new cotton tipped applicator and gauze are used at each site.

Peeled area is rinsed with cold water after appearance of frost or either earlier than that if there is intolerable burning sensation or erythema.

*Immediate post operative care:* At the end of each session, face is washed with tap water and a thin layer of sun screen is applied gently.

The use of trichloroacetic acid (TCA) as a periorbital and eyelid peel for skin rejuvenation is gaining significant acceptance among oculoplastic surgeons, dermatologists, and other surgery groups. In spite of the current enthusiasm, there remain potentially serious complications resulting from any periorbital peel so the lowest-concentration of TCA is applied to avoid cicatricial ectropion (Δαίλεψ et al., 1998).

Excellent results have been obtained by superficial repetitive chemosurgery using 20%-35% TCA in treating hands and arms (Χολλινσ, 1989).

## **Alpha-Hydroxy Acids (AHAs):**

*Structure and source:* Alpha hydroxy acids are naturally occurring in many foods but synthetically mass produced carboxylic acids. This include; i) glycolic acid present in sugar cane, ii) lactic acid in

sour milk, iii) citric acid in fruits, iv) malic acid in apples, v) tartaric acid in grape, vi) citric acid in citrus fruits, vii) mandelic acid, viii) pyruvic acid ix) ascorbic acid. The shortest carbon chain acids, glycolic and lactic, are the most commonly used in dermatology. 70% glycolic acid can cause epidermolysis in 3:7 minutes depending on skin type and thickness of stratum corneum but the same concentration of lactic acid is slower to cause epidermolysis (ζαν Σχοττ ανδ Ψυ, 1989; ζαν Σχοττ ετ αλ., 1996 & Σηαρθυιε ετ αλ., 2005).

The acid strength of AHA is determined by proton dissociation in solution and is usually expressed as pka of the AHA. Since pka is a negative log of the dissociation constant, the difference of one unit of pka equals ten fold difference of the strength. An AHA is considered stronger when pka number is lower (ζαν Σχοττ ετ αλ., 1996). The lower pH products (below pH 2) create more necrosis than the partially neutralized products with a pH above 2 so, the use of partially neutralized glycolic acid solutions seems prudent, since they have a better safety profile than low pH solutions, which contain more free glycolic acid (Βεχκερ ετ αλ., 1996).

***Topical effects of (AHAs):*** In spite that glycolic acid (GA), one of the alpha-hydroxy acids, is widely used as an agent for chemical peeling and there are several reports about its clinical effect, its biological mechanism remains mostly unclear. ζαν Σχοττ, 1996 showed that AHAs action on the epidermis and dermis as the following a) Epidermal effect by decreasing thickness of hyperkeratotic stratum corneum by reducing corneocyte cohesion at lower levels of the stratum corneum, decreasing epidermal thickness when increased for example in ichthyosis and increasing its thickness when photodamaged by its effect

on cathepsin D-like (CD) and chemotrypsin like (SCCE) proteinases. b) Dermal responses which can be detected 2-3 months from peeling and becomes more detectable there after in the form of increased plumpness of the skin not only by direct acceleration of collagen synthesis by fibroblasts, but also by modulation of dermal matrix degradation and collagen synthesis through keratinocyte-released cytokines (ζαν Σχοττ ετ αλ., 1996; Οκάνο ετ αλ., 2003 & Ηορικοσηι ετ αλ., 2005).

### **Glycolic acid:**

The glycolic acid is hydrophilic AHA, spreading easily in the aqueous intercellular phase without the need of plasmatic proteins (Περσονελι, 1993).

***Preparation:*** Topical compositions containing glycolic acid may be formulated as solution, lotion, cream, ointment, gel or other forms. To prepare a solution from glycolic acid (wt/vol) method is followed by adding the distilled water to the desired grams of glycolic acid crystals to form 100cc of solution (ζαν Σχοττ ετ αλ., 1996 & ζοσσεν ετ αλ., 2000).

**Indications of glycolic acid skin peeling:** Glycolic acid chemical peels have been widely accepted as a useful modality in many cutaneous conditions characterized by abnormalities of keratinization [ichthyosis, follicular hyperkeratosis, verrucae vulgaris and other conditions characterized by retention of stratum corneum], hyperpigmentation [melasma, follicular hyperkeratosis, seborrheic keratoses, keratoses commonly known as "age spots," and actinic keratoses], photodamage, acne and rosacea (ζαν Σχοττ ανδ Ψυ, 1989; Ατζορι ετ αλ., 1999 & Τυνγ ετ αλ., 2000).

Alpha-hydroxy acid (AHA) peels have the advantage of being superficial and can be combined with other cosmetic procedures in the office to maximize benefits such as a) Retinaldehyde (RAL), a precursor of retinoic acid 0.1% and GA 6% RALGA (Diacneal) in the treatment of acne vulgaris and postinflammatory hyperpigmentation. b) 5-Fluorouracil (5-FU) have been proven efficacious in the treatment of actinically damaged skin c) GA 70% was used for preconditioning the skin before applying TCA 35% in medium depth peels (Μαρρερο ανδ Κατζ, 1998; Μονηιετ, 2004 & Κατσαμβασ, 2005).

***Application technique of glycolic acid*** (Φυλτων, 1994; Διτρε ετ αλ., 1996; Οβαγι, 1996 & Χαλλενδερ, 2004).

***Preparation:*** The skin is degreased by scrubbing with a cotton gauze soaked in [one part acetone to three parts alcohol] promoting more uniform penetration of peeling agent.

***Equipments:*** Bottles containing appropriate concentration of GA(20%,35%,50%and70%), cotton tipped applicators, square cotton gauze,small glass cup to hold small quantities of GA, a readily accessible container of sterile water and an electric fan.

***Procedure:***

- \* The agent is applied rapidly covering the entire face within about 20 seconds with a large cotton applicator. It was distributed as the following; forehead was treated at first then cheeks followed by the nose then upper lip and chin.
- \* GA penetration is time dependant ,so it is washed after 3:5minutes or earlier than that if sever erythema occurs ,first the GA is wiped off with copious water soaked gauze then patient splashes water on his

face to ensure complete removal of the acid and to avoid more penetration which results in deep burns.

\* The entire procedure takes approximately twenty minutes per patient.

***Immediate post operative care:*** At the end of each session face is washed and a thin layer of sun screen is applied.

**Amino acid Filaggrin based Antioxidant (AFA):** (Κλειν, 2000, Τακαηασηι ανδ Τεζυκα, 2004; Ραωλινγσ ανδ Ηαρδινγ, 2004 & Χηοι ετ αλ., 2005).

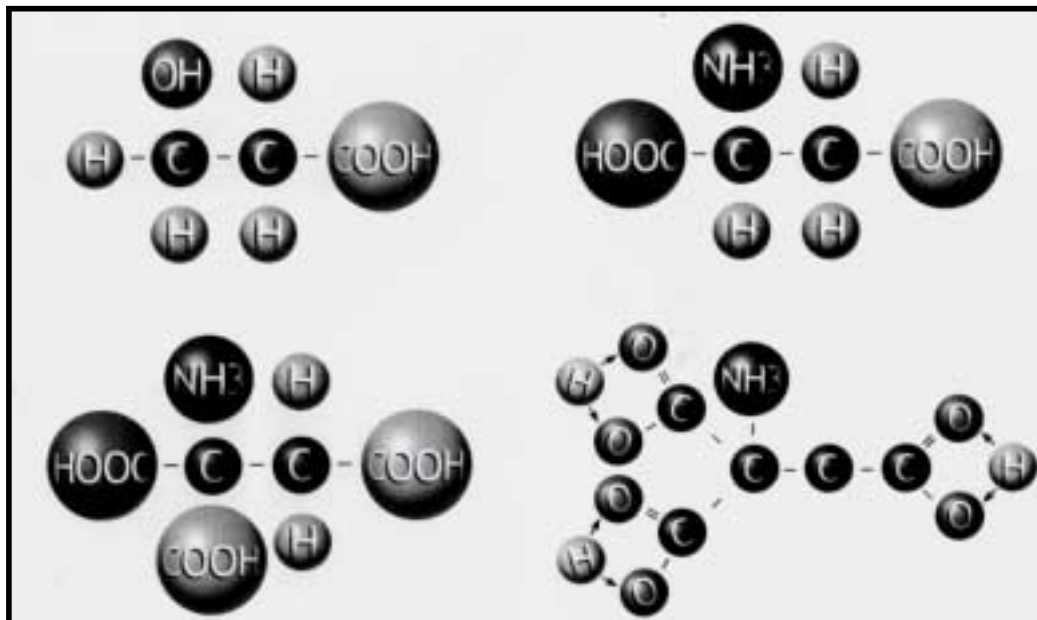
***Definition:*** The term AFAs or Amino Fruit Acids is a neologism and although the term accurately describes the chemistry of AFAs ,it is in a way ,a misnomer for AFAs are not fruit alpha hydroxyl acids such as glycolic or lactic acid or other AHAs. AFAs are a totally new,rapidly effective antioxidant created by dissolution and acidification of natural acidic amino acids,the same acidic amino acids that occur in the stratum corneum as a result of proteolysis of filaggrin (histidine-rich protein) and are the same acidic amino acid that are described in every dermatology biochemistry textbook as the main moisture retention factor in human skin.

***Source:*** Acidic amino acids that are used in AFAs synthesis are actually found in the seeds and buds of immature sugarcane and other fruits, but not in the mature plants, thus botanically, certain acidic amino acids are actually precursors of AHAs.

***Structure:*** AFAs are carboxylated amino acids .However ,they do bear a striking molecular resmbalance to AHAs.They are described as "Tri Carboxylic Acid" or as an alpha, di-carboxyl, alpha amino acetic

acid. AFAs are proved to be effective because they chemically have three potential hydrogen ion denoting carboxyl moieties. These positively charged hydrogen ions are mostly responsible for its dramatically enhanced antioxidant action if compared to other antioxidant formulations e.g. Alpha Hydroxy Acids (AHAs) that have one polar carboxyl radical. These hydrogen ions are also necessary to collagen hydroxy- proline.

Also, AFAs retain an amino radical which is responsible for moisture retention prosperities of the AFAs.



**Fig. (1):** A comparison of an AHA molecule, glycolic acid (upper left), to that of a typical acidic amino acid, arginine succinic acid (upper right), and to that of the two depictions of the tri-carboxylic AFA molecule (bottom left and bottom right).

#### *Action of AFAs:*

-They act as exfoliants and antioxidants with significantly reduced irritation.

- AFAs supplements the natural amino acid filaggrin moisturizing mechanism of the stratum corneum, so patients experience far less dryness with increase in moisture retention and improvement in the tone and texture of their skin. Filaggrin was named in recognition of its role as keratin filament aggregator, but it also has a second major role in the skin, as it is proteolyzed into various acidic amino acids that migrate and accumulate in the stratum granulosum. These amino acids constitute what is generally described as the "primary moisture retention factor of the human skin". It was Dr. Beverly Δαλε, 1994, who first described the fact that these acidic amino acids that are capable in penetrating into the stratum granulosum and significantly increasing moisture retention.
- AFAs significantly decrease the appearance of fine lines and improve skin texture.
- They provide outstanding results on photo-pigmentation or aged spots. They have been so dramatic as to prove superior in many cases, to the results used to getting with prescription of hydroquinone formulations.

***Who is good candidate for AFA peel?***

- Any person who is concerned about his appearance would benefit from the AFA peel.
- People with uneven pigmentation, fine lines or sun damaged skin do particularly well, as one of the main causes of aging is the promotion of filaggrin proteolysis in the upper layers of the stratum spinulosum.

***Peeling procedure:***

First, third and fifth sessions are the same (AFA Clay Mask and step two gel):

- The face is cleansed with AFA cleanser to be sure that all make-up was removed, with avoidance of rubbing or abrading the skin.
- AFA Clay is applied evenly to the skin, using the applicator provided. Contact with eyes is avoided; a thick layer is not necessary. Clay mask is left on face for 5:6 minutes then gently removed with water.
- Soft towel is used to pat the skin dry, without rubbing. The skin is allowed to air dry for several minutes before proceeding to step two.
- A thin even layer of the gel based AFA Peel is applied to the skin; starting at the periphery of the face. It is applied to the sensitive area of the eyes last. The peel is applied with the pads with the kit or with gloved finger tips, with avoidance of rubbing into the skin. The peel is washed with cool water after 1:2 minutes or earlier than that if any erythema or discomfort exists.
- The entire procedure takes approximately 25 minutes per patient.

***Immediate post operative care:***

Once removed, the AFA Toner is misted to further comfort the skin and the sunblock is applied gently.

**Second session AFA 40 Antioxidant gel:**

- The face is cleansed with AFA cleanser to be sure that all make-up is removed, with avoidance of rubbing or abrading the skin.
- Soft towel is used to pat the skin dry, without rubbing. The skin is allowed to air dry for several minutes.
- A thin even layer of the AFA 40 antioxidant gel is applied to the skin; starting at the periphery of the face. It is applied to the sensitive area of the eyes last. The peel is applied with the pads with the kit or with gloved finger tips, with avoidance of rubbing into the skin. The peel is washed with cool water after 1:2 minutes or less than that if any erythema or discomfort exists.
- The entire procedure takes approximately twenty minutes per patient.

***Immediate post operative care:***

Once removed the AFA Toner is misted to further comfort the skin. Gently apply the sunblock.

**Fourth session:** The same steps as the second session but with application of AFA 50 Antioxidant gel.

**Sixth session:** The same steps as the second session but with application of AFA 60 Antioxidant gel.

## Salicylic acid

**Structure:** Salicylic acid is a  $\beta$ -hydroxy acid which has been a mainstay in dermatologic therapy for many decades. In concentration 3:5% it is keratolytic and can be used as enhancer for topical penetration of other agents. Ordinarily, salicylic acid alone is not potent enough to act as an adequate wounding agent for chemical peeling. Swinhart, 1992, described the use of 50% salicylic acid paste under occlusion to peel lentiginos and actinic keratosis. Then, the peeling solution of 35% salicylic acid in ethanol has been used. Recently, chemical peeling with salicylic acid in polyethylene glycol (PEG) vehicle is used clinically to improve the cosmetic appearance of skin that has been damaged by exposure to the sun by reorganization of the epidermis and rebuilding of the superficial dermal connective tissue (Ισοδα ετ αλ, 2001 & Δαινιχητ ετ αλ., 2003).

Salicylic acid is lipid soluble; therefore, it is a good peeling agent for comedonal acne as it is able to penetrate the comedones better than other acids. The anti-inflammatory and anesthetic effects of the salicylate result in a decrease in the amount of erythema and discomfort that generally is associated with chemical peels (Υεδα ετ αλ., 2002).

### PROCEDURE

**Method of paste application:** The skin is pretreated with tretinoin 0.1% and degreased with alcohol and acetone. Large keratosis is pretreated with 20% TCA that will enhance penetration of the salicylic acid. The salicylic acid paste is applied to the affected areas with a tongue blade after cotton balls have been placed between fingers to

protect the palms, plastic wrap followed by gauze roll wrap secures the ointment in place on the arms, the dressing is kept dry for 48 hours and then removed. The resulting desquamation and maceration heal with the application of antibiotic ointment or biosynthetic dressing within 4 weeks, 90% of cutaneous lesions resolve and no scarring will be noted (Αρονσοην, 1984).

On another hand, solution can be applied with cotton tipped applicator that cause stinging for about 1:3 minutes, followed by superficial anathesia to light touch which can be washed within 5 minutes .Peeling begin from 3-5 days that continue for 10 days and can be repeated after 2:4 weeks (Σωινεηαρτ,1992).

Adverse effects usually only found with high-dose oral ingestion. If patient experiences excessive salicylate absorption (salicylism) resulting in; ringing in the ear, muffled hearing, and dizziness or headache, few glasses of water and rest can resolve the problem. So, a new formulation consisting of 30% salicylic acid in polyethylene glycol (PEG) vehicle would be safer for topical use than old preparations (Κλιγμαν ετ αλ., 1996 & Υεδα ετ αλ., 2002).

## **Solid carbon dioxide**

Solid carbon dioxide (dry ice) is physical modality of peeling and not true chemical peeling agent which has added the benefits of being inexpensive and environmentally friendly(Ροοκ ετ αλ., 1972 & Φυλτον ανδ Ραηιμι, 1999).

Carbon dioxide produces a deeper wound than Jessner's solution, and CO<sub>2</sub> + TCA medium depth peeling, is slightly deeper than Jessner's + TCA (Βροδψ, 1989).

Combining solid carbon dioxide with trichloroacetic acid promotes both epidermal and dermal regeneration for treatment of actinic degeneration, acne scarring, rhytides and pigmentary aberrations (Βροδψ ανδ Χαιλεψ, 1986).

***Method of preparation:***

CO<sub>2</sub> snow is prepared either by releasing the gas from a cylinder through a chamois leather bag and then transferring it to wood or bakelite funneled tube in which the snow is hammered hard by means of sparkle machine in which individual cylinders discharge the gas through a small opening into a collecting tube (Ροοκ ετ αλ., 1972).

***Mode of application:***

Five or ten blocks of ice are broken to hand size for slushing in acetone, ethyl acetate, or sulfur. With or without alcohol prior to application, acetone serves to dissolve sebum and lowers the temperature of the CO<sub>2</sub> by accelerating the change of CO<sub>2</sub> from a solid to gas. The dry ice is wrapped in a small hand towel and dip it in an approximate 3:1 solution of acetone and alcohol. Either the lesion or the entire face may be easily slushed by using slow and even strokes. Varying epidermal depth can be obtained by pressure during application. Five to eight seconds of moderate pressure per acne area is adequate to freeze comedones (Σταγνονε, 1989).

The dry ice is dipped into the solution multiple times during the treatment to allow easy slipping on the skin. The skin reaction ranges from mild erythema to vesiculobullae formation. This treatment speeds removal of comedones and acne resolution. Care should always be exercised to apply less pressure when peeling over bony prominences (Βροδψ, 1989)

## **Retinoids:**

**Structure:** All transretinoic acid, is not true chemical wounding agent, it may be employed with chemical peeling both before and after (Ωεισσ ετ αλ., 1991). To date, three generations of retinoids have been developed: the nonaromatics (retinol, tretinoin, and isotretinoin), the monoaromatics (etretinate and acitretin), and the polyaromatics (arotinoid, adapalene, and tazarotene) (Ριγοπουλος ετ αλ., 2004).

**Action at cellular level:** Treated skin showed the elimination of epidermal dysplasia and atypia ,melanin granules dispersion ,elimination of microscopic actinic keratosis, formation of new blood vessels(angiogenesis),new dermal collagen formation(type I and III),and other changes. Two concentrations of topical tretinoin (retinoic acid) cause similar improvement but different degrees of irritation, so, lower concentrations are preferred to minimize irritation(Κλιγμαν ετ αλ., 1986 & Γριφφιτησ ετ αλ., 1995).

**Indications:** Topical retinoids have become a popular method for treating melasma,acne, photoaging as well as for specific disease processes, such as scars or striae (Φλψνν ανδ Χολεμαν, 2000, Δελ Ροσσο,2002, Λεψδεν, 2004 & Κηυνγερ ετ αλ., 2004).

*Short-contact tretinoin therapy is a novel modality in treating chronic ulcers as it reverses the inhibitory effects of glucocorticoids on wound healing and accelerates the formation of healthy granulation tissue. Pretreatment with tretinoin before epidermal injury such as chemical peeling and dermabrasion has shown accelerated wound healing (Παθουεττε ετ αλ., 2001).*

***Adverse effects:***

- The most common one is local irritation, which can be minimized by starting with a mild formulation then concentration can be gradually increased (Τηιβουτοτ, 1994).
- Erythema, dryness, and peeling. They are most common during the first 1-2 weeks of therapy and can be minimized with use of the cream formulation, alternate day application, short contact therapy, mild cleansers, and combination therapy. These effects often resolve after approximately 3 weeks (Τηιβουτοτ, 1994).
- Mild thinning of the stratum corneum that may increase sensitivity to sunlight, necessitating proper sunscreen use (Σψκεσ ανδ Ωεβστερ, 1994).
- Exacerbation of inflammatory lesions (pustular flare) within 2 to 4 weeks of initiation of therapy may also occur (Βερσον ανδ Σηαλιτα, 1995).
- Pyogenic granulomas may develop after 2-3 weeks of therapy initiation. The lesions usually resolve when topical tretinoin is ceased (Τεκνετζισ ετ αλ., 2004).

- Birth defects have occurred in some of patients treated with topical tretinoin, but causation was not proven so, it should not be administered during pregnancy, lactation or in women who are not practicing adequate contraception (Ακηαῶαν ανδ Βερσηαδ, 2003).

## **Jessner's solution or Combes' peel**

***Structure and storage:*** Jessner's solution is composed of 14 g of resorcinol, 14 g of salicylic acid, and 14 ml of 85% lactic acid mixed in enough 95% ethanol to bring the quantity to 100 cc. This formulation was prepared to minimize the toxicities of each individual agent. This solution must be stored in a dark bottle as light will discolor the solution and cause staining. Repetitive layers may be applied for a slightly deeper peel; this can also be used in combination with TCA for a medium depth peel (Δεχηερδ ανδ Χαληουν, 2000 & Μονηιερ, 2004).

***Indications:*** It produces similar epidermal changes to tretinoin and can be useful in tretinoin intolerant patients. It can be used in the treatment of acne, postinflammatory hyperpigmentation, photodamaged skin and actinic keratosis (Σλαγγελ ανδ ΜχΜαρλιν, 1984).

***Application:*** It is easily accomplished by rapid brushing of one coat of solution liberally on the desired area. It produces an even but light white frost when applied with stable brush, but a very weak, slower and uneven frost occurs with two cotton tipped applicators. After 3:4 minutes, to see extent of frosting, a second coat is brushed and this process may be continued till the end point of color is reached, increasing the number of coats advancing from one in the first week to

three in the third week increases the reaction, heavier pressure and quantity of solution increase the depth of penetration. The number of coats applied is determined by the patient schedule and desire for rapid results (Διννερ ανδ Αρτζ, 1994).

The advantages of using Jessner's solution are that only a single solution is needed, timing the duration of application is unnecessary, and dilution or neutralization is not performed (Διννερ ανδ Αρτζ, 1994).

### **Modified Unna's Resorcinol paste**

**Structure:** Resorcinol (m-dihydroxybenzene) is an isomeric with catechol and hydroquinone. It is structurally and chemically related to phenol, soluble in water, alcohol, ether and fats. In alkaline solution it possesses a strong affinity to oxygen and is a reducing agent. It has shown to disrupt the weak hydrogen bonds of keratin and is therefore a keratolytic in concentration as low as 5% (Ροοκ ετ αλ., 1972 & Φυλτον, 1994).

**Indications:** Can be used in the treatment of acne, melasma and sun damaged skin (Λετεσσιερ, 1996).

Different formulas and concentrations can be used, Peeling paste formula [Resorcinol 40 g, Zinc oxide 10g, Kaolin 5g, Olive oil 12g, Wool fat 10g, and Petrolatum 10g] (Πασχηαρ, 1957) or Letessier Modified Unna's Resorcinol paste [Resorcin 40g, Zinc oxide 10g, Ceysstite 2g, and Benzoin axungia 28g] (Λετεσσιερ, 1996).

**Procedure** (Καράμ, 1993):

- ✗ The patient is pretreated with topical tretinoin for 21 days before peeling to increase reactivity of the skin and decreases application time needed.
- ✗ A test site is performed on skin behind the ear, paste is left for 15 minutes, and test site is evaluated in 4 days for erythema to detect contact sensitivity to resorcinol.
- ✗ At the time of peel, patient is placed in supine position to avoid syncope.
- ✗ Alcohol or acetone may be applied as degreasing agent.
- ✗ Paste is warmed by immersing container in hot water for 2:3 minutes to facilitate its application.
- ✗ The paste is applied to the face by gloved fingers and left on for 25 minutes in the first day then; time is decreased by 5 minutes each day till the third day. If the back is treated for three days, time should be increased to 50, 60 and 70 minutes respectively. Less time may be appropriate for more sensitive patient.
- ✗ As paste dries, skin is wiped by tongue depressor and dry gauze to leave a grey "resorcin membrane" film. Avoidance of water and or cream application for 4:7 days after peel is recommended. Micronised water sprays may soothe and prevent patient from picking the skin if necessary.

This type of peeling has serious side effects if applied daily in large doses such as hypothyroidism, and methemoglobinemia (Ματαράσσο ανδ Γλολυ, 1991).

## MEDIUM – DEPTH PEELING

**Definition:** Medium depth peeling is the application of a wounding agent or agents to produce an initial epidermal and upper reticular dermal wound (Ρυβιν, 1992 & Ωιεστ, 2004).

**Indications:** Indications for medium-depth chemical peels include both medical conditions, such as diffuse photodamage with contiguous actinic keratoses, scarring, molluscum contagiosum and cosmetic conditions such as the aging face, melasma, postinflammatory hyperpigmentation and solar lentiginosis(Ωανγ ανδ Χαρεψ, 1994; Οτλεψ ανδ Ροενιγκ, 1996 & Αλ-Ωαιζ ανδ Αλ-Σηαρθι,2002).

**Modalities :**Phenol peeling remains the gold standard of chemical peeling because no other chemical agent can compare in the treatment of patients with moderate and deep rhytids. However, phenol peeling can be very painful and is associated with many tradeoffs. Also, TCA itself is an agent more likely to be fraught with complications especially scarring in strengths of 50% or higher so, it has fallen out of favor as a single agent chemical peel (Βροδψ, 1995). So, TCA and phenol peelings have been modified to improve their results. For this reason, the combination products have been found equally effective in producing this level of control damage without the risk of side effects(Εδισον, 1996 & Μονηιετ, 2004).

### **Agents used for medium depth peeling**

***I-Four combination peels***; currently being used which are as effective as the other medium depth peels with less chance of scarring and pigment dyschromia (Μονηειτ, 2004):

**\*Jessner's and TCA 35 %** (Μονηειτ, 1995): First, the face is degreased with hexachlorophene with alcohol (Septisol) or povidone-iodine followed by an acetone scrub, then JS can be applied with two moist cotton tipped applicators or more rapidly with either a 2 x 2-inch or 4x4inch gauze pad and one coat only is used to achieve light but even frosting. Next, trichloroacetic acid 35% is applied evenly with one or two cotton tipped applicators or with a single 4 x 4-inch gauze pad if heavier application is desired. Even application should eliminate the need for reapplication, but if frosting is incomplete or uneven as in keratosis, for example, TCA can be reapplied carefully. Dry ice pack or cold gel pack offers symptomatic relief when applied for about 5 minutes until the patient is comfortable. A soothing emollient may then be applied if desired.

This peel is indicated in the treatment of actinic damage, rhytides, and pigmentary dyschromias (Λαωρενχε ετ αλ., 1995).

**\*CO<sub>2</sub> and TCA 35%** (Βροδψ, 1995): All makeup is removed with acetone scrub for 1 minute. Then, block of solid CO<sub>2</sub> is broken to hand size and continually dipped in a 3:1 solution of acetone and alcohol so that the dry ice will move freely over the skin. Varying pressure is applied to induce microepidermal vesiculobullous formation. When freezing an individual scar, it is permissible to freeze the rims for 10 to 15 seconds to afford greatest TCA penetration so that the scar edges will

be clinically blunted. Patients may not tolerate hard pressure for long periods over certain areas such as the upper portion of the forehead which is very sensitive. If freezing hard is absolutely necessary here, a nerve block of the forehead may be helpful. The actual time and pressure will vary as all areas of the face may be iced with patient tolerance being the chief limiting factor. An electric fan to blow away the acetone vapors can facilitate patient breathing and reduce discomfort when freezing around the nose, mouth and glabella.

Next the skin is lightly rewiped with dry gauze and 35% TCA is applied with either two cotton applicators or with cotton gauze held with a gloved hand in the standard fashion. After 10 minutes when the patient is again comfortable, the skin may be electively retreated with 35% TCA if actinic elastosis and keratoses are considerable (Brody, 1989).

The burning sensation that accompanies the application of the TCA is lessened by the previous CO<sub>2</sub> and can be minimized by the immediate application of an ice pack after adequate frosting has occurred. No aqueous solutions are applied to avoid inadvertent dilution and after 5 minutes a soothing emollient can be used.

Satisfying clinical results can be obtained in a) Correcting mild to moderate actinic keratoses. b) Flattening the edges of depressed scars. c) Improving fine rhytides. d) Improving pigmentation. e) Peeling extensive molluscum contagiosum seen in human immunodeficiency virus (HIV) positive patients or patients with the autoimmune deficiency syndrome (AIDS) (Γαρρετ et al., 1992; Σαδικ, 1996 & Αλ-Ωαιζ ανδ Αλ-Σηαρθι, 2002).

**\*Liquid nitrogen + TCA 35 %** are another combination of medium depth peeling in which freezing with liquid nitrogen has also been used to add depth to TCA peel (Φυλτων, 1994).

**\*Glycolic and TCA 35 %**(Χολεμαν ανδ Φυτρελλ, 1994): The glycolic and TCA combination is a predictable method that allows even penetration of 35% TCA into the papillary dermis for the treatment of pigmentary dyschromias, actinic damage, and mild rhytides. It differs from previous combinations in that no prepeel defating is necessary, it produces the least wounding depth, and it is the least likely to produce pigmentary dyschromias as a complication. The chief advantage of this peel is the stratum corneum debridement that the 70% glycolic acid performs, allowing even TCA penetration.

**The procedure:** At first, 70% glycolic acid is applied using a rectal swab over the treated area. After a strict 2-minutes contact period, the solution is removed with tap water. Next 35% TCA is applied to the entire face using 4 x 4-inch gauze pads in the usual fashion up to the lid margins. Cool compresses or packs are used to alleviate burning.

The neck may be optionally treated with 70% glycolic acid for 2 minutes followed by 20% TCA if photoaging is significant. Petrolatum is applied over the entire area, and the patient is discharged.

**II-TCA 50%** is seldom used because of a higher risk of scarring and it is not capable of producing in a single application the same results as the availability of the combination peels (Χολλινσ, 1989). Peeling with 60% to 75% TCA is much more risky and not recommended as a chemical peel, although it shows effect in spot treatment of localized actinic

keratoses, and it can also remove amateur tattoos (Πιγγοτ ανδ Νορρις, 1988).

**III-Full strength phenol (88%)** is a very caustic agent that causes immediate keratin agglutination, preventing further penetration of the agent deeper into the dermis. Again, the increased risk of scarring and pigment dyschromia makes this agent less attractive to the practitioner. If diluted and mixed with other complimentary chemicals, this agent can be used effectively as a deep peeling agent **but** cardiac and renal precautions must be enforced (Στεγμαν ανδ Τρομοπιτχη, 1984 & Στεγμαν ετ αλ., 1990).

**IV-Pyruvic Acid ( $\alpha$ -Keto Acid):** Pyruvic acid ( $\text{CH}_3\text{-CO-COOH}$ ), is an  $\alpha$ -Keto acid, a chemical group that has properties of both acids and ketones (Γριφφιν ετ αλ., 1989 & Βροδψ, 1992). It converts physiologically to lactic acid, an  $\alpha$ -hydroxy acid. Although lactic and pyruvic acids convert to each other, pyruvic acid has additional properties that make it particularly potent as a topical peeling agent. Pyruvic acid is available in pure form as a liquid at 95% to 99% strength. After standing over time, it may decompose to form carbon dioxide and acetaldehyde. The carbon dioxide gas will build up pressure, and the bottle can explode (Μιλστειν, 1990).

Pyruvic acid has been recently used as a medium chemical peeling agent in subjects with inflammatory acne, moderate acne scars, greasy skin, actinic keratosis, warts and moderate facial skin aging (Χοτελλεσσα ετ αλ., 2004 & Γηερσειχη ετ αλ., 2004).

Advantages: Pyruvic acid does not seem to have systemic toxicity, and has destructive wound depth as Baker's phenol (Γριφφιν ετ αλ., 1989)

Disadvantages of pyruvic acid are pungent irritating vapors and yellowish discoloration of the skin which can be removed by washing (ζαν Σχοττ ανδ Ψυ, 1989).

The mechanism of action of pyruvic acid is uncertain.

**The procedure** (Γριφφιν ανδ ζαν Σχοττ, 1991):

The solution may be applied with cotton-tipped applicators to tretinoin-prepared skin after mild degreasing. After 2 to 5 minutes or whenever adequate frosting has occurred, the area is soaked with water more for patient comfort than neutralization. Reepithelialization occurs between 7 and 14 days. Focal reapplication may be performed after healing is complete for persistent lesions.

**After-care for medium-depth chemical peels** (Καπλαν, 1984 & Ρααβ, 1991):

A sequence of events that occur after medium depth chemical peeling include erythema an hour after, considerable edema for the first 48 hours and crusting forms after several days when the edema partially resolves, slight edema and erythema persist for 30 to 60 days, and solar restriction is imperative until the erythema has resolved. Crust separation generally begins between the fourth and the eighth postoperative day and is completed usually by days 7 to 12, depending on the area and the peel.

The patients is encouraged to minimize crusting by washing twice daily with antiseptic compresses like tap water, hydrogen peroxide, or dilute 0.25% acetic acid soaks and then applying a soothing ointment.

Overgreasing may produce acne lesions during healing. Some physicians use synthetic membrane dressings (e.g., Vigilon, Meshed Omiderm for the first 2 to 4 days after the peel), but it has been found that this is more useful in dermabrasion or laser and offers no advantage in medium-depth peeling.

Tretinoin, sunscreens, and optionally hydroquinone in the regimen are reinstated as soon as the patient can tolerate them.

Make up can be applied at any time to any area that has resurfaced during the healing course.

Repeat medium-depth peels may be performed in 6 months if there are skip areas, but if all erythema and edema have subsided, the patient can be repeeled sooner but not before 90 days. If the patient is peeled too soon with another peel of equal depth while erythema is still present, we have seen scarring as a result because the dermal collagen has not completely reorganized. This is not a risk in superficial peeling where it is acceptable to re peel erythematous skin with continual epidermal sloughs incurring little or no risk of scarring.

- Aspirin or ibuprofen is to be taken 3 or 4 times daily to reduce swelling.
- Sleeping on several pillows the first night is advised.
- Total sunblock and a hat should be used to prevent hyperpigmentation immediately after healing.
- Prescription creams can be applied after the first week, but the skin will be more sensitive than usual.

If pain begins, which may signal a fever blister, the patient must call his doctor immediately.

## DEEP CHEMICAL PEELING

**Definition:** Deep chemical peeling is the chemical peel that penetrates deep into the reticular dermis to correct most severe actinic damage utilizing, a formula containing phenol, or carbolic acid. The most commonly phenol used is the Baker's formula (**Matarasso and Glogau, 1991**).

**Structure and modalities (Baker and Gordon, 1987, Maloney , McCollough ,1995& Raymond, 2001):** Baker Gordon peel produces the most dramatic results and is the most effective peeling agent currently used. The phenol produces a new zone of collagen that is thicker than that produced by laser.

***The Baker Gordon solution is made of:*** phenol 88%, 2 ml distilled water, 8 drops septisol, and 3 drops croton oil.

This formula penetrates into the middle reticular dermis and requires special monitoring devices, such as an ECG monitor and pulse oximeter, because of the potential of the phenol to cause arrhythmias. The Baker Gordon formula is not often used today because of resurfacing laser technology; however, a deep peel works well on deep perioral rhytides.

### **Deep peels modalities can be:**

***Occluded:*** Occluded method uses zinc oxide tape or other artificial barrier product to prevent evaporation of the phenol from the skin, thus enabling the solution to penetrate deeper.

***Nonoccluded:*** Two variants of the Baker Gordon peel are:

A-Litton's formula, which replaces Septisol with glycerin (Λιττον, 1962&1963).

B-Beeson McCollough formula, which uses aggressive defatting and heavier application of Baker Gordon solution (Βεεσον 1985).

**The indications of deep peel:** It can be used in a) Actinically damaged skin[Actinic keratosis, Basal cell epithelioma]. B) Pigmentary changes[Melasma or coloasma, Ephiledes or freckles, Lentigines and lentigo maligna, postinflammatory hyperpigmentation, Periorbital hyperpigmentation,and Nevroid conditions]. C) Enlarged adnexal pores, has been noted to decrease in size(Βακερ ανδ Γορδον, 1986 & Στεγμαν ετ αλ. , 1990) .

It is absolutely contraindicated in a) Patients with unrealistic expectation and poor comprehension of the postoperative course. B) Physical parameters that discourage deep chemical peels such as history of bad wound healing, poor health, and history of hepatorenal and /or cardiac disease (Ρυβενστειν ετ αλ., 1986 & Ματαρασσο ανδ Βροδψ, 1996).

### **Technique for full-face application:**

#### ***Prepeeling preparation:***

- 1- The patient is placed in a sitting position, and a line of small dots is placed slightly inferior to the mandible. The peel is extended to this point to minimize possible permanent color change, which would fall into the shadow cast by the mandible (Αλτ, 1989).

## 2- Intravenous Fluids.

Because phenol is partially detoxified in the liver and excreted by the kidney and because phenol may induce cardiac arrhythmias, the good health of these organs should be established before peeling. A preoperative history and physical examination to rule out cardiac and hepatorenal disease is performed, and a recent electrocardiogram, complete blood count, hepatorenal profile, and electrolyte values are obtained, hydration with 500 cc of lactated Ringer's solution before the procedure and 1000 cc during and after the peel will prevent phenol toxicity to these organ systems and ensure an increased output of alkaline urine. Occasionally 250 to 500 cc of dextrose in water may prevent hypoglycemia and nausea (Ασκεν, 1989).

3-Sedation and Analgesia: - Intramuscular or intravenous meperidine 50 to 100mg, and diazepam 2 to 5 mg, have been used extensively for many years. The intravenous combination of fentanyl citrate (an analgesic) and midazolam (a sedative) can be titrated to the needs of the patient and administered by an anesthetist or anesthesiologist. Oral fentanyl citrate is available but produces nausea and vomiting and may be impractical (Γερωέλσ ετ αλ., 1994). The patient is instructed not to eat on the day of surgery. Regional supraorbital, infraorbital, mental, superior alveolar and preauricular block anesthetics as bupivacaine or etidocaine can be used. Epinephrine-containing local anesthetics might exacerbate cardiac arrhythmias.

Cardiac monitoring equipment, a pulse oximeter, and blood pressure monitoring are state of the art for intravenous sedation and for monitoring vital signs as phenol is excreted. After an intravenous

infusion of lactated Ringer's solution is begun, Versed can be administered and titrated to avoid respiratory depression at 1 mg per dose to a maximum of 5 mg. Sublimaze is given in 50 µg increments to a maximum dose of 250 µg over a period of 90 to 120 minutes.

#### 4-Cleansing the Skin:

The face should be washed thoroughly with soap and water the night before and the morning of the procedure. No makeup should be employed on the morning of the peel. The fine facial hair is shaved first to avoid the discomfort of depilating these hairs during tape removal after surgery (Αλτ, 1989). A thorough 3-minute acetone scrub or a combination of acetone followed by alcohol to degrease the skin is utilized immediately before the application of wounding agent until a sandpaper-like sound is heard. Adequate degreasing of each cosmetic unit is imperative for good results and an even peel (Μχ χολλουγη ανδ Λανγσδον, 1988 & 1989).

#### ***The procedure:***

*1-Application of Wounding Agent* (Μχ χολλουγη ανδ Λανγσδον, 1988; Γολδμαν ανδ Φρεεδ, 1989; Στεγμαν ετ αλ., 1990; Ζυκοωσκ ετ αλ., 1993 & Ταψλορ, 1995):

It should be accomplished with moist but not very wet cotton-tipped applicators. There is no question that phenol penetrates immediately through the papillary dermis to the reticular dermis. Clinically, in actinically damaged human skin one cannot obtain removal of the thickest rhytides of photoaging IV, in the perioral area for example, without continued rubbing and the subsequent application of a greater quantity of phenol with a very moist cotton-tipped applicator past

a white color until a gray-white color is seen. A single application with one cotton-tipped applicator to the individual deepest rhytids may be used before the application to the rest of the cosmetic unit. If the rhytides are not very deep and only a photoaging III variety, in the periorbital area for example, a single application with one cotton-tipped applicator that has been “wrung out” against the lip of the peel container with no continued rubbing is adequate. This might be termed a “light” versus a “heavy” application of phenol because the gray-white end point is not achieved here. In relatively non-sun-damaged skin, the light application is less likely to be a reality because it is the sun damage that retards wounding agent penetration.

The face is divided into six cosmetic units: forehead, left cheek, right cheek, perioral, nose, and periorbital areas. Peel solution is usually applied in this order-moving from the least sensitive to the most sensitive areas.

Phenol does not affect the growth of hair. The solution should be feathered into all hair-bearing areas, including the scalp and eyebrows. An electric fan to vent the phenol fumes accompanied by good central ventilation in a room with outdoor air access is important for the comfort of the staff.

To minimize renal and cardiac toxicity, 10 to 15 minutes are allowed between cosmetic units, so it takes 60 to 90 minutes for the entire procedure. One or two fresh single cotton tipped applicators are used for each application of solution. These many applicators are discarded during the procedure and are soaked with substantial amounts of wasted phenol.

A flow sheet or face peel chart on the operative report that indicates times at which areas are treated is necessary.

An immediate burning sensation is present for 15 to 20 seconds and quickly subsides. Pain returns in 20 minutes and persists for 6 to 10 hours. Rebound stinging may occur if the patient overuses the topical anesthetic at home multiple times.

The applicators are never passed over the eyes of the patients. Baker's solution is usually needed for the crow's feet area, but we switch to full-strength phenol for the upper or lower eyelid unit as determined by actinic damage or a history of previous peels.

**2-Taping the Mask** (Μοσιενκο ανδ Βακερ, 1978 & ΔιΓερονιμο, 1981):

Taping is applied to each segment as the peel progresses, although one can wait until the entire face is covered with Baker's solution. Waterproof zinc oxide nonporous tape is the most occlusive. Shorter-length tapes act as a hinge when overlapped allowing a slight amount of motion and better adherence. Tape must adhere properly, or skip areas may result. These areas can be spot peeled when the tape is removed. Taping is stopped immediately adjacent to the hair-bearing areas to avoid traction alopecia at the time of the removal. The eyebrows, eyelids, and earlobes should be peeled but not taped. Microfoam tape can be used to occlude the perioral area because the tape is elastic and will both stretch and contract with lip movement. We apply tape in short vertical overlapping strips and then optionally cover with several long horizontal strips to anchor the area.

Tape can be placed to a line 1 to 2 cm parallel to the inferior border of the mandible, which corresponds to the line of cosmetic

application in most women. It is preferred to use the sawtooth taping method along the mandibular region; this produces an irregular line that may be less noticeable.

Most surgeons do not perform deep peeling on the neck because of the risk of scarring.

### **3-Corticosteroid administration during peeling** (Στυζιν ετ αλ., 1989):

Many physicians administer 6 mg of betamethasone in conjunction with a deep peel. Στυζιν ανδ ηισ χοωορκερσ1989 have chosen to do this to reduce edema, but controlled studies have never been performed.

### **4-Tape mask removal** (Σζαχηοωιεζ ανδ Ωριγητ, 1989):

Patients may return in 24 hours for psychologic support.

Ice packs applied over the tape relieve the burning.

A liquid or soft diet is generally encouraged to minimize mastication until tape removal.

Although the pain subsides within 6 to 8 hours, the edema is severe, and the eyelids are frequently swollen. The patients should sleep with the aid of oral hypnotics, and analgesics if necessary.

Analgesia is generally not required by most patients to remove the mask if the face was shaved first. Optionally; some physicians remove the mask at 24 hours, although this is more painful and may delay healing. A gray and deeply edematous face with pinpoint bleeding is cleansed with saline or hydrogen peroxide.

### **After-care** (Στεγμαν ανδ Τρομοπιτη, 1984 ,Αλτ, 1989 & Ρααβ, 1991):

Wet to dry soaking gently three to five times daily with tap water while standing in the shower or dilute antiseptic skin cleansers (Betadine) can be used to dry the exudative edema, followed by an occlusive moisturizer to reduce the healing time. However, the use of Bacitracin or Polysporin ointment is preferred inspite of a low risk of contact allergy with more rapid reepithelialization. Petrolatum or petrolatum-containing ointments (A&D ointment) may not be as effective.

Therefore the original thymol iodide powder, forming an overlying dry crust, or second "mask," that was used by lay peelers and in Baker's original description should seldom be used today. Its use may be associated with an increased healing time or increased degree of hypopigmentation or depigmentation.

Biosynthetic occlusive dressings have been successfully implicated to prevent desiccation and speed epithelialization in dermabrasion. The use of a newer synthetic wound dressing, Meshed Omiderm after dermabrasion has been heralded as a revolutionary type of dressing that is not removed for the entire healing period fully permeable to fluid, ointment is applied to the surface of the dressing, and it is held in place at the edges. The dressing is removed after reepithelialization has occurred. This dressing may prove to be useful immediately after tape removal. Whether dermal quality is enhanced or lessened with more rapid reepithelialization is unknown.

The patient should resist the uniform temptation to pick at the face. Pruritis is common and is relieved by noncomedogenic moisturizers, hydrocortisone ointments, ice packs, and aspirin. Daily cream-based sunscreens and tretinoin are reinstiuted as soon as tolerated

within 1 or 2 weeks of reepithelialization. Complete avoidance of sunlight is imperative during the healing period. Petechiae may result from strenuous physical exercise within a month after peeling. Milia are a common occurrence. It is suspected but unproved that fewer milia result if tretinoin is used before peeling. Tretinoin will prolong erythema if used after peeling, but the patients should return to the maintenance regimen within 21 to 30 days after the peel or as soon as tolerated. Repeat peeling may be performed in 12 to 18 months. Individual rhytides or spot areas can be retouched at 6 months.

## **Wound healing:**

**Definition:** Interaction of a series of complex events that leads to the resurfacing, reconstitution and proportionate restoration of tensile strength of wounded skin. Partial thickness wound that penetrates partially not completely into the dermis heals by secondary intention, by reepithelialisation from residual adnexal epithelium or epithelium derived from adjacent uninjured skin (Χοσλέν, 1991).

### **Stages of wound healing after chemical peeling (Βροδψ, 1997β):**

**Coagulation, Inflammation:** Due to activation of clotting factors, monophages ,lymphocytes,and inflammatory mediators such as C5a, leukotriene B4, and kallikrein (Ραψμονδ, 2001).

**Reepithelialisation:** This process begins within 24 hours of wounding as certain mediators are released during inflammation, which may stimulate keratinocyte cell movement from the wound margins and from residual adnexal epithelium at the base of the wound. They relay on a matrix in the wound bed, which is formed of fibrinocetin cross linked

to fibrin, collagen, and elastin. Water content of wound bed is a major factor in the speed of epithelial cell migration (Οἰκέφει ετ αλ., 1985).

***Granulation tissue formation:*** It is the loose collection of cellular component including fibroblasts, inflammatory cells, fibrinogen, glycosaminoglycans (GAGs), and collagen. It begins in the second or third day of peeling and is maintained until reepithelialisation is complete (Χλαρκ, 1985 & Φολκμαν ανδ Κλαγσβρυν, 1987).

***Angiogenesis:*** After peeling the resumption of blood flow is essential to supply oxygen and nutrients to the healing wound. Endothelial cells migrate directly in the wound and travel along fibrinogen matrix. Angiogenic wound factors which are released from insitu fibroblasts, macrophages, and endothelial cells themselves may be important in this directed migration. The capillary ingrowth with the granulation tissue may explain persistent erythema after chemical peeling (Σηολλεψ ετ αλ., 1978 & Φολκμαν, 1982).

***Collagen remodeling:*** Collagen and matrix remodeling begin at the advent of granulation tissue formation and continue for months after reepithelialisation. This remodeling is responsible for the texture of the skin after peeling. As collagen is laid down, fibrinogen gradually disappears. Water is resorbed and collagen fibers particularly types I and III lie closer together. They reorient in a parallel fashion to the skin surface (Δοιλλον ετ αλ., 1985 & Χοσλεν, 1991).

**Complications of chemical peeling:** (Βροδψ, 2001 & Σαβινι, 2004):

Despite the great cosmetic improvement that can be achieved from chemical peeling, several complications and side effects must be put in consideration.

***Pigmentary change:*** Pigmentary change is not an uncommon complication, especially with the deeper peeling agents. In some cases, the peeled area remains stark white. Taking proper precautions (as described earlier) can prevent undesirable pigmentary changes.

***Scarring:*** By matching the patient and peeling agent properly, the risk of scarring can be decreased. Also, to further decrease the risk of scarring, the patient should be advised to refrain from picking at the healing skin. Patients with a history of keloids should not undertake medium or deep peels because of the risk of scarring.

***Infection:*** By using bacitracin for the medium and deep peels and cleaning the face with a povidone wash, the risk of infection is decreased. *Cold sores* can be prevented with acyclovir (400 mg PO bid), beginning 2 days prior to the peel and continuing 7 days after the peel. *Candidiasis* infection also can develop, for which a short course of ketoconazole can be used.

***Prolonged erythema:*** Patients usually do not complain of erythema because it generally subsides in 30-90 days, but sometimes erythema continues. Prolonged erythema is usually not permanent, and topical hydrocortisone can be used to speed the healing process.

***Acne:*** Some patients develop acne after a chemical peel. This usually occurs between days 3-9. Cultures should be taken, and an antibiotic that covers gram-positive bacteria should be prescribed.

***Milia:*** Small inclusion cysts can appear in the healing process 2-3 weeks after a chemical peel and may be aggravated by ointments due to occlusion of the sebaceous glands.

