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THE USE OF GLYCOLIC ACID AS A PEELING AGENT

Howard Murad, MD, Ava T. Shamban, MD, and Paul Scott Premo

Over the past several years, many patients have become concerned about the cosmetic appearance of their skin. Popular magazines widely read by the lay person have increased the awareness of the public about different methods of skin rejuvenation, including chemical peels. Recently alpha-hydroxy acids (AHAs) have been incorporated into a variety of creams, lotions, and cleansers in general use. They are also being used as a new modality of chemical peeling. Through the ages, AHAs have been used in a variety of cultures. In Egypt Cleopatra bathed in sour milk, and during the French revolution the ladies of the court applied fermented wine to their faces.[3, 21, 33]

AHAs are a special group of nontoxic organic acids found in natural foods and are often commercially referred to as "fruit acids."[33, 34] Several members of the AHA group include glycolic acid, occurring naturally in sugar cane, lactic acid (sour milk), malic acid (apples), tartaric acid (grapes), and citric acid (citrus fruit) (Table 1). AHAs differ in molecular structure, glycolic acid representing the smallest AHA and composed of a two-carbon molecule. Each has one or more carboxyl groups and a hydroxyl group on the adjacent carbon molecule[34] (Table 2).

The exact mechanism of action of AHAs is still unknown; however, it has been shown that at low concentrations the AHAs act to diminish corneocyte cohesion at the lower levels of the stratum corneum, and it has been suggested that this is by interfering with the formation of ionic bonds.[34] There are also some preliminary data demonstrating that one of the AHAs, ammonium lactate, increases the production of glycosaminoglycans.[13] In addition, there is one report that glycolic acid has anti-inflammatory activity with antioxidant properties.[27] AHAs at high concentrations can exert more profound effects on the skin, dependent on exposure time. Some of these effects include complete epidermolysis and possibly even some dermal effects such as increased collagen synthesis.[19, 33]

It is only recently that the clinical applications of AHAs have expanded to include their use as alternative chemical peeling agents.[18, 22] With consideration to all the AHAs, glycolic acid is currently the most commonly used, and this article is dedicated to the details of its use as a chemical peeling agent. Glycolic acid is a versatile chemical peeling agent and is primarily used by the physician at either a 50% or 70% nonneutralized concentration. In contrast to other peeling agents, glycolic acid is frequently applied as a series of peels separated by 1 to 4 weeks, whereas trichloroacetic acid (TCA) peels usually have a longer interval be-

Table 1. ALPHA-HYDROXY ACIDS AND THEIR NATURAL SOURCES

Alpha-hydroxy Acids	Natural Occurring Source
Glycolic acid	Sugar cane
Lactic acid	Sour milk
Malic acid	Apples
Tartaric acid	Grapes
Citric acid	Citrus fruit

Dr. Shamban is a prior recipient of a Shulton-La Prairie Fellowship awarded by the Dermatology Foundation in 1986.

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Table 2. ALPHA-HYDROXY ACIDS

Glycolic Acid	Lactic Acid	Malic Acid	Tartaric Acid	Citric Acid
CH_2OH | $COOH$	CH_3 | $CHOH$ | $COOH$	$COOH$ | CH_2 | $CHOH$ | $COOH$	$COOH$ | $CHOH$ | $CHOH$ | $COOH$	$COOH$ | CH_2 | $HOC—COOH$ | CH_2 | $COOH$

tween their applications. Many of the risks and complications associated with other peeling agents are minimized with the use of glycolic acid. These are discussed in detail later in this article. As previously mentioned, glycolic acid acts to diminish corneocyte cohesion at 5% to 15% concentrations and causes epidermolysis when used at higher concentrations.[34] With this in mind, many defects of the epidermis and papillary dermis are improved, including ichthyosis, actinic and seborrheic keratoses, lentigines, melasma, postinflammatory hyperpigmentation, superficial rhytides, acne, warts, and overall cutaneous improvement.[20, 22, 24, 25, 26, 35] Virtually every patient is a candidate for glycolic acid peels, including Asians, African-Americans, Hispanics, and others with deeply pigmented skin. In addition, almost every part of the body can be peeled, including the back, chest, arms, and legs.[17]

INDICATIONS FOR GLYCOLIC ACID PEELS

There are many indications for a glycolic acid peel. Arguably, the most common is facial rejuvenation, or a general improvement in the appearance of the skin. Next, melasma and lentigines are common indications and can be treated successfully in a variety of skin types and colors with the glycolic acid peel (Figs. 1 and 2). Acne responds quite well to short application serial glycolic acid peels, and they can be an important adjunct to therapy with topical and oral antibiotics (Figs. 3, 4, and 5). Actinic keratoses may be treated with this peel, eliminating the need for long-term, uncomfortable alternatives that have unavoidable side effects that are often socially and cosmetically annoying (Fig. 6). Flat warts may be treated with this peel, as well as mild acne scarring. Superficial

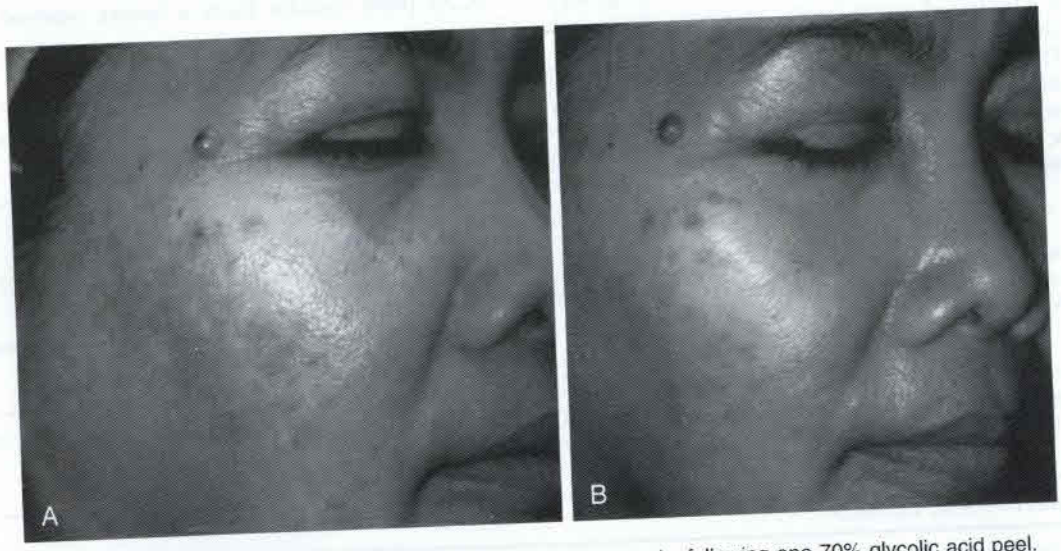
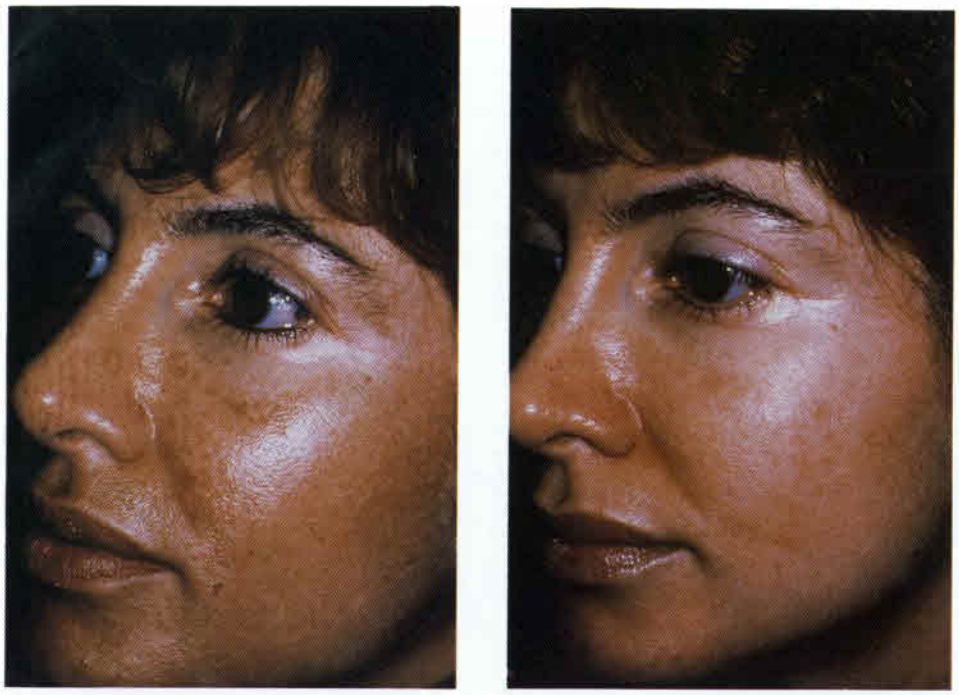
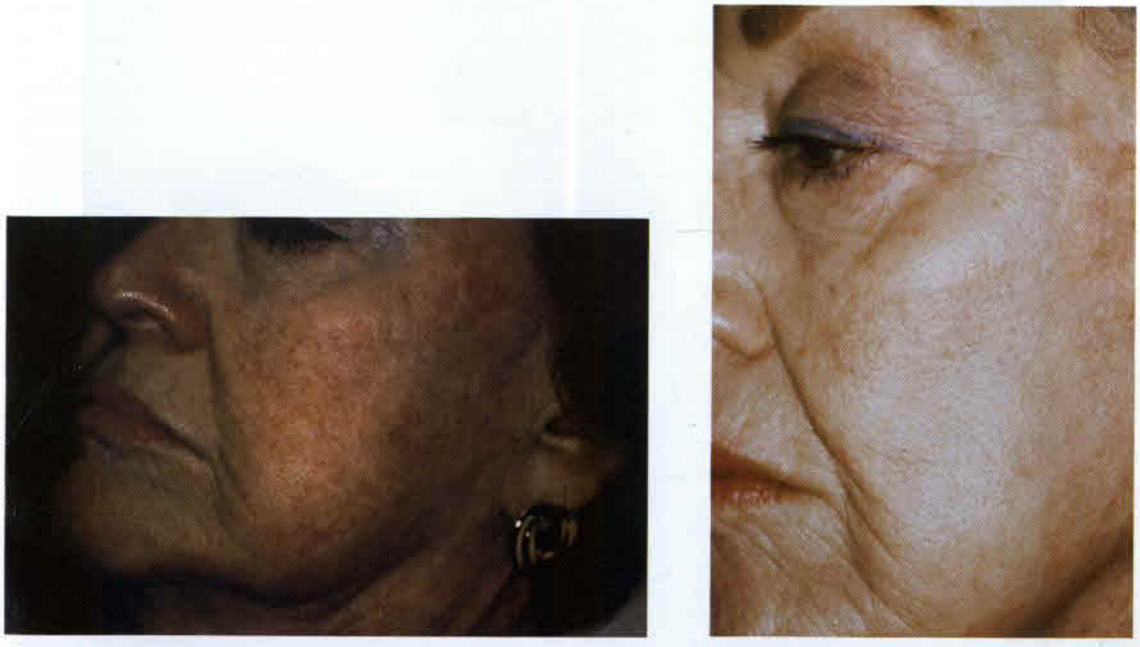


Figure 1. *A*, Typical melasma in a Filipino woman. *B*, Four weeks following one 70% glycolic acid peel.



A B

Figure 2. *A,* Melasma in an Hispanic woman. *B,* Four months later following a series of three 50% glycolic acid peels and topical at-home use of a 2% hydroquinone, 10% glycolic acid gel.



A B

Figure 6. *A,* Actinic keratosis in photodamaged skin of a Caucasian woman. *B,* One year later following single 50% glycolic acid peel and at-home twice-daily use of 2% hydroquinone, 10% glycolic acid gel.

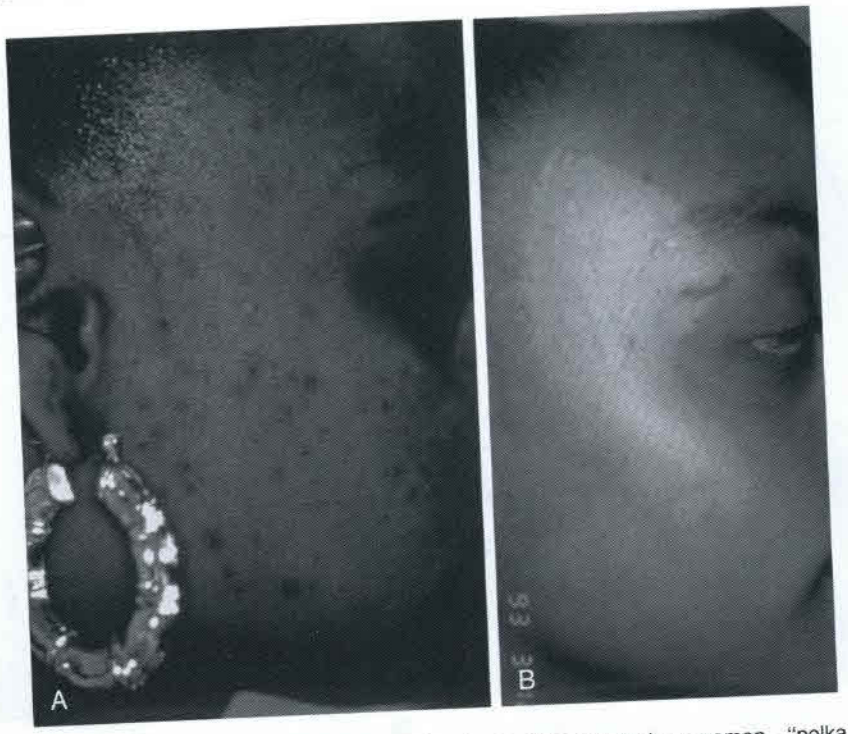


Figure 3. *A*, Acne with postinflammatory hyperpigmentation in an African-American woman—"polka dot" syndrome. *B*, Three months later following at-home topical application of 2% hydroquinone with 10% glycolic acid gel.

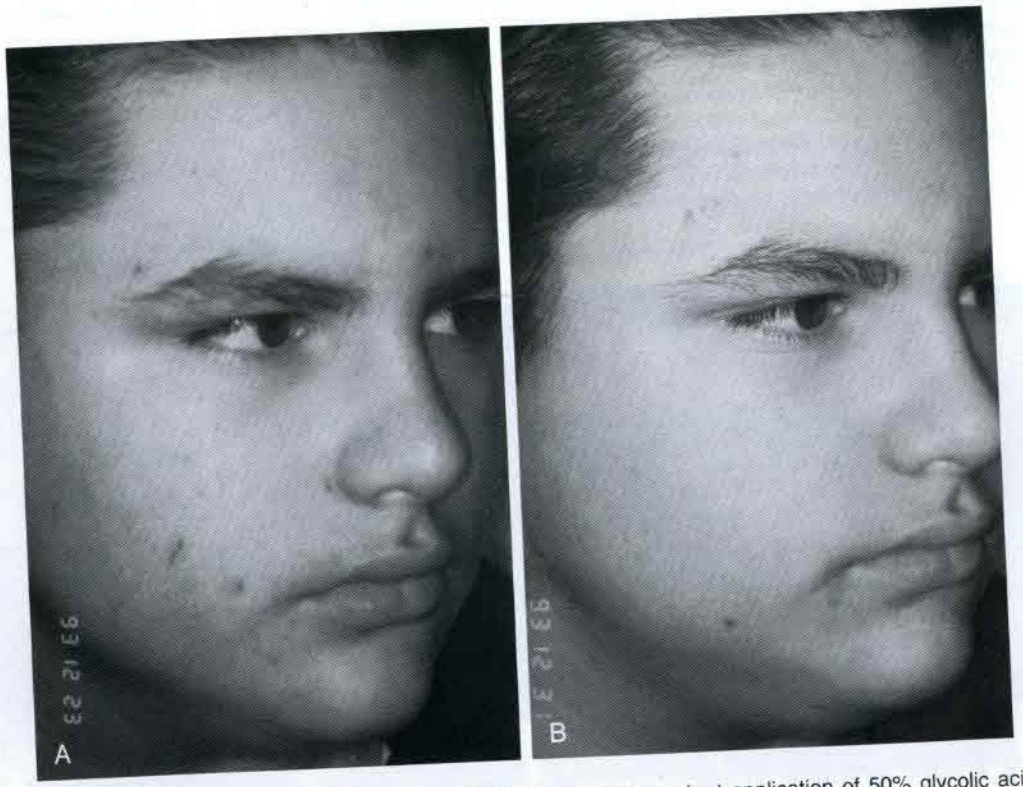


Figure 4. *A*, Acne in Caucasian male. *B*, One month later following one short application of 50% glycolic acid, 15% lactic acid, 5% salicylic acid peel, and home application of 10% glycolic acid gel and 1% salicylic acid.

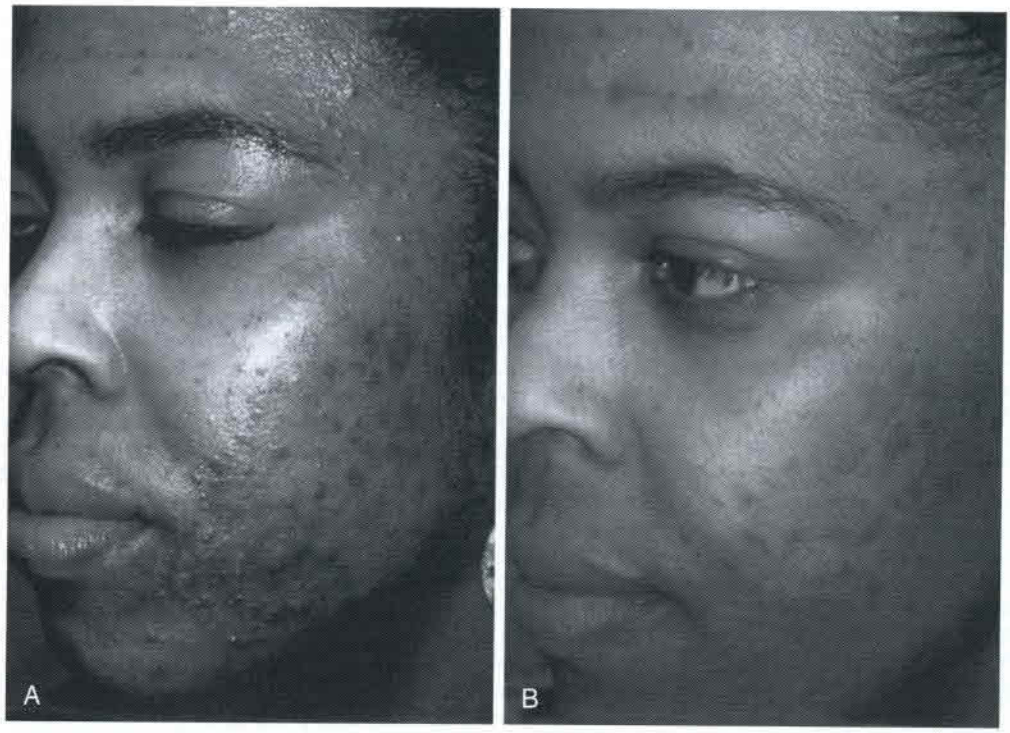


Figure 5. *A*, Cystic acne with postinflammatory hyperpigmentation in an African-American woman. *B*, Appearance after a series of six applications of 50% glycolic acid peels while on oral erythromycin. Photo taken 6 months after start of treatment.

rhytides may also improve with the use of the serial glycolic acid peel, depending on the skin type and individual patient response (Fig. 7). Hyperkeratosis palmaris et plantaris can be successfully treated with short-term 70% glycolic acid application to the palms and soles. Application of glycolic acid peels can enhance the effect of local treatments such as topical steroids in lichen simplex chronicus and psoriasis, and topical antifungals in dermatophyte infections involving the palms and soles.

TECHNIQUES FOR GLYCOLIC ACID PEELS

Prepeel Planning

Before performing a glycolic acid peel on a patient, it is important to assess the skin type, the amount of photodamage, and the cutaneous disorder that is being treated. Generally, patients with older, photodamaged skin, Glogau's classifications III and IV (Table 3), can tolerate higher concentra-

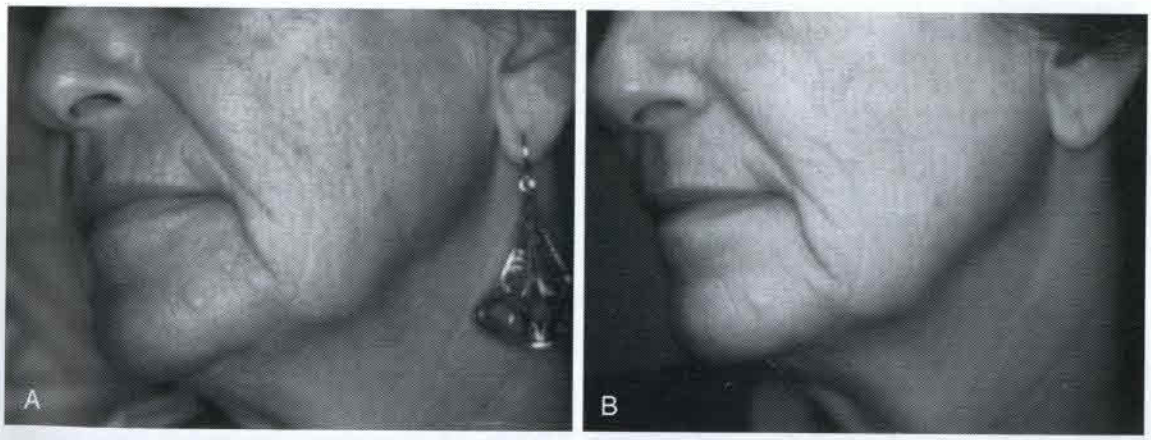


Figure 7. *A*, Superficial rhytides in a Caucasian female. *B*, Appearance following a series of four 50% to 70% glycolic acid peels.

Table 3. GLOGAU'S CLASSIFICATION (EVALUATION OF PHOTOAGING)

Group I. Mild (usually age 28–35 yr)
No keratoses
Little wrinkling
No scarring
Little or no makeup
Group II. Moderate (usually age 35–50 yr)
Early actinic keratoses, slight yellow skin discoloration
Early wrinkling, parallel smile lines
Mild scarring
Little makeup
Group III. Advanced (usually 50–65 yr)
Actinic keratoses, obvious yellow skin discoloration with telangiectasia
Wrinkling, present at rest
Moderate acne scarring
Wears makeup always
Group IV. Severe (usually 65–70 yr)
Actinic keratoses and skin cancers have occurred
Wrinkling, much cutis laxa of actinic, gravitational, and dynamic origin
Severe acne scarring
Wears makeup that does not cover but cakes on

Courtesy of Richard G. Glogau, MD, *as adapted in* Brody HS: Chemical Peeling. St. Louis, Mosby–Year Book, 1992; with permission.

tions of glycolic acid with longer exposure times. The accumulation of solar elastosis in the upper papillary dermis and the hyperkeratotic epidermis typically seen in photodamaged skin may impede the penetration of glycolic acid, resulting in both increased resistance and increased patient tolerance to the peel.[18] Patients with fair, ruddy, or generally sensitive skin, Fitzpatrick skin types I and II (Table 4), may be less tolerant and may quickly develop erythema with higher concentrations and shorter exposure time. Patients with overly sebaceous skin appear to have an increased tolerance to glycolic acid peels, apparently due either to the amount of surface sebum or to a hyperkeratotic stratum corneum. This obstacle can be eliminated prior to peeling with appropriate skin preparation procedures discussed later.

In summary, the important variables that determine the strength of the glycolic acid peel and the length of time it remains on the skin are (1) treatment site stratum corneum thickness and (2) the type and histologic location of the disorder(s): epidermal defects such as keratoses, warts, and dyschromias require less strength or less exposure time than dermal defects such as superficial rhytides. Lastly, the skin type and amount of photodamage also influence the administration of the glycolic acid peel.

Medications and Combination Therapies

Patient sensitization to glycolic acid may be heightened from certain topical or oral medications prior to chemical peeling: topical tretinoin, 5-fluorouracil, AHA preparations, or oral 13-cis-retinoic acid (Accutane) may increase patient skin sensitivity. A recommended 6 month to 2 year rest period after oral retinoids is advisable prior to glycolic acid peels. Chemical peels done immediately after Accutane use have been associated with a higher rate of scarring.[3] However, pretreatment with topical tretinoin or AHA preparations (8%–12% partially neutralized glycolic acid or 12% ammonium lactate or lower concentrations of non-neutralized glycolic acid) may improve the outcome of the peel.[3, 8, 17, 18] Although TCA has been used for many years in the treatment of actinic keratoses, combination therapy of 5-fluorouracil (5-FU) and high concentration AHA peels is also quite effective.[2] Together they appear to adequately treat actinic keratoses while reducing treatment time by as much as 50% compared with use of 5-FU alone.[10] Systemic hormone replacement therapy and oral contraceptives may increase the risk of postpeel hyperpigmentation. In this instance, an initial lower concentration of glycolic acid may be used in combination with sunscreens and hydroquinone. Prophylactic acyclovir for labial herpes simplex is necessary and advised prior to glycolic acid peels if the patient has a history of facial herpetic lesions. A daily course of acyclovir, 200 mg 5 times a day, 2 days prior to peel and 3 days postpeel, is recommended.

SKIN PREPARATION

Two to Four Weeks Prior to Peel

Ideally patients should be pretreated with twice daily at-home applications of glycolic acid appropriate for their skin type for 2 weeks prior to the peel. These preparations vary in vehicle and are supplied as creams, lotions, gels, or astringents. Recommendation of the appropriate glycolic acid preparation for home use is vitally important to ensure satisfactory results. Topical tretinoin may also be used sequentially or concurrently with gly-

Table 4. FITZPATRICK CLASSIFICATION (EVALUATION OF SKIN TYPE)

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 easily
VI	Black	No burn, tan very easily

*Asian Indian, Asian, Hispanic, or light African descent, for example.

Adapted from Fitzpatrick TB: Dermatology in General Medicine. New York, McGraw-Hill, 1993; with permission.

colic acid preparations as a pretreatment. Some patients need the addition of hydroquinone to their prepeel routine. Patients with actinic damage who exhibit multiple keratoses may be treated with topical 5-fluorouracil (5-FU) as an adjunct therapy prior to the glycolic acid peels. A series of 4 to 6 applications of glycolic acid in moderate concentrations (20%–40% partially neutralized) by a staff nurse, esthetician, or medical assistant is another alternative skin preparation regimen used prior to application of higher concentrations of glycolic acid. Prepeel glycolic acid procedures or topical tretinoin enable the patient to better tolerate the glycolic acid peels in addition to partially reducing stratum corneum thickness and may accelerate healing.[11, 15] The patient's response to pretreatment also may be used as an important indicator of the patient's tolerance, sensitivity, or resistance to the glycolic acid peels. Patients are instructed to avoid sun exposure, and daily use of sun protection factor 15 sunscreen is encouraged. They may continue their basic skin care routine. Before a chemical peel is performed, it is extremely important to discuss in detail every aspect of the peel procedure with the patient, including appearance immediately following the peel, 2 weeks after the peel, and long-term effects of the peel. The patient's realistic expectations of the entire procedure help to ensure more patient satisfaction and lessen the possibility of litigation.

Immediately Prepeel

Proper skin preparation prior to the application of the peeling agent is imperative in order to obtain superior results from the peel. Prepeel prepping removes surface sebum, debris, and to some extent stratum corneum, thus facilitating penetration of the peeling agent and insuring a more uniform peel. A variety of prepping agents may be used either in combination or alone. The most commonly used are acetone, ethanol, ethanol–salicylic acid solution, chlorhexidine, or Jessner's solution (Fig. 8). Jessner's solution removes the most stratum corneum; acetone, ethanol, and ethanol–salicylic acid solution remove some stratum corneum and are also very effective degreasing agents. Chlorhexidine is germicidal and removes surface sebum and debris. Surface abrasion by scrubbing with sterile gauze with any of the aforementioned agents will greatly reduce stratum corneum and ultimately yield a much deeper peel.[30] Another method of surface abrasion is scraping with a sharp instrument followed by the application of a CO_2 slush.

The procedure we follow is to first cleanse the patient's skin with a mild nonsoap cleanser to remove all cosmetics. Depending on the patient's tolerance, sensitivity, cutaneous disorder(s), and desired peeling depth, the skin is prepped with any of the previously mentioned degreasing agents alone or in combination. Cotton-tipped applicators, cotton balls, or gauze can be used to apply the prepping agent.

Prior to the application of the peel, a tray may be set up with gauze and water for quick removal of the glycolic peel (Fig. 9). Also, a small portable electric fan should be accessible to provide relief from stinging and pruritus commonly experienced during the peel procedure. The availability of an eye flush system in the event of inadvertent eye contact with glycolic acid is important.

Glycolic Acid Peel Application

After the patient has been adequately prepped, either 50% or 70% nonneutralized or partially neutralized glycolic acid is applied depending on the disorders to be treated. The glycolic acid gel is applied rapidly with a large cotton-tipped applicator or gauze pad, and smaller cotton swab applicators are used for isolated areas such as eyelids, upper lip, and rhytides (Fig. 10). A small fan brush applicator may be used; however, cotton applicators appear to retain the glycolic gel more effectively and are disposable. The glycolic acid is applied to one site at a time, beginning with the forehead and advancing down to the cheek, chin, and nasal areas in a clockwise fashion within 20 seconds. Periorbital rhytides may be stretched out with the hand to allow consistent application of the glycolic acid in these areas and enhance the

Figure 8. Skin preparation agents from left to right: cleansing lotion, acetone, alcohol, Jessner's solution, and 5% salicylic acid solution.

Figure 9. Tray set-up for glycolic acid peel. From left to right: cleansing lotion, 70% glycolic acid, 50% glycolic acid, alcohol, acetone.

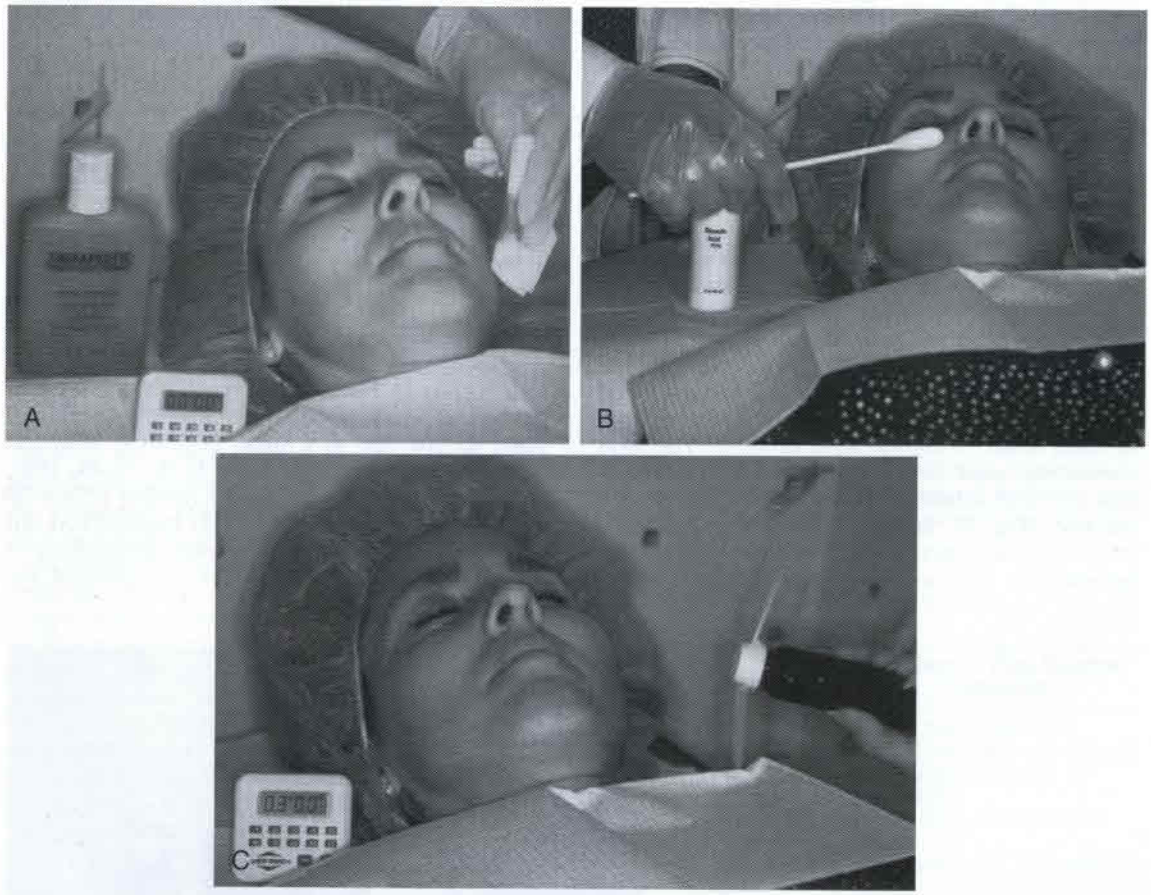


Figure 10. Application of glycolic acid. *A,* Skin is cleansed first. *B,* 70% glycolic acid is applied with a large-tip cotton applicator. *C,* A fan is used to alleviate any stinging or itching sensation.

outcome. Also, the glycolic acid may be applied as a second or third layer to specific affected locations such as actinic keratoses, hyperpigmented macules, cystic acne lesions, or scars. Care must be taken to ensure against direct eye contact with the acid solution. Glycolic acid may also be applied to other fine creases such as the nasolabial folds and perioral lines. When glycolic acid is applied to other areas of the body, either a large gauze pad is used or the glycolic acid is applied directly to the body and spread with a glove (Fig. 11). A timer is started upon the first contact with the glycolic acid, and the patient experiences a stinging or pruritic sensation. The small portable fan can alleviate most of this discomfort. The glycolic acid is left on for varying amounts of time, dependent on the indication and individual patient cutaneous characteristics. Maxillary skin tends to be quite sensitive, and the glycolic acid often needs to be removed from this area slightly before the rest of the face. When erythema is observed clinically it indicates epidermal depth of involvement, and the glycolic acid is removed if a lighter, more superficial peel is desired. Dermal penetration may appear as a mild blanch; the white frost seen with a TCA peel does not occur here. Table 5 gives some guidelines about the length of time various strengths of glycolic acid may be applied in the treatment of various skin disorders. However, every patient reacts differently to the glycolic acid peel, and the physician must constantly monitor the patient during the peel to assess skin color change and epidermolysis.

After the appropriate exposure time, the glycolic acid is removed and neutralized with water-soaked gauze, followed by the application of a mild soapless cleansing lotion. The patient then rinses the skin with cool running water until all cleanser and glycolic acid gel are removed. Some practitioners use sodium bicarbonate as a neutralizing solution instead of water. Patients usually experience a stinging sensation during the rinsing procedure. When this sensation subsides, the glycolic acid has been adequately neutralized and removed. Patients with severe erythema are given a soothing ointment, topical antibiotic ointment, or mild topical corticosteroid cream, depending on the observed inflammatory response. The ointment is applied to the affected areas as needed for 2 to 4 days postpeel. Patients are also instructed to apply a moisturizing sun protection factor 15 sunscreen daily.

Superficial glycolic acid peels need consistent and repetitive applications to provide long-term benefits.[29] Initially, patients with extreme skin sensitivity may begin with low concentration glycolic acid peels with shorter exposure times. Eventually, as patient tolerance increases, longer exposures or increasing the concentration of the glycolic acid to 70% may be initiated. Actinically damaged skin will tolerate longer exposures with 70% glycolic acid.

POSTPEEL CARE

Short-term Care

Immediately following the peel, after all the glycolic acid has been washed off, sunscreen is applied and the patient is allowed to leave, with strict instructions to avoid any sun exposure. Usually only a mild erythema appears, which allows the patient to resume a normal lifestyle immediately, with the exception of sun avoidance. Mild cleansing with a lotion cleanser may be performed the next day with subsequent application of sunscreens.

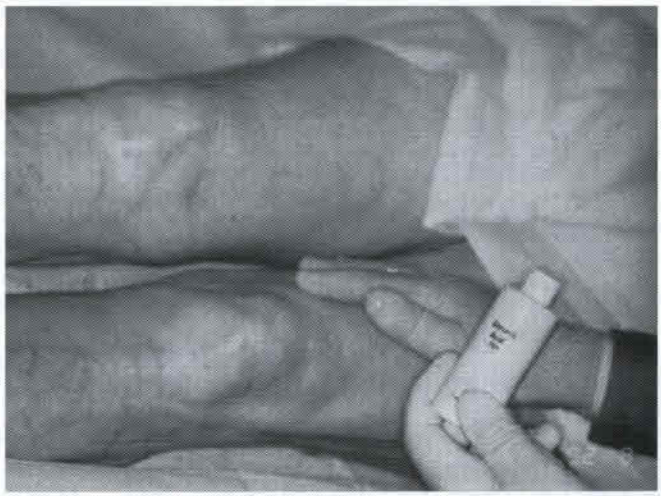


Figure 11. Application of glycolic acid to the body.

If a deeper erythema results from the peel, a soothing ointment, antibiotic ointment, or mild topical corticosteroid cream is used. The patient is asked to return in 2 days for clinical evaluation and possible need for any further care. Any significant irritation or edema may be treated with a semipermeable dressing or continued application of topical antibiotic ointment. Close follow-up is important in these cases to monitor any untoward events such as hyperpigmentation or persistent erythema, indicating potential scarring.

Long-term Care

The most important aspect of long-term care is sun avoidance. Both physical blockage of the sun through the use of hats and parasols and chemical blockage using ultraviolet A and B sunscreen are extremely important to prevent postpeel development of pigmentary dyschromias such as hyperpigmentation or the reappearance of melasma or lentigines. If such complications do occur then topical application of hydroquinone-glycolic acid preparations or tretinoin with hydroquinone and a mild corticosteroid may alleviate them.[12]

After healing has occurred, the patients frequently resume their prepeel regimen of topical, at-home use of glycolic acid or tretinoin to maintain the desired effect. A second peel, often in a series of four, takes place anywhere from 1 to 4 weeks following the initial peel to augment the effects of the prior peel or peels. Alternatively, the patient may elect to undergo a series of superficial glycolic acid exfoliations (20%–40% partially neutralized) administered by a staff nurse or esthetician. In such a fashion, through a series of peels, the cutaneous effects of a deeper peel may be attained without the drawbacks of the deeper peels. It is important to impress upon the patient the continued need for appropriate skin care, including sunscreens, glycolic acid use, and tretinoin use, regardless of whether they intend to have future peels.

Complications

There are many potential complications seen in any kind of chemical peel. These include, in order of severity, scarring, infection, postinflammatory hyperpigmentation or hypopigmentation, and persistent erythema.[4, 9, 14, 32] Scarring, although infrequent, is a possible complication in a higher strength glycolic acid peel, either 50% or 70%, when left on for a period of time not well tolerated by a given skin type. For example, a 50% glycolic acid peel left on for 4 minutes on a fair-skinned young individual may produce a complication, whereas a 70% glycolic acid peel remaining on the skin for 4 minutes on a sun-damaged elderly patient may have an imperceptible effect.

Scarring can occur after any wounding to the epidermis, and it is important to monitor the patient postpeel for any persistent erythema or raised firm red areas, indicating early scarring. If this does occur, early treatment with a cortisone-impregnated tape or intralesional corticosteriod in low concentrations is imperative. Some practitioners are also using silicone sheeting as treatment for early scarring. The incidence of scarring, although it occasionally occurs, is less than that following deeper peels such as phenol or 50% TCA peels and has not been reported with the use of low concentrations of glycolic acid applied for a very short period of time.

Infection is a possible untoward event following a chemical peel. If a history of herpes simplex is not elicited and prophylaxis is not instituted, an outbreak may occur. If treated after the peel, then scarring may occur. When the face is not cleansed properly following the peel, bacterial infection may result. This must be treated immediately with oral antibiotics.

Postinflammatory hyperpigmentation and persistence of prepeel dyschromias are other important complications. As already discussed, complete sun avoidance is crucial to a good result, but if hyperpigmentation persists, it is usually treated with good results with a glycolic acid formulation

Table 5. GLYCOLIC ACID PEEL EXPOSURE TIME

Clinical Indications	70% Glycolic Acid (Nonneutralized) (min)	50% Glycolic Acid (Nonneutralized) (min)	70% Glycolic Acid (Partially Neutralized, pH 2.5)
Keratoses	3–5	5–7	up to 10+ min
Hyperpigmentation	1–2	3–4	10 min repeated
Photodamage (Favré Rachouchet)	3–5	5–7	up to 10+ min
Fine rhytides	3–5	5–7	10+ min
Keratoses (hands/feet)	10+	15+	—
Warts	7–10	10	—
Acne	1	2–3	up to 10 min
Acne scars	3–4	5–7	10 min repeated
Skin rejuvenation	4–6	7–10	10+ min
Body (torso/extremities)	7–10	10+	10 min repeated

containing hydroquinone or tretinoin, and hydroquinone typically twice a day at home.

Postinflammatory hypopigmentation is an extremely uncommon complication of a glycolic acid peel. It is considered to be a side effect of a phenol peel and occasionally occurs following a high concentration TCA peel.[32] In our experience the only instance occurred following an inadvertent splash of 70% glycolic acid on a patient's arm that was not washed off for several hours.

Atrophic texture changes and milia are other potential sequelae generally not seen with a glycolic acid peel. Also, demarcation between peeled and unpeeled areas is generally not obvious to the eye following a glycolic peel.

Combining Peeling Agents

Owing to the flexibility of glycolic acid as a chemical peeling agent, it can be combined with other peeling agents to modulate the effects of the peel. This technique of combining peeling agents can enhance the penetration and depth of both agents while decreasing the toxicity and morbidity associated with traditional deeper peels.[8]

Various combinations of peeling agents have been employed through the years in an attempt to improve results. Preoperative prepping with tretinoin, Jessner's solution, carbon dioxide, and glycolic acid has been shown to enhance the penetration of TCA.[6, 8, 29] Several practitioners currently use glycolic acid to prewound the skin before applying TCA. This apparently allows the TCA to penetrate more deeply, while yielding a more uniform frost.[8] The glycolic acid–TCA combination can provide the surgeon with a new method of medium-depth peeling. This dual procedure of superficial peeling with 70% glycolic acid followed by TCA can be used as a substitute for pretreatment with Jessner's solution or solid CO_2. In our office we apply TCA in a strength of 20% to 30% as a prewounding agent, followed by the application of glycolic acid in a 50% to 70% strength. In this way we believe that the glycolic acid can more deeply penetrate to the dermis.

Topical tretinoin is commonly used as a pretreatment to enhance the outcome of chemical peels. Recent studies suggest that "retinizing" the skin may improve wound healing and reepithelialization.[11, 15] Pretreatment with glycolic acid preparations (10%–15%) for at least 2 weeks prior to a TCA or glycolic acid peel can be used as a substitute for tretinoin.[5] This is especially beneficial for the noncompliant patient who is tretinoin intolerant.

Research has demonstrated that the combination of 35% TCA prepped by Jessner's solution significally reduced the potential for scarring associated with higher concentrations of TCA.[16]

Histologic Evaluation of Glycolic Acid Peels

Clinical and histologic findings following chemical peels with TCA and phenol have been well described. Brodland et al[1] in 1989 reported on depth of necrosis observed in the pig model following application of various strengths of TCA. Brown et al[7] reported in 1960 on histologic alterations noted in skin following the application of phenol. In 1982, Stegman[31] described histologic events following application of TCA, phenol, Baker's solution, and dermabrasion in both sun-damaged and non–sun-damaged skin. He found that a layer of enlarged papillary dermis formed, whose thickness depended on the strength of the wounding agent, and that the effects were similar in both sun-damaged and non–sun-damaged skin.

Although there have been several reports describing clinical results of glycolic acid peels, histologic events accompanying the glycolic acid peel and later changes have not been documented.[3, 17, 18, 20, 22] We have completed a study examining TCA 35% and 70% glycolic acid applied to a non–sun-damaged area of the arm of a 52-year-old Caucasian, Fitzpatrick type II skin.[23] Our goal was to determine the depth of wounding observed with both glycolic acid and TCA and to ascertain its relevance to short- and long-term cutaneous effects. Also, our aim was to quantify the amount of inflammatory response elicited and the amount of new collagen and elastin deposition. Finally, we wanted to evaluate when and if the skin appeared to revert to its original prepeel condition.

Methods

The skin was prepared first by cleansing with chlorhexidine and then degreasing with acetone. First, 35% TCA was applied and then 70% glycolic acid was applied immediately inferior to the TCA site, except for a margin of untreated skin. The glycolic acid was left on. Three-millimeter punch biopsies were taken at both sites, as well as a control site that had been degreased and cleansed with acetone, at time intervals of 2 days, 2 weeks, 2 months, and 19 months. During this period there were no sunscreens, tretinoin, or AHAs applied. All biopsies were submitted for histopathologic evaluation to determine collagen and elastin deposition, as well as a hematoxylin and eosin stain. Biopsies taken at all stages were consistently uniform.

HISTOLOGIC EVALUATION

Results

Results from histopathologic examination of skin cleansed and degreased appear in Figure 12. At 2 days, the TCA induced upper epidermal ne-

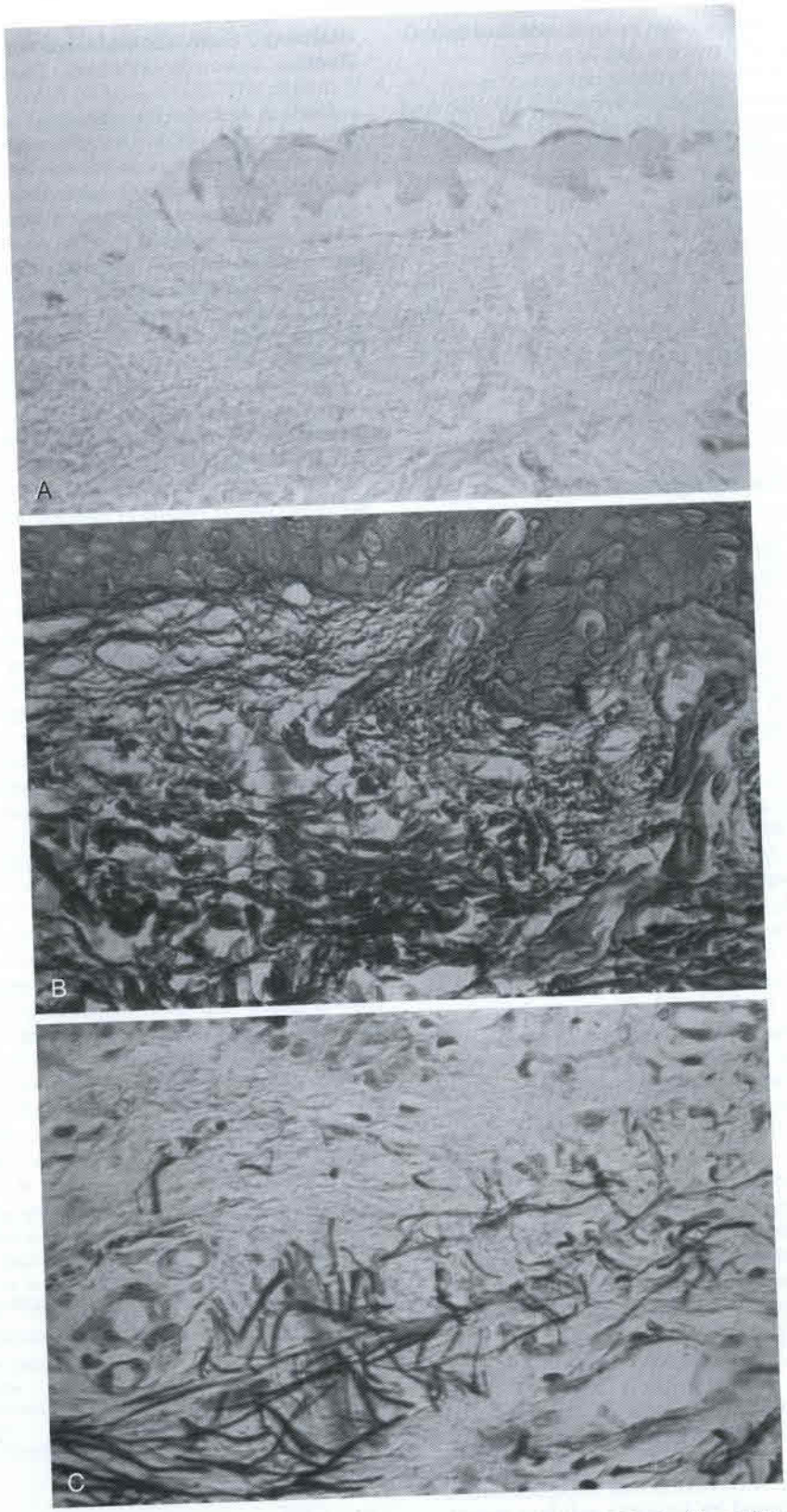


Figure 12. Normal skin. *(A,* Hematoxylin and eosin; *B,* trichrome; *C,* Verhoeff–van Gieson.*)*

Table 6. STRATUM CORNEUM AND EPIDERMAL THICKNESS

	Stratum Corneum Thickness (mm)		Epidermal Thickness (mm)	
	35% TCA	70% Glycolic Acid	35% TCA	70% Glycolic Acid
2 d	0.08	0.04	Necrotic	Edematous
2 wk	0.08	0.05	0.25	0.1
2 mo	0.05	0.1	0.1	0.11
2 yr	0.03	0.03	0.1	0.1

crosis to a 0.09-mm depth. There was also a perivascular infiltrate of lymphocytes and histiocytes. In contrast, the glycolic acid–treated skin demonstrated epidermal spongiosis, with individual necrotic epithelial cells and a perivascular infiltrate of lymphocytes and histiocytes (Fig. 13). The trichrome and elastin stain revealed separation of fine connective tissue fibers in the papillary dermis and a decreased number of elastic fibers, respectively. Therefore, in marked contrast to the TCA-treated skin, in which the changes are primarily located in the epidermis, the effects of glycolic acid appear to be taking place in the papillary dermis.

At 2 weeks a markedly acanthotic epidermis with focal spongiosis can be seen in the TCA-treated specimen, whereas the glycolic acid–treated skin demonstrated only a mild acanthosis, with an increased number of clear cells, possibly representing Langerhans cells (Fig. 14). The trichrome and elastic stain demonstrated persistence of the edema in the papillary dermis. Stratum corneum thickness was essentially the same, whereas at this stage the epidermis was thicker in the TCA specimen (Table 6).

At 2 months the epidermis appeared normal in the TCA-treated specimen but there was a proliferation of blood vessels and a mild inflammatory infiltrate. The trichrome stain illustrated a slight increase in thickness of the collagen fibers, and the elastic stain revealed thickening of the elastic fibers as well. In the glycolic acid specimen there were some areas of thickened stratum corneum, with increased thickness of collagen fibers visible with the trichrome stain. Also noted in the papillary dermis were increased numbers of elastic fibers. At this stage the dermal changes seen with both glycolic acid and TCA were quite similar (Fig. 15).

At 19 months changes in papillary collagen and elastin and all epidermal changes had essentially reverted back to normal, prepeel conditions (Fig. 16). At all stages biopsies were taken of untreated skin, which were consistently uniform.

The results of this small study are quite relevant to our current use of these two popular peeling agents. Of particular interest is the finding in the glycolic acid–treated skin that even without any epidermal necrosis there was still increased collagen and elastin deposition in the papillary dermis seen especially well at 2 months. Perhaps it is not necessary to undergo the discomfort and longer recovery time of a TCA peel to obtain similar benefits observed in the dermis with both agents. Another interesting finding is that at 19 months the skin had essentially returned to its prior untreated appearance. This finding supports clinical observations made from superficial peels of relatively short-term benefits and the need for repeated peels or daily use of sunscreens or topical agents such as tretinoin and glycolic acid to maintain these benefits. We did not look at histologic changes seen with serial glycolic acid peels. It would be interesting to see how the histology correlates with observed clinical improvement, however. The mechanism of action by which glycolic acid influences collagen and elastic fiber deposition is uncertain. One in vitro laboratory study of cultured fibroblasts exposed to glycolic acid suggests a stimulation of production of collagen in fibroblasts.[19] On the other hand, the presence of epidermal spongiosis instead of necrosis seen with glycolic acid in this study may not account completely for observed clinical improvement in cases of pigmentary dyschromias and other epidermal conditions such as actinic and seborrheic keratoses. Because this study was done on upper arm, non–sun-damaged skin rather than facial skin, it is conceivable that mild epidermal necrosis may occur at other locations, which can account for clinical epidermal improvement.

Owing to glycolic acid's time dependency, cutaneous penetration and necrosis can be amplified by increased exposure time (Table 7). When glycolic acid 70% is exposed to skin for 15 minutes, depth of necrosis may be equivalent to treatment with 35% and 50% TCA.[17] With decreased exposure time, glycolic acid 70% causes less wounding than that seen with 35% TCA.

SUMMARY

Glycolic acid is a member of the AHA family, which occurs naturally in foods and has been used for centuries as a cutaneous rejuvenation treatment. Recently it has proved to be a versatile peeling agent and it is now widely used to treat many

Text continued on page 306

Table 7. VARIABLES IN GLYCOLIC ACID PEELING

Assess skin type, degree of photodamage, cutaneous disorder(s)
Prepeel prepping agents at time of surgery
Glycolic acid concentration and pH
Glycolic acid in combination with other peeling agents
Appplication technique
Exposure time
Postpeel short- and long-term care
Repeated serial peels

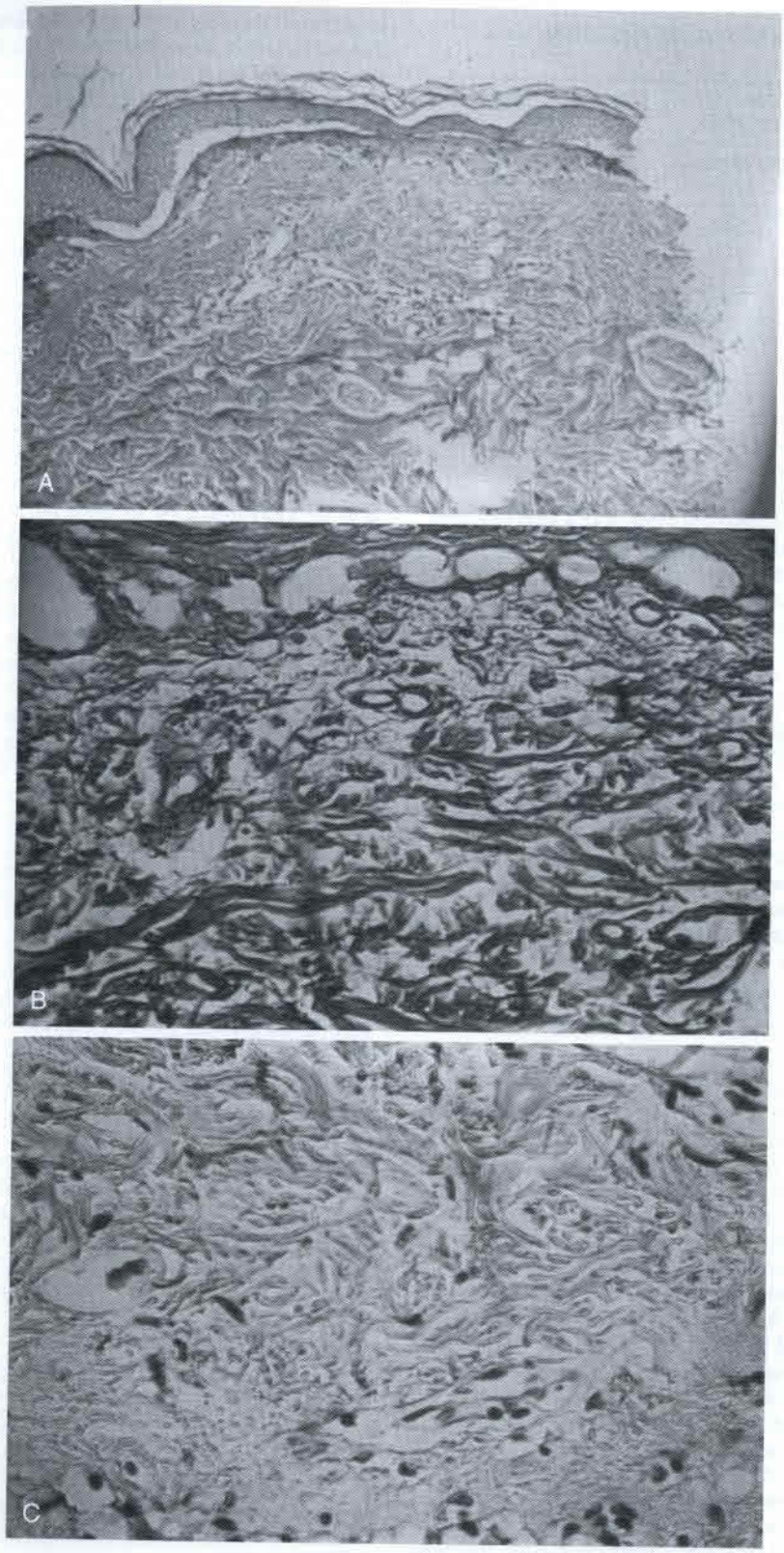


Figure 13. 35% TCA–treated skin at 2 days *(A, B,* and *C)* and 70% glycolic acid–treated skin at 2 days *(D, E,* and *F).* *(A* and *D,* Hematoxylin and eosin; *B* and *E,* trichrome; *C* and *F,* Verhoeff–van Gieson.*)*

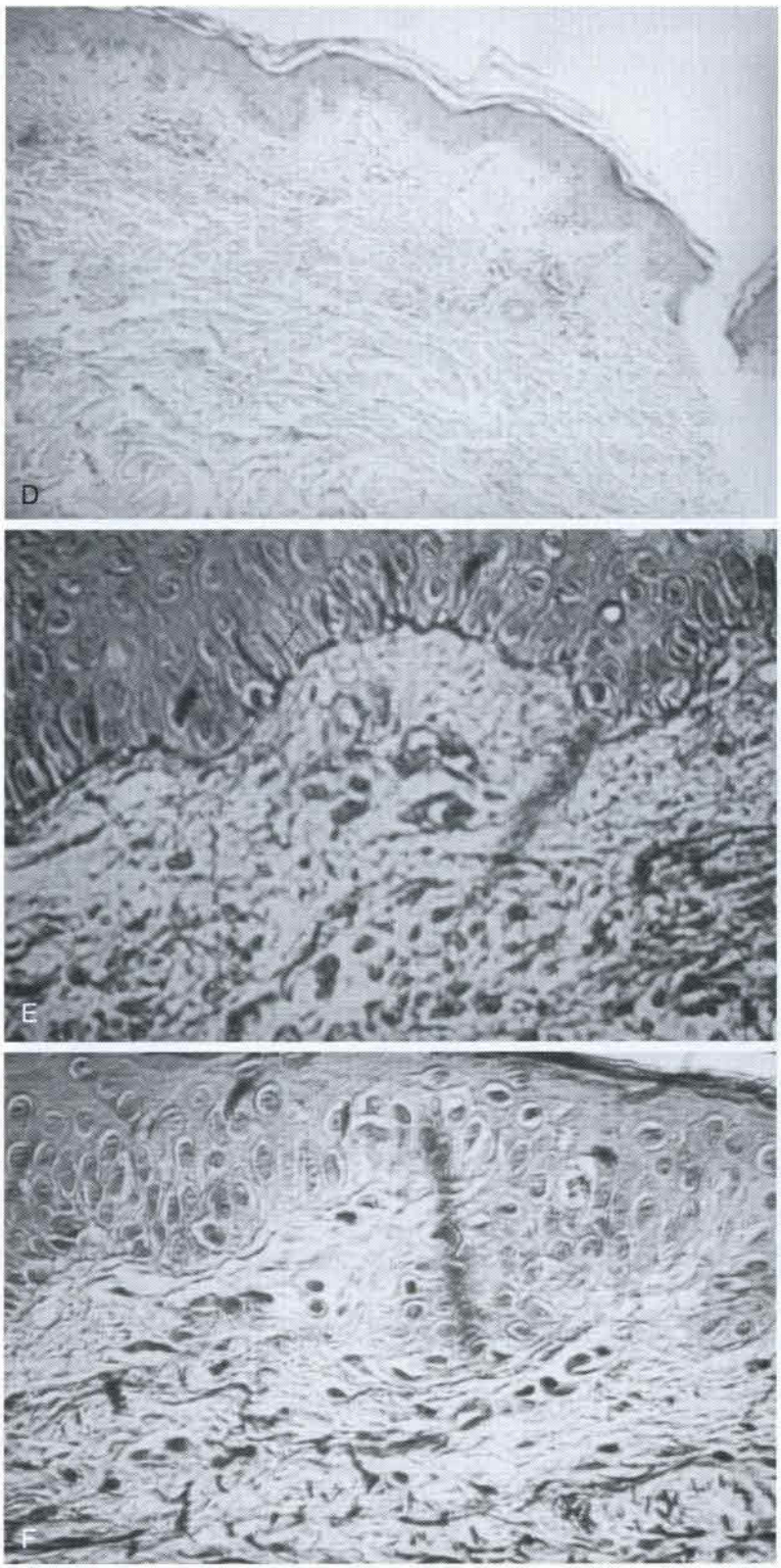


Figure 13 *(Continued).*

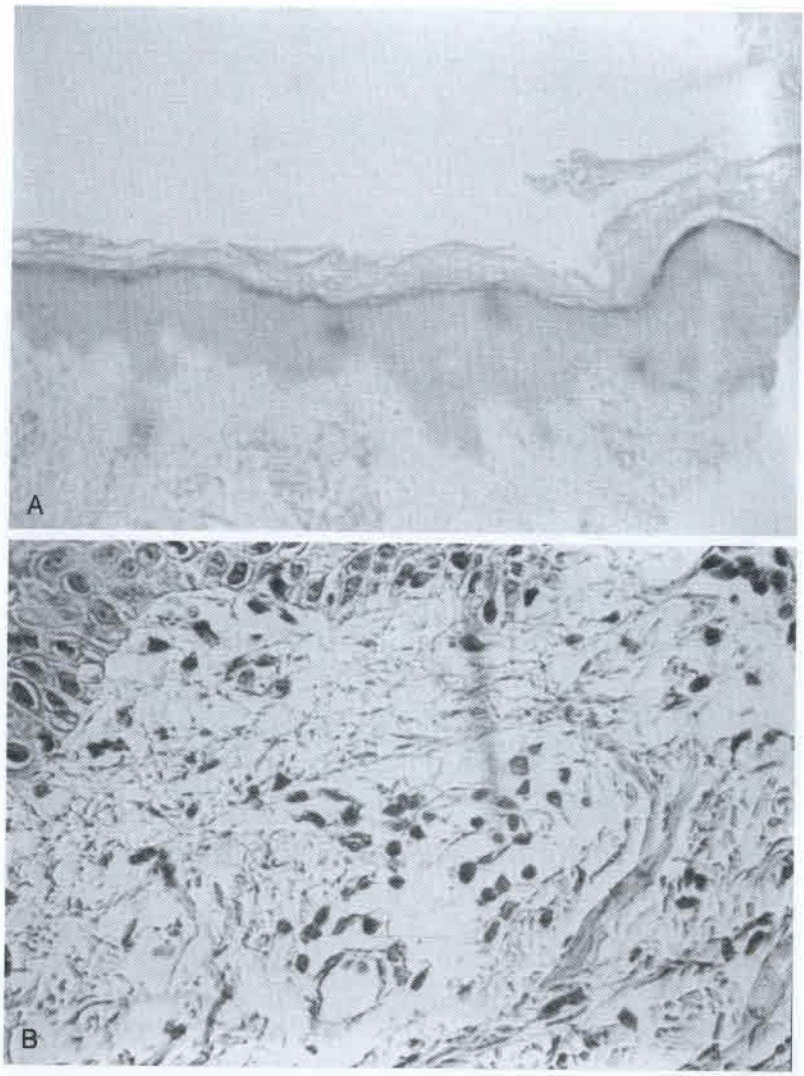


Figure 14. 35% TCA–treated skin at 2 weeks *(A* and *B)* and 70% glycolic acid–treated skin at 2 weeks *(C* and *D).* *(A* and *C,* Hematoxylin and eosin; *B* and *D,* Verhoeff–van Gieson.*)*

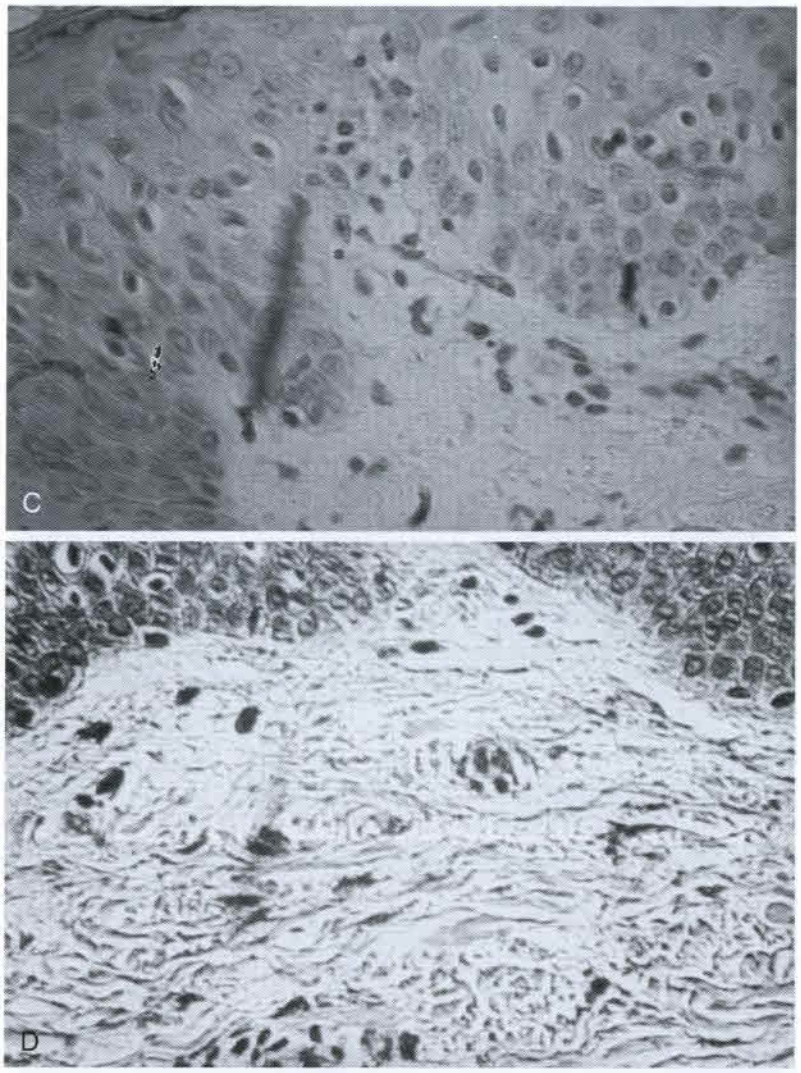


Figure 14 *(Continued).*

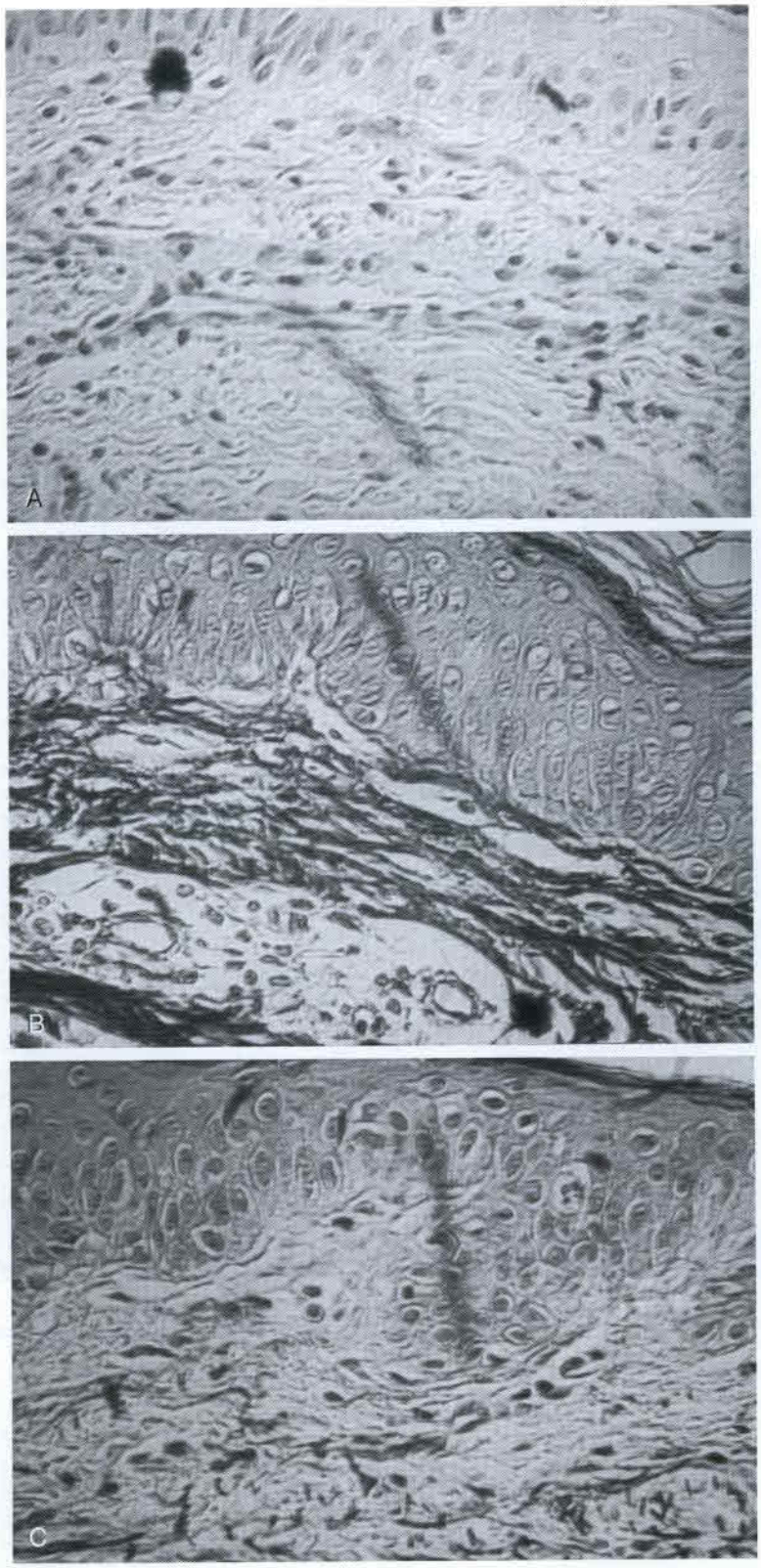


Figure 15. 35% TCA–treated skin at 2 months *(A, B,* and *C)* and 70% glycolic acid–treated skin at 2 months *(D, E,* and *F). (A* and *D,* Hematoxylin and eosin; *B* and *E,* trichrome; *C* and *F,* Verhoeff–van Gieson.*)*

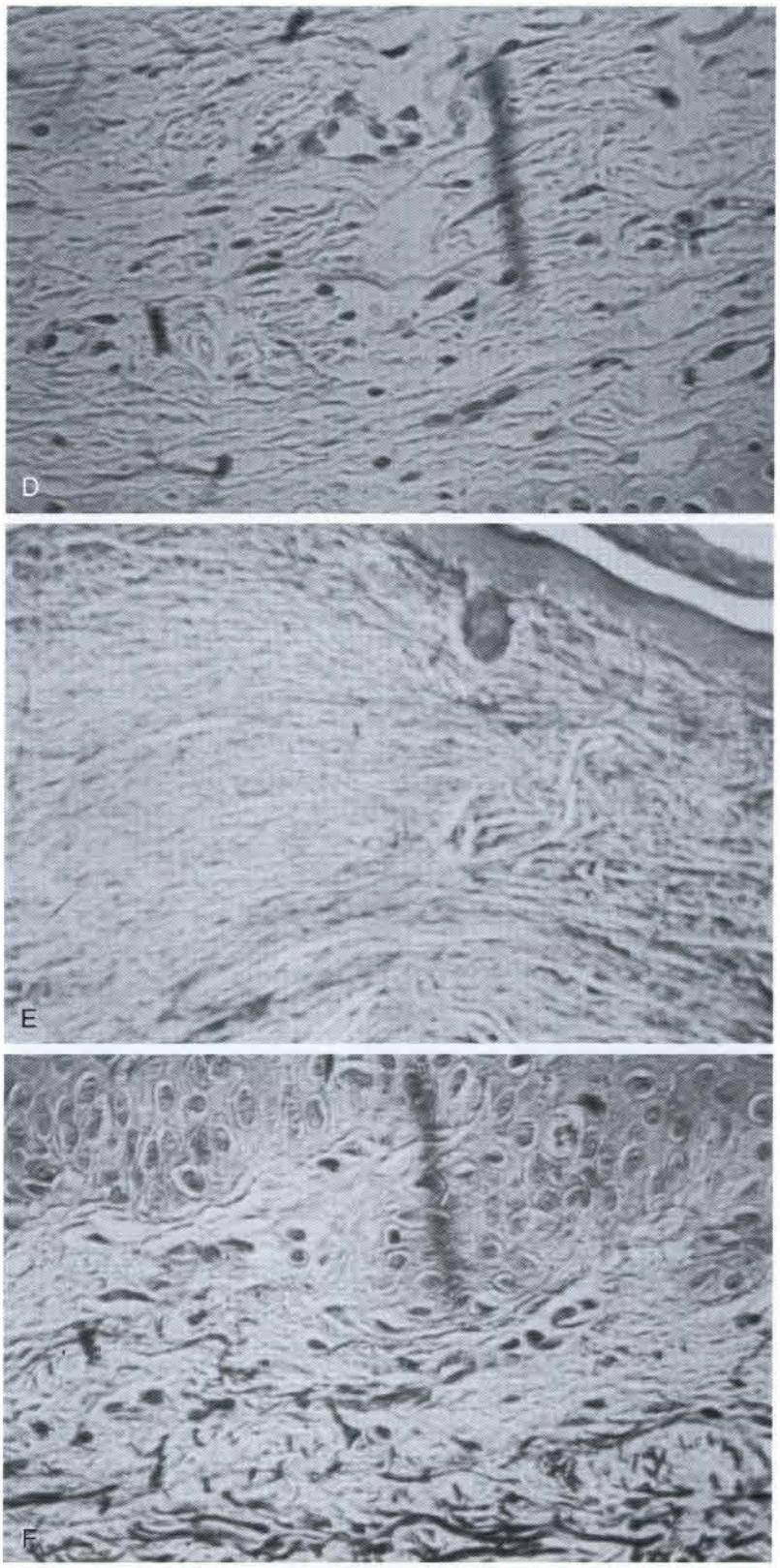


Figure 15 *(Continued).*

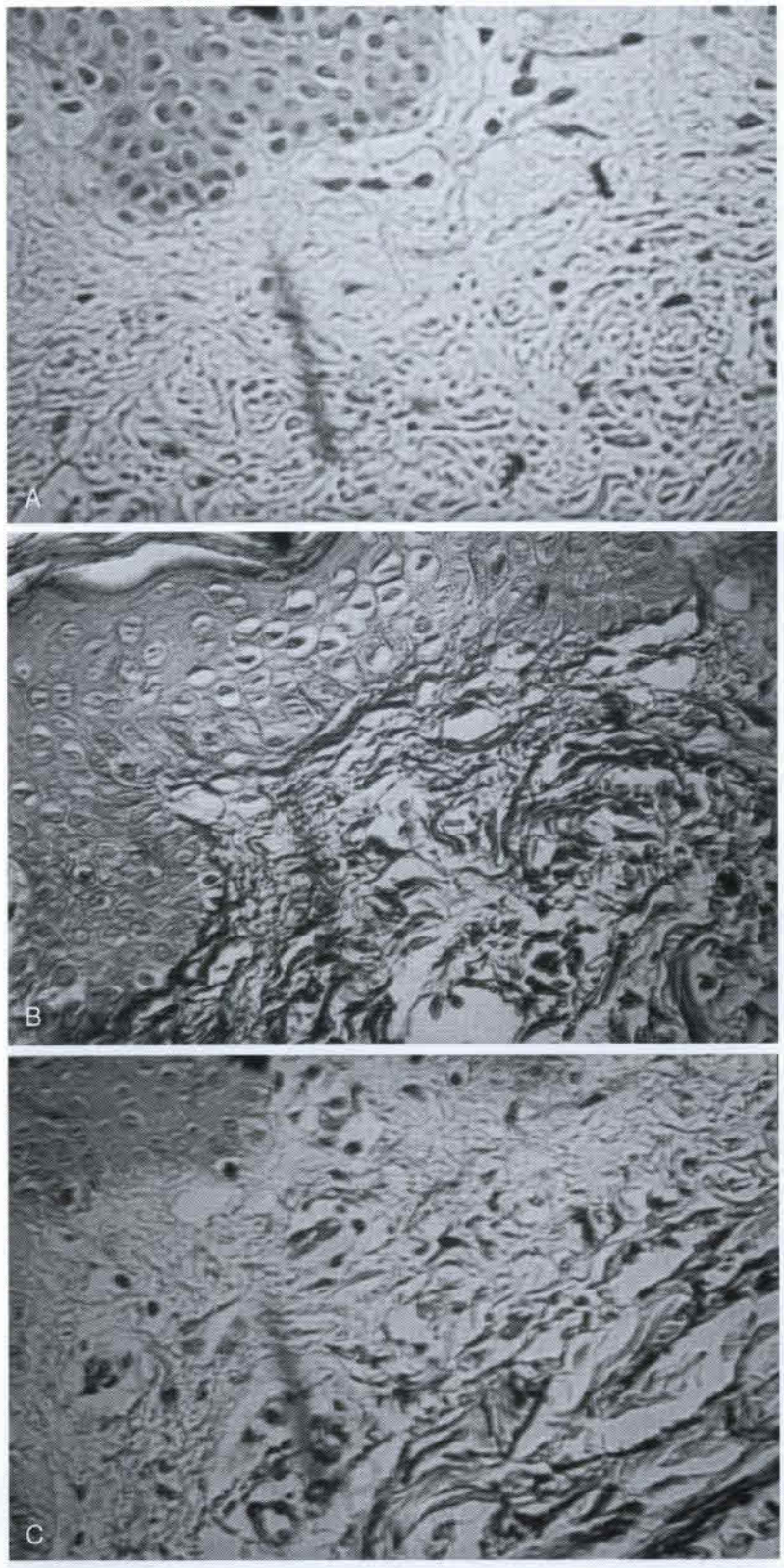


Figure 16. 35% TCA–treated skin at 2 years *(A, B,* and *C)* and 70% glycolic acid–treated skin at 2 years *(D, E,* and *F). (A* and *D,* Hematoxylin and eosin; *B* and *E,* trichrome; *C* and *F,* Verhoeff–van Gieson.*)*

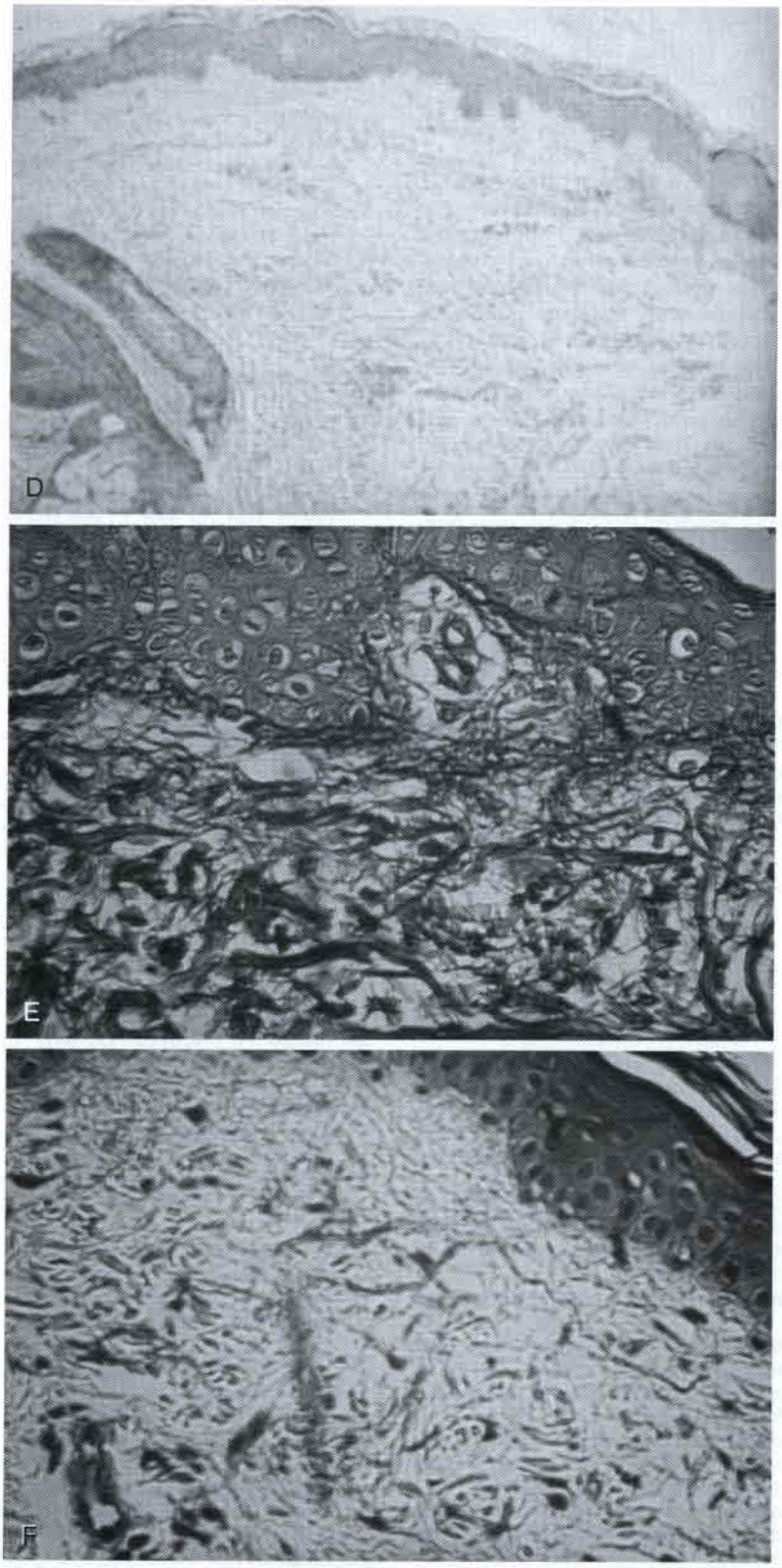


Figure 16 *(Continued).*

defects of the epidermis and papillary dermis in a variety of strengths, ranging from 20% to 70%, depending on the condition being treated. People of almost any skin type and color are candidates, and almost any area of the body can be peeled. Several weeks prior to a peel the skin may be prepared with topical tretinoin or glycolic acid, and immediately prior to the peel the skin may be degreased with a variety of agents. Following the peel the skin is carefully observed for any complications such as hyperpigmentation and infection. Results are maintained with serial peels and at-home use of tretinoin or glycolic acid, as well as sun avoidance. The glycolic acid can be applied simultaneously with TCA and is another technique for a medium-depth peel. Comparison of 35% TCA-treated skin with 70% glycolic acid–treated skin examined histologically at different times reveals similar changes in papillary dermis connective tissue proteins, epidermal necrosis seen only with TCA, and reversion at 2 years postpeel to pretreatment appearance.

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Howard Murad, MD, and Paul Scott Premo have financial interest in Glycolic Acid Skin Care Products distributed and marketed to dermatologists, plastic surgeons, and the professional beauty industry under the name Murad.

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