

profile, the physician should make sure both lips touch the "Steiner line," he said.

When seen in profile, the nasolabial angle should be about 84-105 degrees, he continued: "You want a good nasolabial angle."

To illustrate this, he showed a photograph in which one extended line connected the base of the nose to the tip of the nose. A second line from the base of the nose touched the "Glogau-Klein point" at the center edge of the upper lip. The angle is formed where the two lines intersect.

The G-K point describes the "ski slope" shape of the lip in profile as you move from the skin above the lip down onto the pink vermillion. There is always a little up-

turn, a point of reflection, which becomes lost as one ages, Richard G. Glogau, M.D., told SKIN & ALLERGY NEWS.

The cosmetic implication is that you have to recreate this shape with fillers used in the border of the lip to make the lip young and attractive. Also, if you use too much Botox on the upper lip, the orbicularis muscle flattens and makes an older looking lip. Therefore, it is generally a good idea to combine fillers with the Botox if you are trying to reestablish a youthful looking upper lip, said Dr. Glogau, who is a consultant to Allergan Inc., Medicis, and Inamed Aesthetics.

Dr. Klein cited a study of 100 women

which showed that aging lips lose height (Dermatology 2004;208:307-13). He said the most important aspect of lip augmentation involves building buttresses to restore the lost height and the ends of the lips.

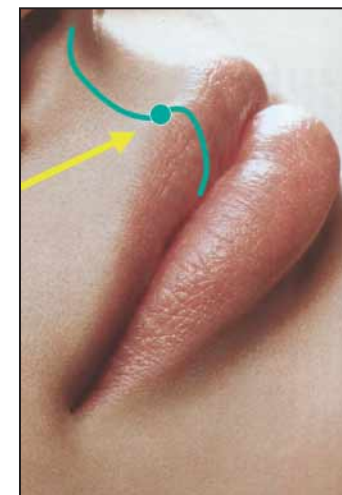
"You want flying buttresses to hold up the lips because of the loss of dentition," he said. "You want to restore the ends and build buttresses to support the lip. That's really important."

The choice of filling agent is less important than the physician's skill in using it, according to Dr. Klein, who disclosed ties as a consultant and/or investigator for Allergan Inc., Genzyme, Inamed Aesthet-

ics, Anika Inc., Medicis, SkinMedica, and OrthoNeutrogena.

"It is not what you use. It is how you use it," he said, recommending physicians become really skilled in one or two products rather than plow through what he described as a delicatessen menu of filling agents on the market.

Except for correction of scars, Dr. Klein opposes the use of permanent fillers. He



COURTESY DR. RICHARD G. GLOGAU AND DR. ARNOLD W. KLEIN

The Glogau-Klein point shows dimensions of the aesthetic lip.

warned that these agents could become increasingly visible or create an unnatural appearance as facial contours change over time. "For aesthetic indications I believe permanent fillers are a formula for disaster," he said.

Plasma Method Irons Out Lines And Acne Scars

LAKE BUENA VISTA, FLA. — Plasma skin resurfacing reduces acne scars and fine lines while minimizing downtime and adverse events, according to data presented at the annual meeting of the American Society for Laser Medicine and Surgery.

"Plasma skin regeneration provides an effective long-term facial rejuvenation for acne scarring and fine lines," said M. Potter, M.D., of RAFT Institute of Plastic Surgery in London.

The plasma device works by passing ultrahigh energy through nitrogen gas, generating plasma used to treat scars and lines with short pulses.

In this study, Dr. Potter treated a total of 11 patients (10 women)—3 for acne scars, 7 for fine lines, and 1 patient for both. The treatment was performed under anesthesia. Energy varied between 1 and 4 J.

All patients were assessed at 10 days and 3 and 6 months post treatment. "A precise measure of skin irregularity was recorded using silicon molds. ... Wrinkle depth was assessed using a light microscope technique to give an accurate measurement," Dr. Potter said.

In patients with fine lines, the mean pre-treatment wrinkle depth was 0.25 mm. At 10 days, there was a mean improvement in wrinkle depth of 39%. At 6 months, mean improvement was 24%. "Acne is always difficult to treat, but these patients had an improvement of 35% at 10 days and 23% at 6 months," Dr. Potter said.

—Kerri Wachter

conjunctivitis, corneal epithelial abnormality, cortical cataract, decreased night vision, diplopia, itchy eyes or eyelids, nuclear cataract, pannus, papilledema, photophobia, posterior subcapsular cataract, recurrent styes and subepithelial corneal lesions. Any patient treated with Soriatane who is experiencing visual difficulties should discontinue the drug and undergo ophthalmologic evaluation. **Pancreatitis:** Lipid elevations occur in 25% to 50% of patients treated with Soriatane. Triglyceride increases sufficient to be associated with pancreatitis are much less common, although fatal fulminant pancreatitis has been reported. There have been rare reports of pancreatitis during Soriatane therapy in the absence of hypertriglyceridemia. **Pseudotumor Cerebri:** Soriatane and other retinoids administered orally have been associated with cases of pseudotumor cerebri (benign intracranial hypertension). Some of these events involved concomitant use of isotretinoin and tetracyclines. However, the event seen in a single Soriatane patient was not associated with tetracycline use. Early signs and symptoms include papilledema, headache, nausea and vomiting and visual disturbances. Patients with these signs and symptoms should be examined for papilledema and, if present, should discontinue Soriatane immediately and be referred for neurological evaluation and care. Since both Soriatane and tetracyclines can cause increased intracranial pressure, their combined use is contraindicated (see CONTRAINDICATIONS). **PRECAUTIONS: Information for Patients:** Patients should be instructed to read the Medication Guide supplied as required by law when Soriatane is dispensed. **Females of reproductive potential:** Soriatane can cause severe birth defects. Female patients must not be pregnant when Soriatane therapy is initiated; they must not become pregnant while taking Soriatane, and for at least 3 years after stopping Soriatane (see boxed CONTRAINDICATIONS AND WARNINGS). **Females of reproductive potential should also be advised that they must not ingest beverages or products containing ethanol while taking Soriatane and for 2 months after Soriatane treatment has been discontinued.** This allows for elimination of the acitretin which can be converted to etretinate in the presence of alcohol. Female patients should be advised that any method of birth control can fail, including tubal ligation, and that microdosed progestin "minipill" preparations are not recommended for use with Soriatane. Female patients should sign a consent form prior to beginning Soriatane therapy (see boxed CONTRAINDICATIONS AND WARNINGS). **Nursing Mothers:** Studies on lactating rats have shown that etretinate is excreted in the milk. There is one prospective case report where acitretin is reported to be excreted in human milk. Therefore, nursing mothers should not receive Soriatane prior to or during nursing because of the potential for serious adverse reactions in nursing infants. **All Patients: Depression and/or other psychiatric symptoms such as aggressive feelings or thoughts of self-harm have been reported.** These events, including self-injurious behavior, have been reported in patients taking other systemically administered retinoids, as well as in patients taking Soriatane. Since other factors may have contributed to these events, it is not known if they are related to Soriatane. Patients should be counseled to stop taking Soriatane and notify their prescriber immediately if they experience psychiatric symptoms. Patients should be advised that a transient worsening of psoriasis is sometimes seen during the initial treatment period. Patients should be advised that they may have to wait 2 to 3 months before they get the full benefit of Soriatane. **Decreased night vision has been reported with Soriatane therapy.** Patients should be advised of this potential problem and warned to be cautious when driving or operating any vehicle at night. **Visual problems should be carefully monitored (see ADVERSE REACTIONS).** Patients should be advised to avoid excessive alcohol intake to contact lenses during the treatment period and sometimes after treatment has stopped. Patients should not donate blood during and for at least 3 years following therapy because Soriatane can cause birth defects and women of childbearing potential must not receive blood from patients being treated with Soriatane. Because of the relationship of Soriatane to vitamin A, patients should be advised against taking vitamin A supplements in excess of minimum recommended daily allowances to avoid possible additive toxic effects. Patients should avoid the use of sun lamps and excessive exposure to sunlight (non-medical UV exposure) because the effects of UV light are enhanced by retinoids. Patients should be advised that they must not give their Soriatane capsules to any other person. **For Prescribers: Phototherapy:** Significantly lower doses of phototherapy are required when Soriatane is used because Soriatane-induced effects on the stratum corneum can increase the risk of erythema (burning). **Laboratory Tests:** If significant abnormal laboratory results are obtained, either dosage reduction with careful monitoring or treatment discontinuation is recommended, depending on clinical judgment. **Blood Sugar:** Some patients receiving retinoids have experienced problems with blood sugar control. In addition, new cases of diabetes have been diagnosed during retinoid therapy, including diabetic ketoacidosis. In diabetics, blood-sugar levels should be monitored very carefully. **Lipids:** In clinical studies, the incidence of hypertriglyceridemia was 66%, hypercholesterolemia was 33% and that of decreased HDL was 40%. Pretreatment and follow-up measurements should be obtained under fasting conditions. It is recommended that these tests be performed weekly or every other week until the lipid response to Soriatane has stabilized (see WARNINGS). **Liver Function Tests:** Elevations of AST (SGOT), ALT (SGPT) or LDH were experienced by approximately 1 in 3 patients treated with Soriatane. It is recommended that these tests be performed prior to initiation of Soriatane therapy, at 1- to 2-week intervals until stable and thereafter at intervals as clinically indicated (see CONTRAINDICATIONS AND WARNINGS). **Drug Interactions:** Ethanol: Clinical evidence has shown that etretinate can be formed with concurrent ingestion of acitretin and ethanol (see boxed CONTRAINDICATIONS AND WARNINGS). **Gliclazide:** In a study of 7 healthy male volunteers, acitretin treatment potentiated the blood glucose lowering effect of gliclazide (a sulfonylurea similar to chlorpropamide) in 3 of the 7 subjects. Repeating the study with 6 healthy male volunteers in the absence of gliclazide did not detect an effect of acitretin on glucose tolerance. Careful supervision of diabetic patients under treatment with Soriatane is recommended. **Hormonal Contraceptives:** It has not been established if there is a pharmacokinetic interaction between acitretin and combined oral contraceptives. However, it has been established that acitretin interferes with the contraceptive effect of microdosed progestin "minipill" preparations. Microdosed "minipill" progestin preparations are not recommended for use with Soriatane. **It is not known whether other progestational contraceptives, such as implants and injectables, are adequate methods of contraception during acitretin therapy.** **Methotrexate:** An increased risk of hepatitis has been reported to result from combined use of methotrexate and acitretin. Consequently, the combination of methotrexate with acitretin is also contraindicated (see CONTRAINDICATIONS). **Phenytoin:** If acitretin is given concurrently with phenytoin, the plasma binding of phenytoin may be reduced. **Tetracyclines:** Since both acitretin and tetracyclines can cause increased intracranial pressure, their combined use is contraindicated (see CONTRAINDICATIONS AND WARNINGS). **Pseudotumor Cerebri, Vitamin A and oral retinoids:** Concomitant administration of vitamin A and/or other oral retinoids with acitretin must be avoided because of the risk of hypervitaminosis A. There appears to be no pharmacokinetic interaction between acitretin and cimetidine, digoxin, or glyburide. **Investigations into the effect of acitretin on the protein binding of anticoagulants of the coumarin type (warfarin) revealed no interaction.** **Carcinogenesis, Mutagenesis and Impairment of Fertility: Carcinogenesis:** A carcinogenesis study of acitretin in Wistar rats, at doses up to 2 mg/kg/day administered 7 days/week for 104 weeks, has been completed. There were no neoplastic lesions observed that were considered to have been related to treatment with acitretin. An 80-week carcinogenesis study in mice has been completed with etretinate, the ethyl ester of acitretin. Blood level data obtained during this study demonstrated that etretinate was metabolized to acitretin and that blood levels of acitretin exceeded those of etretinate at all times studied. In the etretinate study, an increased incidence of blood vessel tumors (hemangiomas and hemangiosarcomas at several different sites) was noted in male, but not female, mice at doses approximately one-half the maximum recommended human therapeutic dose based on a mg/m² comparison. **Mutagenesis:** Acitretin was evaluated for mutagenic potential in the Ames test, in the Chinese hamster (V79/HGPRT) assay, in unscheduled DNA synthesis assays using rat hepatocytes and human fibroblasts and in an in vivo mouse micronucleus assay. No evidence of mutagenicity of acitretin was demonstrated in any of these assays. **Impairment of Fertility:** In a fertility study in rats, the fertility of treated animals was not impaired at the highest dosage of acitretin tested, 3 mg/kg/day (approximately one-half the maximum recommended therapeutic dose based on a mg/m² comparison). Chronic toxicity studies in dogs revealed testicular changes (reversible mild to moderate spermatogenic arrest and appearance of multinucleated giant cells) in the highest dosage group (50 then 30 mg/kg/day). No decreases in sperm count or concentration and no changes in sperm motility or morphology were noted in 31 men (17 psoriatic patients, 8 patients with disorders of keratinization and 6 healthy volunteers) given 30 to 50 mg/day of acitretin for at least 12 weeks. In these studies, no deleterious effects were seen on either testosterone production, LH or FSH in the 31 men.⁴⁴ No deleterious effects were seen on the hypothalamic-pituitary axis in any of the 18 men where it was measured.⁴⁵ **Pregnancy: Teratogenic Effects: Pregnancy Category X (see boxed CONTRAINDICATIONS AND WARNINGS).** **Nursing Mothers:** Studies on lactating rats have shown that etretinate is excreted in the milk. There is one prospective case report where acitretin is reported to be excreted in human milk. Therefore, nursing mothers should not receive Soriatane prior to or during nursing because of the potential for serious adverse reactions in nursing infants. **Pediatric Use:** Safety and effectiveness in pediatric patients have not been established. No clinical studies have been conducted in pediatric patients. Ossification of interosseous ligaments and tendons of the extremities, skeletal hyperostoses, decreases in bone mineral density, and premature epiphyseal closure have been reported in children taking other systemic retinoids, including etretinate, a metabolite of Soriatane. A causal relationship between these effects and Soriatane has not been established. While it is not known that these occurrences are more severe or more frequent in children, there is special concern in pediatric patients because of the implications for growth potential (see WARNINGS: Hyperostosis). **Geriatric Use:** Clinical studies of Soriatane did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently than younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. A two-fold increase in acitretin plasma concentrations was seen in

healthy elderly subjects compared with young subjects, although the elimination half-life did not change. **ADVERSE REACTIONS:** During clinical trials with Soriatane, 513/525 (98%) of patients reported a total of 3545 adverse events. One hundred sixteen patients (22%) left studies prematurely, primarily because of adverse experiences involving the mucous membranes and skin. Three patients died. Two of the deaths were not drug related (pancreatic adenocarcinoma and lung cancer); the other patient died of an acute myocardial infarction, considered remotely related to drug therapy. In clinical trials, Soriatane was associated with elevations in liver function test results or triglyceride levels and hepatitis. **Postmarketing Reports: Cardiovascular:** Acute myocardial infarction, thromboembolism (see WARNINGS), stroke. **Nervous System:** Myopathy with peripheral neuropathy has been reported during Soriatane therapy. Both conditions improved with discontinuation of the drug. **Psychiatric:** Aggressive feelings, and/or suicidal thoughts have been reported. These events, including self-injurious behavior, have been reported in patients taking other systemically administered retinoids, as well as in patients taking Soriatane. Since other factors may have contributed to these events, it is not known if they are related to Soriatane (see PRECAUTIONS). **Reproductive:** Vulvo-vaginitis due to *Candida albicans*. **Skin and Appendages:** Thinning of the skin, skin fragility and scaling may occur all over the body, particularly on the palms and soles; nail fragility is frequently observed. **Hypervitaminosis A** produces a wide spectrum of signs and symptoms primarily of the mucocutaneous, musculoskeletal, hepatic, neuropsychiatric, and central nervous systems. Many of the clinical adverse reactions reported to date with Soriatane administration resemble those of the hypervitaminosis A syndrome. The following information lists by body system and frequency the adverse events reported during clinical trials of 525 patients with psoriasis. **Adverse Events Frequently Reported During Clinical Trials (Percent of Patients Reporting):** BODY SYSTEM: CNS: 10% to 25%; Rigors, *Eye Disorders:* 10% to 25%; Xerophthalmia, *Mucous Membranes:* >75%; Cheilitis; 25% to 50%; Rhinitis; 10% to 25%; Dry mouth, Epistaxis, *Musculoskeletal:* 10% to 25%; Arthralgia, Spinal hyperostosis (progression of existing lesions), *Skin and Appendages:* 50% to 75%; Alopecia, Skin peeling; 25% to 50%; Dry skin, Nail disorder, Pruritus; 10% to 25%; Erythematous rash, Hyperesthesia, Paresthesia, Paronychia, Skin atrophy, Sticky skin. **Adverse Events Less Frequently Reported During Clinical Trials (Some of Which May Bear No Relationship to Therapy) (Percent of Patients Reporting):** BODY SYSTEM: *Body as a Whole:* 1% to 10%; Anorexia, Edema, Fatigue, Hot flashes, Increased appetite, <1%; Alcohol intolerance, Dizziness, Fever, Influenza-like symptoms, Malaise, Menstrual, Muscle weakness, Weight increase. *Cardiovascular:* 1% to 10%; Flushing; <1%; Chest pain, Cyanosis, Increased bleeding time, Intermittent claudication, Peripheral ischemia, *CNS:* 1% to 10%; Headache, Pain; <1%; Abnormal gait, Migraine, Neuritis, Pseudotumor cerebri (intracranial hypertension), *Eye Disorders:* 1% to 10%; Abnormal/blurred vision, Blepharitis, Conjunctivitis/irritation, Corneal epithelial abnormality, Decreased night vision/night blindness, Eye abnormality, Eye pain, Photophobia; <1%; Abnormal lacrimation, Chalazion, Conjunctival hemorrhage, Corneal ulceration, Diplopia, Ectropion, Itchy eyes and lids, Papilledema, Recurrent styes, Subepithelial corneal lesions. *Gastrointestinal:* 1% to 10%; Abdominal pain, Diarrhea, Nausea, Tongue disorder; <1%; Constipation, Dyspepsia, Esophagitis, Gastritis, Gastroenteritis, Glossitis, Hemorrhoids, Melena, Tenesmus, Tongue ulceration. *Liver and Biliary:* <1%; Hepatic function abnormal, Hepatitis, Jaundice. *Mucous Membranes:* 1% to 10%; Gingival bleeding, Gingivitis, Increased saliva, Stomatitis, Thirst, Ulcerative Stomatitis; <1%; Altered saliva. *Anal disorder:* Gum hyperplasia, Hemorrhoids. *Musculoskeletal:* 1% to 10%; Arthritis, Arthrosis, Back pain, Hyperostosis, Myalgia, Osteodynia, Peripheral joint hyperostosis (progression of existing lesions); <1%; Bone disorder, Olecranon bursitis, Spinal hyperostosis (new lesions), Tendinitis. *Psychiatric:* 1% to 10%; Depression, Insomnia, Somnolence; <1%; Anxiety, Dysphonia, Libido decreased, Nervousness. **Reproductive:** <1%; Atrophic vaginitis, Leukorrhea. **Respiratory:** 1% to 10%; Sinusitis; <1%; Coughing, Increased sputum, Laryngitis. **Skin and Appendages: 1% to 10%; Abnormal skin odor, Abnormal hair texture, Bulbous eruption, Cold/dammy skin, Dermatitis, Increased sweating, Infection, Psoriasisiform rash, Purpura, Pyogenic granuloma, Rash, Seborrhea, Skin fissures, Skin ulceration, Sunburn; <1%; Acne, Breast pain, Cyst, Eczema, Fungal infection, Furunculosis, Hair discoloration, Herpes simplex, Hyperkeratosis, Hypertrichosis, Hypoesthesia, Impaired healing, Otitis media, Otitis externa, Photosensitivity reaction, Psoriasis aggravated, Scleroderma, Skin nodule, Skin hypertrophy, Skin disorder, Skin irritation, Sweat gland disorders, Vitiligo, *Verrucae, Special Senses/Other:* 1% to 10%; Earache, Taste perversion, Tinnitus; <1%; Ceruminosis, Deafness, Taste loss. **Urinary:** <1%; Abnormal urine, Dysuria, Penis disorder. **Laboratory:** Soriatane therapy induces changes in liver function tests in a significant number of patients. Elevations of AST (SGOT), ALT (SGPT) or LDH were experienced by approximately 1 in 3 patients treated with Soriatane. In most patients, elevations were slight to moderate and returned to normal either during continuation of therapy or after cessation of treatment. In patients receiving Soriatane during clinical trials, 66% and 33% experienced elevation in triglycerides and cholesterol, respectively. Decreased high density lipoproteins (HDL) occurred in 40% (see WARNINGS). Transient, usually reversible elevations of alkaline phosphatase have been observed. The following information lists the laboratory abnormalities reported during clinical trials. **Abnormal Laboratory Test Results Reported During Clinical Trials (Percent of Patients Reporting):** BODY SYSTEM: *Electrolytes:* 10% to 25%; Increased: Phosphorus, Potassium, Sodium; Increased and decreased: Magnesium; 1% to 10%; Decreased: Phosphorus, Potassium, Sodium; Increased and decreased: Calcium, Chloride. **Hematologic:** 25% to 50%; Increased: Reticulocytes; 10% to 25%; Decreased: Hematocrit, Hemoglobin, WBC; Increased: Hemoglobin, Neutrophils, WBC; 1% to 10%; Increased: Bands, Basophils, Eosinophils, Hematocrit, Hemoglobin, Lymphocytes, Monocytes; Decreased: Hemoglobin, Lymphocytes, Neutrophils, Reticulocytes; Increased or decreased: Platelets, RBC. **Hepatic:** 25% to 50%; Increased: Cholesterol, LDH, SGOT, SGPT; Decreased: HDL cholesterol; 10% to 25%; Increased: Alkaline phosphatase, Direct bilirubin, GGPT; 1% to 10%; Increased: Globulin, Total bilirubin, Total protein; Increased and decreased: Serum albumin. **Miscellaneous:** 50% to 75%; Increased: Triglycerides; 25% to 50%; Increased: CPK, Fasting blood sugar; 10% to 25%; Decreased: Fasting blood sugar, High occult blood; 1% to 10%; Increased and decreased: Iron, Renal; 10% to 25%; Increased: Uric acid; 1% to 10%; Increased: BUN, Creatinine. **Urinary:** 25% to 50%; WBC in urine; 10% to 25%; Acetonuria, Hematuria, RBC in urine; 1% to 10%; Glycosuria, Proteinuria. **OVERDOSAGE:** In the event of acute overdose, Soriatane must be withdrawn at once. Symptoms of overdose are identical to acute hypervitaminosis A, i.e. headache and vertigo. The acute oral toxicity (LD₅₀) of acitretin in both mice and rats was greater than 4000 mg/kg. In one reported case of overdose, a 32-year-old male with Darier's disease took 21 x 25 mg capsules (525 mg single dose). He vomited several hours later but experienced no other ill effects. **All female patients of childbearing potential** who have taken an overdose of Soriatane must: 1) Have a pregnancy test at the time of overdose, 2) Be counseled as per the boxed CONTRAINDICATIONS AND WARNINGS and PRECAUTIONS sections regarding birth defects and contraceptive use for at least 3 years duration after the overdose. **REFERENCES:** 1. Berbis Ph, et al. *Arch Dermatol Res* (1988) 280:388-389. 2. Maier H, Honigsman H. Concentration of etretinate in plasma and subcutaneous fat after long-term acitretin. *Lancet* 348:1107, 1996. 3. 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