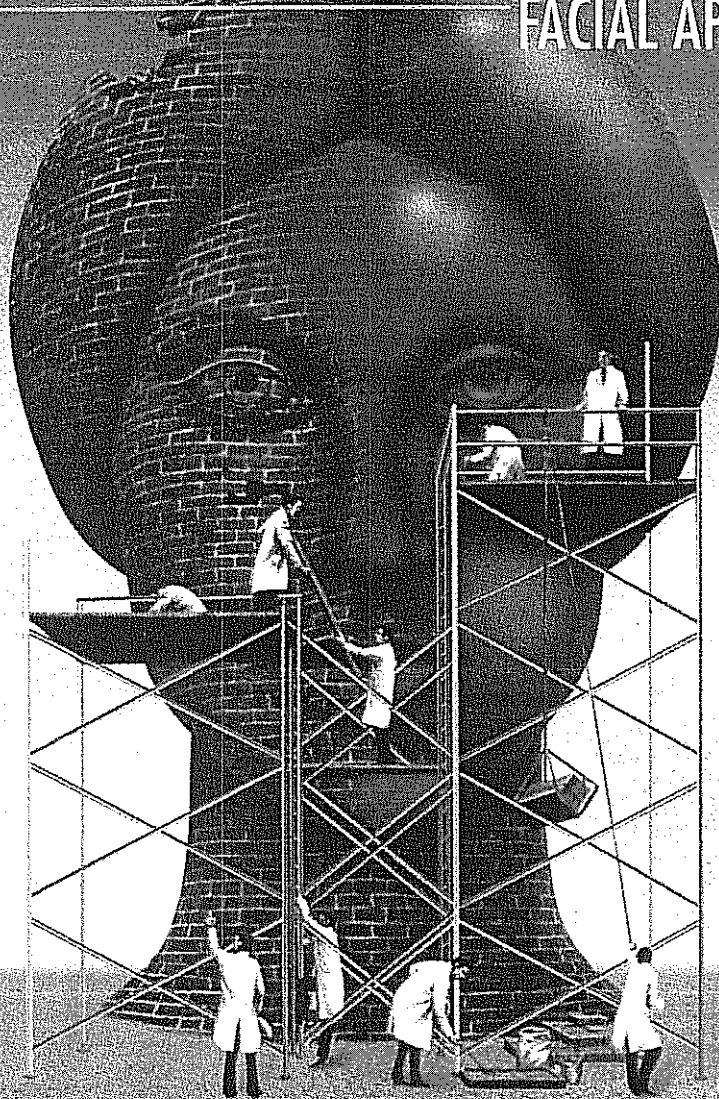


INNOVATIONS IN IMPROVING FACIAL APPEARANCE

Sunday, July 29, 2001
Anaheim, California



ABSTRACTS AND SELECTED SLIDES

Highlights from a CME activity held during ACADEMY 2001

Jointly sponsored by the A. Webb Roberts Center for Continuing Education of Baylor Health Care System, Dallas, and ApolloCom Associates, LLC



PROGRAM OVERVIEW

Our abilities to improve facial appearance continue to progress rapidly as new therapies are introduced and existing treatments are refined. At the activity which was designated for CME credit, the distinguished program faculty discussed the efficacy and tolerability of topical retinoid therapy in acne and photodamage and the role of botulinum toxin and filling agents in improving facial aesthetics.

ACCREDITATION

The CME activity on which these highlights are based was planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the A. Webb Roberts Center for Continuing Education of Baylor Health Care System, Dallas, and ApotheCom Associates, LLC.

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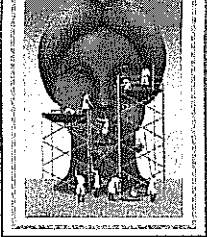
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FACULTY DISCLOSURE INFORMATION

In accord with the Policy on Disclosure of Faculty and Sponsor Relationships of the A. Webb Roberts Center for Continuing Education of Baylor Health Care System, Dallas, the standards of the ACCME, and the guidelines of the AMA, all faculty have been asked to disclose relationships (e.g. research grant support, speakers bureau, consultant, etc.) with pharmaceutical companies, biomedical device manufacturers, or other corporations. The intent of this policy is not to prevent a speaker with a potential conflict of interest from making a presentation. It is merely intended that any potential conflict should be identified openly so that the listeners may form their own judgments about the presentation with full disclosure of the facts.

The following speakers have, or have had in the last 12 months, relationships with the companies indicated:

Kenneth Arndt, MD, receives grant/research support from Candela Corporation, Cynosure, ESC, Laser Aesthetics, and Laserscope. He discussed unapproved products and unapproved uses of products and made them known during his presentation.

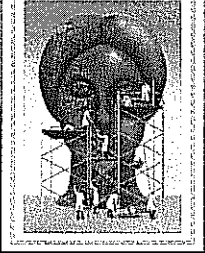
Sewon Kang, MD, receives grant/research support from Allergan, Inc., Galderma, and Johnson & Johnson. He addressed unapproved uses of a product and made this known during his presentation.

James Leyden, MD, receives grant/research support from Allergan, Inc., Dermik, Fujisawa, Galderma, Novartis, Ortho-McNeil Pharmaceutical, Pharmacia, Roche, and SmithKline Beecham. He is a consultant and is on the speakers bureau for the same companies. He may have addressed unapproved uses of a product and made this known during his presentation.

M. Alan Menter, MD, receives grant/research support from Allergan, Inc., Connetics, Genentech, and IDEC Pharmaceuticals. He is a consultant for Centocor and is on the speakers bureau for Roche. He addressed unapproved uses of a product and made this known during his presentation.

Alan Shalita, MD, receives grant/research support from Allergan, Inc., Dermik, Galderma, Ortho-McNeil Pharmaceutical, Stiefel, and Wyeth-Ayerst. He is a consultant for Allergan, Inc., Dermik, Galderma, Johnson & Johnson, Medics, and Stiefel. He is on the speakers bureau for Dermik.

Emil Tanghetti, MD, receives grant/research support from Allergan, Inc. and 3M. He is on the speakers bureau for Allergan, Inc., Cynosure, Fujisawa, Ortho-McNeil Pharmaceutical, and 3M. He addressed unapproved uses of a product and made this known during his presentation.



PRESENTATION ABSTRACTS

Evolution of Topical Retinoids for the Treatment of Acne and Photoaging

Selected Slides 1-3

Alan Shalita, MD

Retinoids are compounds that are either chemically related to vitamin A and/or bind to specific nuclear retinoid receptors. Tretinoin was first introduced more than 30 years ago for the treatment of acne and, more recently, for photoaging. Subsequently, newer retinoids and new chemical formulations have been developed to increase our therapeutic flexibility in the treatment of acne. These newer retinoids also appear to be promising for the treatment of photoaging.

Topical isotretinoin was the first new retinoid to be developed for the treatment of acne, but it is not available in the United States. Adapalene, a naphthoic acid derivative with receptor selectivity, appears to offer the advantage of better tolerability and cosmetic elegance, thereby improving patient compliance. Tazarotene, also a receptor-selective retinoid, is dramatically effective against both non-inflammatory and inflammatory lesions of acne. And finally, microsphere technology has permitted the use of relatively high concentrations of tretinoin with a reduced potential for irritation, thus improving patient compliance.

Today tretinoin is the only retinoid approved for the treatment of photoaging. It is available in emollient creams of 0.05% and 0.02% concentrations. Evidence from clinical trials suggests that the other retinoids may also become treatment options for photoaged skin.

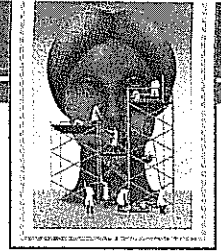
Retinoid Activity in Inflammatory and Non-Inflammatory Acne

Selected Slides 4-6

James Leyden, MD

Retinoid therapy is one of the major advances of the past 30 years. These molecules induce a variety of gene-mediated effects on cell differentiation processes and proliferation, which result in effects that are therapeutically useful in a wide variety of disorders. In the late 1960s, topical tretinoin, the first generation retinoid, was shown to be effective in acne. In the past decade, second generation topical retinoids—adapalene and tazarotene—have also been found to be effective in acne therapy.

Acne is a disease with multiple areas of pathophysiology resulting in clinical expressions ranging from non-inflammatory comedones to inflammatory papules, pustules, and—in some patients—highly destructive inflammatory lesions. Central to the evolution of these varied lesions is the formation of a pre-clinical stage, known as the microcomedo. Abnormal desquamation of follicular epithelia admixing with sebum distends the lumen of sebaceous follicles. This pre-clinical microcomedo provides a microclimate, in which proliferation of *Propionibacterium acnes* occurs. The microcomedo can evolve into either non-inflammatory comedones or inflammatory lesions. The latter occurs because of *P. acnes* production of chemoattractants for lymphocytes and neutrophils and pro-inflammatory cytokines.



Topical retinoids modulate the abnormal desquamation of follicular epithelia, preventing microcomedo formation. By attacking the pre-clinical, precursor stage, topical retinoids produce a reduction in both inflammatory and non-inflammatory lesions.

While dermatologists are well aware of the utility of topical retinoids in the treatment of acne, their use is primarily in patients with a predominance of non-inflammatory lesions. Use in inflammatory acne is curtailed because of concern that inflammation may be aggravated by topical retinoids and because of the clear-cut benefit of antibiotics. Despite the repeated demonstrations in vehicle-controlled trials that topical retinoids are effective in the inflammatory phase of acne, retinoids are rarely used as monotherapy. Some physicians use topical retinoids after a period of antibiotic therapy.

In this study, five investigators who have been involved in numerous acne clinical trials evaluated the effect of several topical retinoids in the inflammatory phase of more than 500 patients. The results of this photanalysis confirm the benefit of topical retinoid therapy in patients with inflammatory acne. Significant improvement was seen with tretinoin, adapalene, and tazarotene even in patients with severe inflammation. Moreover, topical retinoid therapy did not intensify inflammation. These results, coupled with previous reports of increased benefit in those treated with combinations of topical retinoids and antibiotics compared to antibiotics alone, strongly suggest that topical retinoids should be more widely used in patients with inflammatory acne.

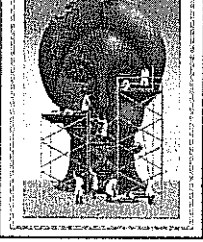
Minimizing Retinoid Irritation

Selected Slides 9-14

Emil Tanghetti, MD

Topical retinoids are the cornerstone of treatment for acne and photodamage. Irritation with dryness and redness is a commonly noted side effect that is typically seen early in therapy, usually within the first 4 to 6 weeks. Without appropriate management, it can lead to premature discontinuation of topical retinoid therapy.

A practical understanding of skin barrier function, vehicles, and the time course of retinization provide a rational and simple approach to maximizing topical retinoid therapy while minimizing irritation. A framework can be provided whereby most patients can tolerate the most potent topical retinoids and reap the benefits of the stronger products. This is achieved by maintaining skin barrier function, understanding the course of retinization, choosing the appropriate vehicle and concentration of drug, and exercising flexibility in initiating retinoids.



Latest Findings for Retinoids in Photodamage

Sewon Kang, MD

Selected Slides 12-16

Exposures to solar ultraviolet radiation, both acute and chronic, cause skin damage. One aspect of repetitive chronic photodamage is accelerated skin aging or photoaging. Its clinical features include fine and coarse wrinkles, dyspigmentation, skin roughness, and sallow color. Topical all-trans retinoic acid (tretinoin) has been shown to improve the photoaged phenotype and, at present, it is the only approved pharmacologic agent for the treatment of this condition.

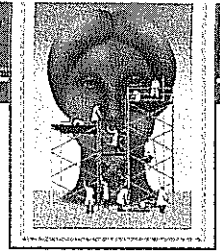
Retinoic acid effects are mediated by intranuclear retinoic acid receptors (RARs). Therefore, in addition to naturally occurring molecules like retinoic acid, synthetic molecules that activate the receptors directly or after metabolic conversion can also mediate retinoidal action. Tazarotene is a synthetic compound that upon metabolism to tazarotenic acid can bind to and activate the receptors. Therefore, it is predicted to impact photodamaged skin similarly to retinoic acid. Several clinical studies have been conducted over the years, involving more than 1,400 subjects with photoaging, which have demonstrated that tazarotene is effective in ameliorating clinical features of photodamaged skin and has a good safety profile. This lecture will provide background information on photoaging and present data from those clinical studies with tazarotene.

Clinical Update on Botulinum Toxin in Facial Aesthetics

Alan Menter, MD

Selected Slides 17-21

A brief introduction to the history, pharmacology, and action of botulinum toxin will be followed by a discussion of results from a recently conducted 1-year, two-period study of the safety and efficacy of repeated treatments of botulinum toxin type A in patients with glabellar lines.



Optimizing Aesthetic Results with Fillers and Botulinum Toxin

Selected Slides 12-24

Kenneth Arndt, MD

An overview will be presented of the various ways in which botulinum toxin type A can offer improvements in facial aesthetics, either as monotherapy or as combination therapy. Sites of injection and injection technique will be discussed.

The various type of fillers—both current and future—will also be reviewed. The areas of the face for which the adjunctive use of botulinum toxin type A may enhance the response to fillers will be outlined. Similarly, the areas of the face for which the adjunctive use of fillers may enhance the response to botulinum toxin type A will be outlined.

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