



# *Journal of* **Drugs In Dermatology**

**NEW METHODS AND TECHNIQUES**

Supplement to July/August 2004 • Volume III • Issue 4

## **CURRENT CONCEPTS IN THE MANAGEMENT OF ACNE**

EXPERT PANEL DISCUSSION ON INCIDENCE, PRESENTATION,  
AND THE STATE OF THE ART OPTIONS IN ACNE MANAGEMENT

**JDDonline.com**

**SUPPLEMENT**

ACNE • LASER • VITILIGO • MELANOMA • PSORIASIS  
• IMPLANTS • NAILS • IMMUNOMODULATORS



# Journal of Drugs In Dermatology

## EDITOR-IN-CHIEF

**PERRY ROBINS MD, NEW YORK, NY**

## MANAGING EDITOR

**DONNA M. MICARI**

## MEDICAL EDITOR

**ELIZABETH K. HALE MD**

## SENIOR EDITORS

**STEVEN R. COHEN MD, NEW YORK, NY**  
**LEONARD M. DZUBOW MD, PHILADELPHIA, PA**  
**C. WILLIAM HANKE MD, INDIANAPOLIS, IN**  
**RONALD L. MOY MD, LOS ANGELES, CA**  
**DAVID L. RAMSAY MD, NEW YORK, NY**  
**JEROME L. SHUPACK MD, NEW YORK, NY**

## ASSISTANT PUBLISHER

**ARIEL BORKOWSKY**

## EDITORIAL STAFF

**MARTHA ARROYO MD**  
**THOMAS CHIN**  
**ALYSA HERMAN MD**  
**NATHALIE NGUYEN MD**  
**FITZGERALDO A. SANCHEZ MD**

## ART DIRECTOR

**SILVAN HARNIK**

OFFICIAL PUBLICATION OF:



## ADDRESS ALL CORRESPONDENCE TO:

JOURNAL OF DRUGS IN DERMATOLOGY, 377 PARK AVENUE SOUTH, NEW YORK, NY 10016

TEL: 212-213-5434 / FAX: 212-213-5435 / EMAIL: EDITOR@DRUGSINDERMATOLOGY.COM / WWW.DRUGSINDERMATOLOGY.COM

COPYRIGHT © 2004, JOURNAL OF DRUGS IN DERMATOLOGY. PUBLISHED BY JOURNAL OF DRUGS IN DERMATOLOGY, INC.

## INTERNATIONAL EDITORIAL BOARD

### NORTH AMERICA

**REX A. AMONETTE MD, MEMPHIS, TN**  
**DIANE S. BERSON MD, NEW YORK, NY**  
**JEAN L. BOLOGNIA MD, NEW HAVEN, CT**  
**JEAN-CLAUDE BYSTRYN MD, NEW YORK, NY**  
**J. ALASTAIR CARRUTHERS MD, VANCOUVER, BC, CANADA**  
**JEAN CARRUTHERS MD, VANCOUVER, B.C., CANADA**  
**ROGER L. CEILLEY MD, DES MOINES, IA**  
**DAVID E. COHEN MD, NEW YORK, NY**  
**MELVIN P. COOLIDGE MD, FAIRFIELD, CT**  
**MADELEINE D. DUVIC MD, HOUSTON, TX**  
**LAWRENCE F. EICHENFIELD MD, SAN DIEGO, CA**  
**DAVID J. GOLDBERG MD, NEW YORK, NY**  
**LEONARD H. GOLDBERG MD, HOUSTON, TX**  
**MITCHEL P. GOLDMAN MD, SAN DIEGO, CA**  
**ADITYA K. GUPTA MD, ONTARIO, CANADA**  
**BRUCE E. KATZ, NEW YORK, NY**  
**DAVID J. LEFFELL MD, NEW HAVEN, CT**  
**RHODA S. NARINS MD, WHITE PLAINS, NY**  
**JORGE J. OCAMPO CANDIANI MD, MONTERREY, MEXICO**  
**PHILIP ORBUCH MD, NEW YORK, NY**  
**MARITZA I. PEREZ MD, DANBURY, CT**  
**ANNA C. PAVLICK MD, NEW YORK, NY**  
**NEIL S. SADICK MD, NEW YORK, NY**  
**NOAH S. SCHEINFELD MD, NEW YORK, NY**  
**ALAN R. SHALITA MD, NEW YORK, NY**  
**DANIEL MARK SIEGEL MD, STONYBROOK, NY**  
**NICHOLAS A. SOTER MD, NEW YORK, NY**  
**JAMES M. SPENCER MD, NEW YORK, NY**  
**BRUCE E. STROBER MD, PHD, NEW YORK, NY**  
**ELLA L. TOOMBS, MD, WASHINGTON, DC**  
**KEN WASHENIK MD, PHD, BEVERLY HILLS, CA**  
**ROBERT A. WEISS MD, BALTIMORE, MD**  
**W. PHILLIP WERSCHLER MD, SPOKANE, WA**  
**RONALD G. WHEELAND MD, TUCSON, AZ**  
**HERSCHEL S. ZACKHEIM MD, SAN FRANCISCO, CA**  
**JOHN ZIC MD, NASHVILLE, TN**

### SOUTH AMERICA

**CLEIRE PANIAGO MD, BRASILIA, BRAZIL**  
**FERNANDO STENGEL MD, BUENOS AIRES, ARGENTINA**

### EUROPE

**ROBERT BARAN MD, CANNES, FRANCE**  
**GUNTER BURG MD, ZURICH, SWITZERLAND**  
**FRANCISCO M. CAMACHO MD, SEVILLE, SPAIN**  
**ALEX CAMPS MD, BARCELONA, SPAIN**  
**JULIAN S. CONEJO MD, SEVILLE, SPAIN**  
**ALINA A. FRATILA MD, BONN, GERMANY**  
**JOHN HAWK MD, LONDON, ENGLAND**  
**MARTINO NEUMANN MD, ROTTERDAM, NETHERLANDS**  
**ANTONIO PICOTO MD, LISBON, PORTUGAL**  
**LUIGI RUSCIANI SCORZA MD, ROME, ITALY**  
**MIGUEL SANCHEZ VIERA MD, MADRID, SPAIN**  
**GERHARD SATTTLER MD, DARMSTADT, GERMANY**  
**ISAAC ZILINSKY MD, TEL AVIV, ISRAEL**

### ASIA

**POONG MYUNG KIM MD, SEOUL, KOREA**  
**JAI IL YOON MD, SEOUL, KOREA**

## GENERAL INFORMATION

Please direct orders for subscriptions, single copies, back issues, changes of address; and claims for missing issues to the Journal of Drugs in Dermatology, 377 Park Avenue South, New York, NY 10016. Claims for missing issues can be honored only up to 3 months for domestic addresses, 6 months for foreign addresses. Duplicate copies will not be sent to replace ones undelivered through failure to notify the Journal of change of address; please notify us of address changes at least 6 weeks in advance to ensure uninterrupted service.

**Journal of Drugs in Dermatology: New Methods and Techniques** is issued bimonthly by Journal of Drugs in Dermatology, Inc., 330 E. 38th St., Suite 41-N, New York, NY 10016. Printed in the USA by Cadmus Science Press, 300 W. Chestnut St., Ephrata, PA 17522.

Yearly subscription prices: US: Individual \$150, Institutional \$300; International: Individual \$200, Institutional \$350. Single issue: \$35. Prices include postage and are subject to change without notice. All subscriptions are entered on a calendar-year basis beginning in January and expiring the following December. Orders received midyear will be charged based on the prorated number of issues left to be mailed for the year; payments received above this amount will be credited towards a future subscription. Any inquiry relating to subscription should be sent to: Journal Subscription Dept. 307 Fifth Avenue., Suite 1505, New York, NY 10016 USA. Postage paid at Ephrata, PA and at additional mailing offices. POSTMASTER: Send address changes to Journal of Drugs in Dermatology, 307 Fifth Avenue, Suite 1505, New York, NY 10016.

## REPRINTS

Reprints are available for purchase from the Journal. For information or to place an order, please contact the Journal Editorial office at (212) 213-5434.

## PERMISSION

Permission for reprinting, re-issuing, copying, or otherwise re-using the intellectual property protected herein may be granted solely upon the express written consent of the Journal of Drugs in Dermatology. Please contact Ariel Borkowsky, 377 Park Avenue South, New York, NY 10016. Tel: (212) 213-5434.

## PUBLISHER'S OFFICE:

Journal of Drugs in Dermatology, Publisher's Office, 530 1st Avenue, New York University Medical Center, Suite 7-H, New York, NY 10016. Tel: (212) 686-4663; Fax: (212) 686-5842.

## INSTRUCTIONS TO AUTHORS

Instructions to Authors will be located in each issue and online at [www.drugsindermatology.com](http://www.drugsindermatology.com).

## ADVERTISING

Advertising inquiries should be addressed to Ariel Borkowsky, Journal of Drugs in Dermatology, 377 Park Avenue South, New York, NY 10016. Tel: (212) 213-5434, Fax (212) 213-5435.

The publisher and the organizations appearing herein assume no responsibility for any injury and/or damage to persons or property as a matter of product liability, negligence, or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein. No suggested test or procedure should be carried out unless, in the reader's judgment, its risk is justified. Because of the rapid advances in the medical sciences, we recommend that independent verification of diagnoses and drug dosages should be made. Discussions, views, and recommendations as to medical procedures, choice of drugs, and drug dosages are the responsibility of the authors. Statements and opinions expressed in the articles and communications herein are those of the author(s) and not necessarily those of the Editor, Publisher, or staff. The Editor, Publisher, and staff disclaim any responsibility for such material and do not guarantee, warrant, or endorse any product or service advertised in this publication nor do they guarantee any claim made by the manufacturer of such product or service.

Although all advertising material is expected to conform to ethical and medical standards, inclusion in this publication does not constitute a guarantee or endorsement by the Journal or its staff of the quality or value of such products or of the claims of any manufacturer.

The paper used in this publication meets the minimum requirements of the American National Standard for Information Sciences Permanence of Paper for Printed Library Materials, ANSI Z39.48-1992

© 2004 Journal of Drugs in Dermatology  
Published by Journal of Drugs in Dermatology, Inc.



# CURRENT CONCEPTS IN THE MANAGEMENT OF ACNE

## TABLE OF CONTENTS:

### DEFINING CHARACTERISTICS OF ACNE

Incidence	S-5
Clinical Features	S-5
Presentations at Different Stages	S-7
Influences	S-9

JDDonline.com

### TREATMENT

Skin Care	S-11
Topical Retinoids	S-13
Combination Treatments	S-15
Oral Antibiotics	S-16
Hormones	S-18
Office-Based Procedures	S-19
Laser Treatment	S-20
Concluding Remarks	S-20

THIS SUPPLEMENT TO THE JOURNAL OF DRUGS IN DERMATOLOGY IS BASED ON A SYMPOSIUM SUPPORTED BY AN EDUCATIONAL GRANT PROVIDED BY DERMIK LABORATORIES THAT TOOK PLACE IN NEW YORK CITY IN NOVEMBER 2003. IN THE FOLLOWING PAGES, SIX DISTINGUISHED DERMATOLOGISTS DISCUSS ACNE: ITS INCIDENCE, PRESENTATION, AND THE STATE OF THE ART OPTIONS IN ACNE MANAGEMENT.

**MODERATOR:****PERRY ROBINS, MD**

Professor of Dermatology, New York University Medical Center.  
New York, New York.

---

**FACULTY:****DIANE BERSON, MD**

Assistant Professor of Dermatology, Weill Medical College,  
Cornell University; New York, New York

**RENA BRAND, MD**

Clinical Associate Professor, New York University Medical Center;  
New York, New York

**ALAN SHALITA, MD**

Professor and Chairman, Department of Dermatology,  
SUNY Downstate Medical Center; New York, New York

**JEROME SHUPACK, MD**

Professor of Dermatology, New York University School of Medicine;  
New York, New York

**KATHERINE WHITE, MD**

Private Practice; New York, New York



## DEFINING CHARACTERISTICS OF ACNE

### *Incidence*

**Dr. Robins:** Approximately 17 million people in the United States currently have acne. Therefore, it constitutes a large part of the dermatologist's daily office visits.

**Dr. White:** Traditionally, people consider acne a teenage condition, but it has become increasingly evident that it also affects the adult population significantly. We have to take that into account and vary treatment accordingly.

**Dr. Berson:** Yes, although most think of it as a disease of adolescence, acne can occur at all different stages of life. Incidence may not actually be increasing among adults—it could just be that adults are coming to us more for acne treatment because they now realize it is an option for them.

**Dr. Robins:** Who are the youngest patients we see with acne?

**Dr. Shalita:** Newborns. Both neonatal acne and infantile acne exist, but they both have a different presentation than the acne we're discussing. The acne we're talking about today begins in preadolescents. We've seen it in children as young as 6 years old. It can start a lot earlier than people imagine.

**Dr. White:** Little girls as young as 8 or 9 years old come into my private office with their first few inflammatory papules or comedones, and they want treatment.

**Dr. Robins:** Should we consider acne in a 9-year-old a disease state? Is it a signal for further endocrinologic evaluation, or part of the normal developmental spectrum?

**Dr. Brand:** I would consider it part of the normal spectrum of early onset, unless the acne is unusually severe.

**Dr. White:** It's worth examining a child who presents with early onset acne for other signs of early sexual maturity, say, breast or pubic hair development. You consider the body habitus of the patient. Often, these children tend to be on the heavier side, or there may be a family history of early menarche, and these factors may play a part in premature acne.

**Dr. Berson:** It can just be part of normal development. I know plenty of young girls with comedones on the forehead and nose at that age who are maturing in a normal manner. It's part of normal maturation.

**Dr. Robins:** Has anyone ever seen an 8- or 9-year-old male acne patient?

**Dr. White:** Yes, although it's more unusual.

### *Clinical Features*

**Dr. Robins:** What are the observable clinical features of acne?

**Dr. Shalita:** As Dr. Bernard Ackerman would say, "Zits and Goobers," which was the title of Dr. Ackerman's book for children. Actually, you can divide acne arbitrarily into noninflammatory vs. inflammatory types, but most patients have a combination of the two. It is rare to see one kind of lesion exclusively in a patient. The noninflammatory lesions are open or closed comedones such as blackheads or whiteheads. The most important noninflammatory lesion, however, is not visi-

ble on the skin surface; that's the precursor lesion, a micro-comedo that can be seen histologically.

The inflammatory lesions include papules, pustules (which are really mature papules), and nodules, which have been referred to erroneously over the years as cysts; we've tried to change that terminology. The most severe forms of acne can lead to a coalescence of lesions, where you get acne conglobata. But even in the absence of acne conglobata, you can get merging lesions that form sinus tracts because of re-epithelial-

ization after chronic inflammation, which can create a serious therapeutic problem.

In terms of overall clinical manifestations, everyone has his or her own classification of acne. We came out with a definition at a consensus conference of the American Academy of Dermatology (AAD) a number of years ago, but I don't know if that definition is necessarily better than any others. I tend to refer to acne as mild, moderate, and severe, or sometimes moderately severe. Then I describe the predominant lesions: comedonal, comedo papular, papularo-pustular, and so on.

**Dr. Berson:** I look at it the same way.

**Dr. Robins:** What are the pathogenic factors?

**Dr. Berson:** We describe the four pathogenic factors: increased keratinization, increased sebum production, growth of the bacteria *Propionibacterium acnes*, and, finally, the development of inflammation. Usually, you see the first two occur during hormonal stimulation at about the time of menarche or puberty, when hormonal stimulation of the sebaceous glands accelerates, producing more sebum. Also, if you look at a histopathology of the follicle wall, you see that the wall thickens at around the time of hormonal stimulation, and keratinization increases.

**Dr. Shalita:** I don't know if I would call it "increased keratinization."

**Dr. Berson:** The follicle wall thickens.

**Dr. Shalita:** The desquamation is off. It's that the cells are turning over more rapidly. They are being shed more rapidly into the follicular lumen and then sticking together. Precisely what changes are occurring in those cells that make them stick together is still being investigated.

**Dr. Berson:** The combination of the follicle being blocked and becoming narrower, and the increase in sebum production into the follicle, leads to the development of the microcomedo precursor lesion that Dr. Shalita discussed. Generally, in the pathogenesis of acne, we think of that lesion becoming gradually larger and larger and then essentially rupturing. This occurs because the anaerobic environment within that follicle is an ideal medium in which *P. acnes* can grow. The lesion gets bigger and bigger and ruptures. We then see the development of inflammation within the dermis surrounding the follicle, the release of inflammatory mediators, and the development of the inflammatory cascade, leading to an increase in inflammatory acne.

**Dr. Shupack:** We should say more about the role of inflammation. In the modern era, we know that inflammatory response depends on a whole nexus of factors. We know that inflammation is a function of the immune system and the world of cytokines, which can induce inflammation, and we know that keratinocytes are rich in cytokines. We also know that stress can influence immunologic response. So having a bacterial antigen is one thing, and having an inflammatory response to the bacteria is something else; there are people who at any given point in their lives may be hyper-responsive to the antigenic stimulus. People go through cycles of being minimally inflammatory or maximally inflammatory, and that aspect of acne has to be expanded on conceptually to reflect what is going on in modern immunology.

**Dr. Shalita:** We've been working on it. First, there are the proinflammatory cytokines released by *P. acnes*. In addition, as you've said, there are other factors. There are interleukins released, toll-like receptors that also play an important role, and a whole immunological response from both T-cells and immunoglobulins. I'm not sure that the human antibody response is very important in acne, because it's directly related to the severity of the disease, which means that the more *P. acnes* that get into the bloodstream, the higher their antibody level is. Then, when the acne is treated and the patient gets better, the immunoglobulin level goes down. So, that is probably a reactive state and not a pathogenic state. Interestingly, patients with really severe acne have depressed cellular immunity. But you also see that in chronic granulomatous disease of childhood and in rheumatoid arthritis; anything involving really bad chronic inflammation alters immune state.

**Dr. Shupack:** But it isn't a one-to-one translation. HIV patients are immunosuppressed, yet their psoriasis, which presumably is based on immunologic response, is aggravated.

**Dr. Shalita:** There are local differences.

---

*The inflammatory response depends on a whole nexus of factors.*

—Dr. Shupack

---

## ***Presentations at Different Stages***

**Dr. Berson:** Acne has a different clinical presentation in adolescents than in adults, but it isn't cut and dried.

**Dr. Brand:** Very often the first clinical presentations are comedones on the forehead and around the nose area. Those are often what bring people in for treatment initially. When you really start looking at the individual lesions involved in acne, they usually have a mixed presentation. But the earliest acne is seen primarily around the forehead and nose. As women get into their 20's and you start seeing their adult acne pattern, you also see different localization. You see a more perioral and jawline distribution than in a younger adolescent.

**Dr. Shalita:** I'm glad you mentioned that. There is a head-to-toe migration of the disease, commonly starting at the forehead and for some reason around the nose and chin. That also creates special therapeutic problems because the neck is a very sensitive area.

**Dr. Shupack:** Dermatologists traditionally think in terms of primary lesions, and everyone seems to accept the comedo as a primary lesion of acne. However, if we are talking about the onset of adolescent acne, probably the first pathogenesis has to do with hormones as opposed to all the other dimensions that come into play once the comedo is formed.

**Dr. Shalita:** Right. The first event that probably occurs in individual follicles is an alteration in the amount of sebum produced. That in turn can alter follicular epithelial differentiation, which starts the formation of the microcomedo. There is also probably an androgen response by the cells in the lining of the follicle. So it's a two-pronged pathogenic event (with both factors related to androgenic hormones), which leads to the microcomedo. Then everything else follows suit, producing an environment in which *P. acnes* can proliferate. But you can also get comedones without any *P. acnes* occurring in a follicle. Bob Lauker PhD, from Northwestern University, showed that a long time ago.

**Dr. Robins:** Do you see adolescent acne sooner in boys or girls?

**Dr. Berson:** We usually see it sooner in girls, because they go through puberty a little earlier and seek medical treatment earlier. They mature more rapidly.

**Dr. Robins:** Skin cancer is more common in men than women. Is acne more common in young women than young men?

**Dr. Shalita:** To know that, you would have to do a random sample of the population. Dr. Marie-Louise Johnson of New York University did such a sample. She covered ages 12 to 25, and found that something like 80 to 85 percent of that population had acne, if you defined having acne as having at least one blackhead. However, I don't remember the statistical difference between the sexes. We see more adult women than men coming into the office for acne, but that doesn't necessarily mean that women have more acne than men. Even though men are a lot more cosmetically conscious today than they were 20 years ago, they don't tend to come in with acne unless it's really stubborn, chronic, and severe.

**Dr. Brand:** There is a subgroup of adult female patients who have such a struggle with cyclical breakouts related to the menstrual cycle. Because the pattern becomes almost predictable for many women, it brings them in for care.

**Dr. White:** I consider acne as potentially becoming more severe in men. They tend to get more of the inflammatory nodular cystic acne. However, they also respond better long-term. Often, when you treat a male adolescent acne patient, once he clears up it doesn't become a problem for him again, whereas women tend to have persistent, low-grade, chronic acne where they get a few breakouts cyclically. It's not severe, but to the woman it's severe enough.

In the adult population, when men come in, they often have severe acne on the trunk, back, and chest, as opposed to facial involvement. In women, you'll see much more perioral, jawline, and neck acne, and some on the back, but not as severe as in the men.

---

*Men tend to get more inflammatory nodular cystic acne.*

—Dr. White

---

**Dr. Berson:** Not as severe but more chronic.

**Dr. Shupack:** Dr. Shalita, when you alluded to the Marie-Louise Johnson studies earlier you used the phrase, "depending on what you define as acne." Can we assume that all humans during adolescence form microcomedones?

**Dr. Shalita:** No, that was studied by Dr. Ronald Marks in England or at the University of Pennsylvania, and I believe follicular biopsies showed that some people don't have any.

**Dr. Shupack:** But they are probably the minority.



**Dr. Shalita:** Absolutely.

**Dr. Shupack:** So they are abnormal.

**Dr. Shalita:** Yes.

**Dr. Shupack:** Acne is a normal physiologic process that occurs to a greater or lesser degree in different individuals, but when it becomes a physical or psychological burden, we say it's a disease state. It's an exaggeration of a normal combination of things including follicular structure, sebum production, genetics, and immune response or inflammatory response at the moment.

**Dr. Shalita:** It's like with flushing and rosacea; in this country, we define flushing as a characteristic of rosacea. In Ireland, however, everybody has flushing, so it's normal; it's not considered part of rosacea.

**Dr. Berson:** You also have to make a distinction between non-inflammatory and inflammatory acne; when you start developing such inflammatory lesions that you have scarring, it stops being "normal."

**Dr. Robins:** About what age are the oldest patients we treat for acne?

**Dr. Berson:** There is postmenopausal acne. Any kind of a hormonal change can stimulate acne.

**Dr. Robins:** How about in men? Men go through a kind of menopause, too. Do men of "postmenopausal" age develop acne?

**Dr. Shupack:** Definitely not.

**Dr. Robins:** Are there also geographic and ethnic differences in acne? Do we see more in the South, less in the North? Do we see it in Eskimos? Do Eurasians have fewer sweat glands? Do they have less acne? Actually, I've seen a lot of Asians with acne.

**Dr. Shalita:** There are certainly a lot of Asians with acne, both here and in the Orient. However, there are two islands, one in the South Pacific and the other in the South Atlantic, where virtually no one gets acne. In these particularly isolated populations, this phenomenon could well be the result of genetic factors. However, an article published last year in the *Archives of Dermatology* claimed that it was due to an almost total absence of carbohydrates in the diet. Perhaps we should put everybody on the Atkins diet and see if acne disappears.

**Dr. White:** We could do that for inflammation, too.

**Dr. Berson:** The islands you describe have a limited population, so the influence of genetics could be strong. So could stress or the lack thereof.

**Dr. Robins:** What about geographic influence? Is there more acne in the North or more in the South?

**Dr. Berson:** I don't know if anyone has studied that.

**Dr. Robins:** There is more skin cancer in the South.

**Dr. White:** That's because it's closer to the equator, and sun exposure is more intense.

**Dr. Robins:** Does proximity to the equator affect acne as well?

**Dr. Shalita:** I don't know if it makes any difference in acne.

**Dr. Shupack:** This could be considered stereotyping, but there are groups of people who seem to naturally produce more oil than others. Some might say it is related to latitude, but what if, say, different members of an ethnic group are not living at the same latitude? Mediterranean types, for example, often are found to have oilier complexions in their youth than other groups. This would suggest the influence of genetics rather than latitude.

**Dr. Robins:** What about African-Americans?

**Dr. Shalita:** They get acne.

**Dr. Shupack:** Absolutely.

**Dr. Robins:** As much as or less than Caucasians? Or is there no difference?

**Dr. Shupack:** I don't think there's any difference.

**Dr. Brand:** One difference in the acne presentation is the significant post-inflammatory hyperpigmentation that can develop in darker-skinned patients.

**Dr. White:** That's problematic.

**Dr. Shalita:** It's also a major problem for Asians and people of the Indian subcontinent.

**Dr. Robins:** What about pollution? Is there any difference in acne levels in areas where the air is polluted?

**Dr. Shalita:** Not except for toxic conditions such as chloracne. There was a major outbreak of chloracne after an explosion in a factory in Turkey. Other than that, I'm not aware of any effects of pollution.

**Dr. Brand:** Often, people who have recently moved to New York say that their acne gets worse. They relate this to stress and environmental changes.

**Dr. White:** Definitely.

**Dr. Brand:** But patients have many misconceptions regarding the cause of acne.

**Dr. Shalita:** In the late 1960s or early 70s when Dr. Shupack and I were residents, there was a whole migration here of young colleens who had peaches-and-cream complexions when they were home in Ireland. Perhaps stress was a big factor, but once they were living in an urban society in New York, working as waitresses and barkeeps and the like, they all started getting acne. However, acne is common in Dublin too.

**Dr. Robins:** Have there been any studies showing that certain countries have more or less acne than others?

**Dr. Shalita:** Not that I'm aware of.

**Dr. White:** I think the differences would arise in the amount of treatment that patients seek and receive.

## Influences

**Dr. Robins:** We should say more about the influence of various factors on acne.

**Dr. Shalita:** We've already touched on stress, hormones, and genetics.

**Dr. Robins:** Let's review them in detail.

**Dr. Berson:** For starters, family history plays a part. If either or both of your parents have had acne, there is a good chance that you will get it. Hormones play a part in the initiation of acne at around the time of adolescence. Moreover, in women predisposed to acne, hormonal factors can definitely influence breakouts at around the time of their menstrual cycle. We can also see flares during perimenopause and menopause.

Women's acne can either flare or improve markedly when they become pregnant, and can improve for many who take the birth control pill. Conversely, we often see women develop a bit more acne after they go off the birth control pill.

**Dr. White:** Usually the flares occur right before menses or with ovulation.

**Dr. Robins:** We haven't talked about medications and diet. There are a lot of fairy tales about diet.

**Dr. Berson:** When someone comes in with new onset acne, if it's a sudden development, there are certain medications that can cause eruptions.

**Dr. Brand:** Steroids, for example.

**Dr. Robins:** Which ones?

**Dr. Brand:** All steroids can exacerbate acne. You tend to see monomorphic inflammatory acne on the chest.

**Dr. Berson:** Some antidepressants can also cause eruptions, as can lithium.

**Dr. Shupack:** Even some of the newer nonsteroidal topical medicines can cause problems. I'd like to back up a second and talk about stress. We all agree that stress makes acne worse, but we went right into hormonal fluctuations without touching on it. Clearly, stress can affect hormonal status, but is that the primary, direct way in which it aggravates acne? I believe it also has an effect on one's immunologic/inflammatory responsiveness through neuroendocrine pathways. It works through that route, in addition to its effects on endogenous corticosteroids and the like.

**Dr. White:** It's multifactorial.

**Dr. Shalita:** But there's no ethical way to investigate that, unless perhaps you were to study the internal reactions of students before and during examinations—their physiologic responses under normal conditions and under conditions of high stress.

**Dr. White:** There was a study of college kids which found that their acne flared when they took exams.

**Dr. Shupack:** But the question is, were they having flares because of stress or did the stress make them wash less often to clean away their *P. acnes*?

**Dr. Shalita:** If you are talking about neuroendocrine transmission, you can measure certain factors in the blood.

**Dr. White:** I simplify it for patients it by saying how stress works and telling them that their adrenal gland, for example, is releasing adrenaline. I explain that along with the adrenaline, the gland releases androgenic hormones that can stimulate acne. I don't think it's that simple, but it's a way to explain things to patients.

**Dr. Shalita:** The hormones don't really work that fast.

**Dr. White:** Exactly. There's a lot more going on with stress that we just don't know about with certainty. When we talk about its impact on psoriasis and eczema and acne, there are all these pathways that we just don't understand yet.

**Dr. Shalita:** But there's a whole list of medications we *do* know about that affect acne. We mentioned lithium and steroids. There are also halogenated hydrocarbons.

As for diet, only a few things have been identified as possible causative factors, and they're questionable. Years ago there was a myth about chocolate and peanuts, as well as some other things. Chocolate was studied at the University of Pennsylvania, where they looked at what was then the \$500 Hershey bar, the big pound bar. They gave it to patients who thought their acne was aggravated by chocolate, and they gave others carob, an imitation chocolate, as a control. No difference was found between the two.

The late Dr. Phil Anderson, of the University of Missouri, studied the effect of several dietary factors on acne. He looked at cheese, milk, and several other foods, and there was no aggravating factor. The only other conceivably related thing I've heard about is peanuts; a colleague told me that certain strains of peanuts have androgen in them. In addition, a study published in the *Archives of Dermatology* described a group of people who have no carbohydrates in their diet and don't get acne.

Back when Weight Watchers had just begun, it included a lot of salt-water fish in its recommended diet, and we saw people breaking out while they were on it. There was a lot of iodine in that diet, and there's been some debate as to whether or not the iodine actually induced acne. In any event, it's hard for anybody to be on a diet exclusively of shellfish because it's so expensive.

**Dr. Shupack:** Iodine sensitivity is known to manifest itself in many different ways. Some people have truly severe allergic reactions, but there are also in-between groups, such as a group that developed acrodermatitis. It's not too much of a jump to conceive of a subpopulation of people who have iodine sensitivity. If we've thought about dietary factors at all, I think we've all on rare occasions seen people whose acne seems to be aggravated by iodine. Interestingly, the foods that are high in iodine are the same ones we've often warned people about: shellfish, kelp, and certain mineral supplements. True iodine sensitivity may occur in only one of a thousand cases, but I think it's true in some.

**Dr. Brand:** I think so as well.

**Dr. Shalita:** Yes, in certain subsets of the population.

**Dr. Brand:** Of all the myths and popular beliefs about acne that I've encountered in the clinical setting, the cleanliness myth and the link to diet are the two most persistent ones.

**Dr. Shalita:** That's very important. Dr. James Leyden at the University of Pennsylvania has clearly demonstrated that excessive washing and scrubbing can actually exacerbate acne.

**Dr. Shupack:** Is the reverse true as well? Can under-washing exacerbate acne? By leaving more sebum and allowing *P. acnes* to proliferate and multiply, can it produce an immune inflammatory response?

**Dr. Shalita:** No.

**Dr. Shupack:** What you want is the happy mean. You should wash enough but not too much.

**Dr. Shalita:** The point is that acne is not a disease of dirt. You just look dirty because you have a lot of blackheads on your face.

**Dr. Brand:** Nor is it a disease of diet, although some individuals may have a food sensitivity that aggravates acne.

**Dr. Shalita:** My sister insists she breaks out from chocolate, so I tell her not to eat it.

**Dr. Berson:** There's a whole philosophy now about inflammation and carbohydrates. One of our colleagues has publicized a regimen involving diet, medications, vitamins, and anti-inflammatory agents. He first talked about it with respect to photodamage, and now he's written a book about it as a therapy for acne. His philosophy is that acne is induced by inflammation, not by all the other factors that are traditionally considered to be influential. Patients who have read the book believe in it, and they're convinced that if they eat a low-carbohydrate diet, their acne will improve.

**Dr. Shalita:** They may be right.

**Dr. Berson:** When you talk about inflammation and how it relates to carbohydrates and carbohydrate metabolism, the question is, will an Atkins type of diet improve someone's acne? A layperson asked me this at a conference, and she swore that when she eliminated carbohydrates from her diet, her acne improved. My feeling is that perhaps she lost weight and looked better and thus had less stress. There are a lot of factors involved, but we really don't know the answer.

**Dr. Shupack:** There's another component involved as well. If you believe something long enough and strong enough, it happens.

**Dr. Shalita:** The power of positive thinking.

**Dr. Brand:** The mind is always an important part of healing. Patients receive multiple benefits from meditation and other stress-reduction activities. A healthy diet is also a good recommendation for everyone.

**Dr. Shalita:** On average, we get 35 percent improvement with acne patients using this vehicle alone. Every time we do an acne study, the control group's improvement rate is so high that the treatment group has to have better than 35-40 percent improvement to be considered successful.

**Dr. Shupack:** For one thing, just being part of a study removes a lot of stress. They feel that the responsibility for their condition is out of their hands.

**Dr. Shalita:** I'd feel the opposite: Not knowing whether I'm getting the real drug or not would make me worried.

**Dr. Shupack:** Maybe the patient improves and the investigator breaks out because of stress.

**Dr. Berson:** Another related topic is attracting a lot of attention in the lay media: omega-3 fatty acids, such as eicosapentaenoic and docosahexaenoic acid.

**Dr. Shalita:** Also alpha-lipoic acid.

**Dr. Berson:** Patients are coming in and saying that they are eating meat, and their acne is getting better.

## TREATMENT

### Skin Care

**Dr. Shupack:** The treatment of acne starts with skin care.

**Dr. White:** And proper cleansing could be considered the most basic step in skin care. You wash gently, with no vigorous scrubbing.

**Dr. Berson:** It is an important part of treatment. I use different cleansing modalities depending on the patient.

**Dr. Brand:** Before I start giving prescriptions, I discuss skin care, and I tailor the cleansing modality and the way I start treatment based on what the acne looks like. For example, if it's a teenager with a significant inflammatory condition, I might add a gentle benzoyl peroxide (BP) cleanser. If it's a patient with a lot more comedonal presentation, I may go with a gentle glycolic acid, alpha-hydroxyl acid cleanser.

**Dr. Shupack:** But what if the patient says, "Doctor, I have combination skin. Do I use one cleanser in the middle of my face and another on my cheek?"

**Dr. Brand:** I just determine which the predominant presentation is and go with that.

**Dr. Shupack:** You can also tell the patient, "That's why I'm giving you a combination of products."

**Dr. Brand:** It's important to find out what patients are already doing for treatment by the time they come to your office. Many people use harsh abrasive scrubs and/or very drying astringents, and it's important to inform them that they need something non-drying and gentle. They need to learn that less is often more.

If you have patients with very oily skin, they are clearly going to need a different kind of cleanser to begin with than someone whose skin is on the dry side. You especially need to advise people that since all acne medications are potentially

drying and irritating, you don't want to exceed their tolerance with a cleanser that's too harsh.

**Dr. Shalita:** Exactly. If you are going to put somebody on a retinoid and a leave-on product containing BP, you really want to use a very gentle cleanser.

**Dr. Brand:** If they get too irritated, they won't use their acne medicines. You want to make sure they are in compliance with the medication, so give them a gentle, mild cleanser.

**Dr. Shalita:** I am not the least bit opposed to using emollients. There are a wide variety of emollients available today.

**Dr. Shupack:** But don't they clog the pores?

**Dr. Shalita:** There are wide varieties that are noncomedogenic and, even more important, nonacnegenic – there's a difference between the two. All you have to do is look at the animal model to see that it is nonacnegenic and noncomedogenic. Not everybody does that, because they don't use the animal models anymore. I believe they use cell models. In any event, there are plenty of those products. If you are using a topical retinoid, it will overcome the mild comedogenic effects of anything else that you are putting on, so unless you are using something potent like coal tar, you are not going to have a problem. This is very important because it enhances patient compliance.

**Dr. Brand:** As you say, it's important to emphasize to people that they can use a moisturizer if they need to. And they should probably include some sunscreen in the moisturizer as well if they are using a topical retinoid.

---

*Before I  
start giving  
prescriptions,  
I discuss  
skin care.*

---

—Dr. Brand



Another point that comes up is hair care products. If people use products that are greasier and then don't wash their hands before putting on makeup, it can aggravate their acne. When making recommendations about particular cosmetics, it's important to educate people about what the terminology means, and then to point them in the right direction. Most large, reputable cosmetic brands are generally well tolerated; users should look for the words 'oil-free,' 'noncomedogenic,' and 'nonacnegenic'.

**Dr. Berson:** I agree with that, as long as you are using a non-comedogenic, nonacnegenic product. When I see the occasional patient who has a hairline exacerbation with a shampoo product, I usually recommend that he or she use a standard shampoo that doesn't include conditioner, and then add the conditioner separately to the area away from the face and not on the hairline. That usually solves the problem.

**Dr. White:** I agree that gentle cleansing and mild cleansers are advisable when you are giving the patient drying medications. But I find that early adolescents like and do well with liquid cleansers containing salicylic acid. Even in the hot summer months, they can use a toner or astringent with salicylic acid, perhaps on their oilier areas. I find that if they can tolerate it along with their medications that may be a helpful adjunct also.

**Dr. Berson:** I also like products that have a mild glycolic acid. It's the same idea but a different modality.

**Dr. Shupack:** Do we really need special cleansing products when potent therapeutic products such as BenzaClin® are available? Why bother with all of the rest?

**Dr. Shalita:** In point of fact, if I have somebody who is on a topical retinoid and a BP combination product, I have him or her use the gentlest cleanser they can use; I don't use any special products.

**Dr. Shupack:** Things like pore-minimizing lotion are a big waste.

**Dr. Shalita:** Those are really marketed for people who have 'acne-prone' skin. For example, a woman is getting one pimple on her chin premenstrually every month as well as an occasional blackhead. So, she goes to some salon periodically to get a facial cleansing, and the laying on of hands makes her feel better. They may use one of the exfoliating lotions that contain a

mild salicylic acid or glycolic acid in it to loosen up the acne, even though the patient is not undergoing active treatment. Then there are a variety of other products for the acne-prone. You may be using only one simple product and want to complement it with a stronger one. For example, there are patients who can't tolerate a topical retinoid and a leave-on BP product, although more and more can tolerate it with the aqueous formulation. For them, I'll possibly use a BP cleanser, so they're still getting the benefit of the benzoyl peroxide, and some of the newer BP cleansers have enough substantivity so that the antibacterial activity lasts overnight. Now, that's not my first-line therapy; it's for somebody who's not tolerating my preferential therapy, which is the leave-on product.

**Dr. Shupack:** Now, what about consumer patients who have been so indoctrinated by magazine reading that they absolutely refuse to give up using a line of products that has been sold to them for \$500? Do you try to reeducate them, or do you just shrug your shoulders and say my treatment is more powerful than all of the above, and let them do whatever they want?

**Dr. Shalita:** I let them do whatever they want. I give them the information I think they should have, and try to educate them, and if they're still going to do what they want to do, fine. However, if they're running into a problem with it or it's going to conflict with whatever I'm recommending, I'll tell them, "Look, you have a choice. You can follow the regimen I give you, which I believe will help, or you can choose not to follow it. All I can do is advise you how to take care of your problem. The rest is up to you."

**Dr. White:** By the time they arrive in my office, they have tried the usual over-the-counter products, the ones they've seen advertised on TV.

**Dr. Shupack:** Or they've been to other dermatologists or GPs.

**Dr. White:** That, too. So, with whatever product or treatment or line of cosmetics that they've been using, they still have acne when they come to my office.

## Topical Retinoids

**Dr. Berson:** I think we all try to incorporate a topical retinoid in our regimen whether the patient has predominantly comedonal acne or inflammatory acne. We were all originally taught that retinoids are comedolytic and can decrease comedonal formation—that they ultimately decrease the development of inflammatory lesions by decreasing precursor lesions. But we now know that retinoids are anti-inflammatory as well. So they can be used as a first-line agent for all types of acne lesions.

You can usually use topical retinoids as a monotherapy for acne, but because most patients have a combination of lesions, we tend to use combination regimens with most. Most of us tend to use a topical retinoid in conjunction with a topical antimicrobial agent.

**Dr. Shalita:** I don't think there's one topical retinoid for everybody. I think it's a distinct advantage to us in the United States that we have such a good selection of retinoids. We don't have topical Isotrex® (isotretinoin), though it's available to the rest of the world, but it's a real advantage to have as large a choice as we do. You can tailor the regimen to the individual patient. Interestingly, topical retinoids are used much less in Europe than in the United States, and the industry has undertaken a major campaign to educate the Europeans. That's really the rationale behind the algorithm that came out in the *Journal of the American Academy of Dermatology (JAAD)* a couple of months ago.

**Dr. Shupack:** Could you be a little more specific? You've mentioned the many choices of topical retinoids. Predominantly, there's tretinoin (all-trans-retinoic acid).

**Dr. Shalita:** And adapalene and tazarotene. Those are the three that we have.

**Dr. Shupack:** You say that there's not one retinoid treatment for all, and I'm sure we've all found that one will work better than another at various times, but is there a way you can pre-select which one you are going to start with?

**Dr. Shalita:** For me it's a lot easier, because virtually every acne patient I see has been somewhere else, so I already have a history. I know if they have sensitive skin or not, and I know what they've used. I saw a patient yesterday who was not getting significant improvement with one topical retinoid, in his case tazarotene. He was using the gel, and it was too irritating, so he wasn't using it all the time. However, he has a lot of really tough comedones, so I know he needs the comedolytic activity of a potent retinoid. I suggested that he use tretinoin solution. I told him, this is liquid fire, but you'll start by using it only once

a week, and then we'll gradually build up frequency. The same thing could have been done with the tazarotene, but sometimes that burns. Most patients that I use topical tazarotene on don't complain; they notice the burning, but it's tolerable, and then it goes away. However, you know that some are going to moan and groan. I think the easiest topical retinoids to use for first-line therapy are adapalene cream or tretinoin in microsphere in the low 0.04% concentration. And then, depending on what the therapeutic success is, I may work my way up to different concentrations and vehicles. I think that the most potent topical retinoid treatments are the higher concentrations of tretinoin and tazarotene.

**Dr. White:** Patient education is so critical, especially if you are using topical retinoids that may be perceived as more potent. Many patients have had unhappy experiences as teenagers, usually a long time ago, with a topical retinoid; I spend a lot of time educating them about how to make the treatment more tolerable. There is a big difference if you start with every-other-night applications. It also helps to have patients wait 20 minutes after washing before applying the topical retinoid. It's helpful to give patients the tools to be able to assess their own skin. Then, for example, if they feel they are getting too dry and irritated they can skip treatment for a night. And it's important to tell them that it's going to take time.

**Dr. Shalita:** The biggest problem in acne therapy compliance is the dermatologist, not the patient. Unfortunately, too many patients have gone through dermatologists' offices and have not been educated. They haven't been told enough information or been given something to take home to read, before being sent home with a bag full of medication.

I think some doctors have what I call clinic-like practices, which process too many patients too fast. At least at the first visit, it is critically important to take your time and explain things to patients. I think Dr. White described this beautifully. That's exactly what you need to do.

**Dr. White:** You also have to spell out the exact doses for them. If you simply tell them that a pea-sized amount of cream is enough for the whole face, people instinctively feel they don't have enough coverage. If they do apply a retinoid to the degree that they feel they have coverage, it's probably way too much. You need to take time to tell them exact amounts.

Also, we usually start with a cream, and then graduate up to a gel; we seem to do well with that regimen.

**Dr. Shupack:** I was going to ask about that. We know that retinoids are a class of drug, and that they are available in dif-

ferent vehicles, including creams, gels, and solutions. They are also available in at least three distinct molecular forms: tretinoin, adapalene, and tazarotene. It would be useful to formulate some order based on irritancy potential, ranking them by vehicle and by molecular form. Which is the most irritating vehicle, and is there any difference among the three molecules? There's no question that if you put tazarotene into a gel, it can be more irritating than something like the Retin-A® microsphere. But what's the order of irritancy, starting with the three molecules?

**Dr. Berson:** As a clinician, I think we all basically accept that adapalene is the mildest and most easily tolerated, certainly in the cream formulation. Adapalene cream is probably at one end of the spectrum and tazarotene gel at the other.

**Dr. Shupack:** How do they stack up against the little wipes, which are basically a solution?

**Dr. Brand:** The various creams are the gentlest in the spectrum. Tazarotene gel and tretinoin liquid would be at the other end. And in between, after adapalene, you would have tretinoin in the Micro 0.004% gel, then tretinoin 0.025% cream. That's basically the spectrum you follow, but it is not a firm and fixed rule. There are patients who find adapalene very irritating but do very well with tazarotene. It can be something else in the formulation that causes the irritation. But that basic spectrum is probably the general rule of thumb.

**Dr. Shupack:** Something we all have to worry about these days is drug plan insurance. All three molecules are approved as a treatment for acne, but insurance companies cast a suspicious eye if the patient is over 26, requiring prior authorization.

**Dr. Shalita:** Over 18 with some plans.

**Dr. Shupack:** So aren't you better off in that regard prescribing tazarotene, since it's approved for treatment of psoriasis and not questioned based on age?

**Dr. Shalita:** It's also approved under a different brand name for treating photodamaged skin.

**Dr. Brand:** Recently, the drug companies have been challenging those prescriptions as well.

**Dr. Shalita:** But tazarotene has been able to get on most insurance formularies; it is on the New York State Medicaid formularies, and neither adapalene nor tretinoin is. I've been fighting for 20 years to get tretinoin on the New York State Medicaid formularies. Insurers say it's a cosmetic.

**Dr. White:** You're right. Until tazarotene was approved for acne or photodamage, if you gave it to acne patients they had a better chance of being covered for it because it was a psoriasis medication. But the plans are catching on to everything, and they know what's used for what.

**Dr. Shalita:** I write down "for acne" on the prescription, and I underline it three times. Ortho actually gives you a letter that you can give to the patient to send to the insurance company.

**Dr. Berson:** Patients can fax that letter to their insurance formulary, meaning you (hopefully) won't have to call the insurer, which takes time.

**Dr. Shalita:** Speaking of time spent, there's truly a disincentive to spend a lot of time explaining things to patients, as Dr. White suggested earlier. For example, in our medical school we are obliged to get involved with all the HMO plans. If I wasn't getting a salary, I couldn't afford to do what I do with acne patients, because I'd basically be paid less than my costs.

**Dr. Brand:** The problem with these creams being used for photoaging is that they're the same as the ones used for acne. That's particularly so with tazarotene; the new version approved for photoaging is actually identical to the acne cream and is made by the same company in the same medium.

**Dr. Berson:** In the tretinoin family, the vehicle for Renova® is a little bit different from, say, the Retin-A microsphere.

**Dr. Shalita:** So be careful.

**Dr. Berson:** They're different. So at least you can justify using an acne product as opposed to a photoaging product. But when you use tazarotene, it is absolutely identical whether you prescribe the .1% cream or the differently named photoaging product.

## Combination Treatments

**Dr. Shalita:** Benzoyl peroxide is the most potent topical antibacterial as a single agent because it is bactericidal, whereas the topical antibiotics are bacteriostatic. The only advantage topical antibiotics have, which is why I like to use them in combination with BP, is that they have anti-inflammatory properties. In terms of antibacterial activity, *P. acnes* are resistant to antibiotics. Dr. Berson clearly demonstrated many years ago that *P. acnes* is resistant to erythromycin, and Dr. James J. Leyden of the University of Pennsylvania published an article in the *British Journal of Dermatology* showing that *Staphylococci* are resistant to erythromycin as well. But if you combine benzoyl peroxide with erythromycin—or now, clindamycin—you eliminate the bacterial resistance to the antibiotic; you eliminate all those strains that were resistant or less sensitive. For some unexplained reason, you get a greater decrease in the bacteria with the combination therapy than you do with BP alone. It's not a huge difference, but there is some difference. Plus, you reap the anti-inflammatory benefits of the antibiotics.

There are really two antibacterial combinations available to us now. We've had the BP-erythromycin combination around for a long time, and it is very effective and very helpful. However, it's an alcohol formulation, so some patients may be experiencing excessive drying, whereas the benzoyl peroxide/clindamycin formulations are both aqueous, so they are better tolerated. I saw some data, I believe from Dr. Leyden, where the benzoyl peroxide/clindamycin combo was slightly superior clinically and bacteriologically to the benzoyl peroxide/erythromycin. And that's basically what I use. I rarely if ever use the topical antibiotic alone. If, for example, I'm going to use the clindamycin wipe as an individual agent, which is very convenient to the patient, I'll have the patient use a benzoyl peroxide cleanser either at the same time or at another time. Clindamycin is much more stable than erythromycin when used in combination with a cleanser or anything else.

**Dr. Shupack:** Benzoyl peroxide has to be either reconstituted at the time of dispensing, or refrigerated. I assume that's to maintain its stability.

**Dr. Shalita:** No, it's the other way around. Benzoyl peroxide is a potent oxidizing agent, so whatever you put with it eventually is going to be oxidized. That's why you have to make it up fresh or have it refrigerated before dispensing it. There's a difference between the two products: one, BenzaClin, is compounded by the pharmacist at the time of dispensing, so theoretically it's a fresh product at the time; while the other product, Duac<sup>TM</sup>, is already mixed by the manufacturer and is kept refrigerated until the time of dispensing.

These are good products, and the overall majority of patients are probably getting the correct medication and enjoying satisfactory improvement.

**Dr. Shupack:** Are two applications a day better than one?

**Dr. Brand:** If you were using only the one combination product, two applications would be better than one. I usually don't use a combination product as the only treatment, so I would generally do one application a day of each product, using one product in the morning and a different one at night. Usually one of them is a retinoid.

**Dr. Berson:** When you're told that benzoyl peroxide is bactericidal and antibiotics are bacteriostatic, you might ask why a combination of the two should be used as opposed to benzoyl peroxide alone? The answer, as Dr. Shalita explained, is that the antibiotic has some anti-inflammatory properties, so the combination product is probably better than benzoyl peroxide alone. And I'd like to point out that when we give someone one of these benzoyl peroxide/antibiotic combination products plus a retinoid, we are essentially giving them three treatments, although in two preparations.

**Dr. Berson:** In the anti-inflammatory category, we should talk about sodium sulfacetamide and sulfur products, because we are seeing a new product every day on the market.

**Dr. White:** There have got to be ten. I've never seen anything like it.

**Dr. Shalita:** It's because the products don't have to be approved by the FDA; they're grandfathered in. These products were already on the market when Dr. Shupack and I started our residency. They're old enough to be studied as part of what one doctor has called "paleodermatology."

I'd just like to reiterate what's been said about the BP/clindamycin and BP/erythromycin combinations being less irritating than BP alone in the same vehicle.

**Dr. Robins:** To make sure we've clarified everything, do either BenzaClin or Duac have any advantages over the other?

**Dr. Shalita:** Each has its own little peculiarities.

**Dr. Brand:** They're both excellent products. One good thing with the benzoyl peroxide and clindamycin formulations is that they don't require refrigeration like the earlier combinations with erythromycin. There's a place for both of these.



**Dr. Shalita:** Actually, you don't have to refrigerate the new erythromycin packs either.

**Dr. Brand:** That's true.

**Dr. Robins:** And they recommend still keeping Duac refrigerated.

**Dr. Shalita:** No, just the pharmacist keeps it refrigerated.

**Dr. White:** What's the reason that pharmacists have to refrigerate it, if once they hand it to someone it doesn't matter?

**Dr. Shalita:** Because as soon as you mix benzoyl peroxide and clindamycin you slow down any breakdown.

**Dr. White:** So once they dispense it to you, you don't need to refrigerate it. But if the pharmacist has it for three months in the pharmacy and doesn't refrigerate it, what happens?

**Dr. Shalita:** There's an expiration date on it.

**Dr. Robins:** Therefore, there is an advantage to mixing it fresh, because then you know are getting the maximum strength.

**Dr. White:** That's true.

**Dr. Shupack:** With Duac, even before it gets to the pharmacist, you have to trust that the interstate carriers of this stuff maintain steady refrigeration.

**Dr. Shalita:** It's shipped in refrigerators.

**Dr. Robins:** Like Botox.

**Dr. Shalita:** Yes.

**Dr. Robins:** What is it refrigerated with, CO<sub>2</sub> dry ice? You get Botox in a box, and they call you the day before to tell you it's coming. They want you to be there to receive it, because it's refrigerated.

## Oral Antibiotics

**Dr. Robins:** We have to discuss oral antibiotics.

**Dr. Shalita:** The problem I started alluding to before, the decreased sensitivity of bacteria to antibiotics, is getting to be a major issue. The bacteria are virtually all resistant to erythromycin, as well as to azithromycin and clarithromycin, even though somebody has said you could use Zithromax® for 10 days a month.

**Dr. Robins:** Four days.

**Dr. Shalita:** Absolute nonsense. It doesn't work any better than the others. It's better-absorbed than erythromycin, but the organism is resistant and you can't get the anti-inflammatory effect. Tetracycline is increasingly resisted, too. There's the least amount of resistance to minocycline, although that resistance is increasing as well. Next best is doxycycline, followed by the other tetracyclines. Trimethoprim sulfate is still okay, but as with the others, if you use it for any length of time you're going to develop resistance. The advantage to minocycline is that it penetrates better and lasts longer than the other antibiotics. It has side effects, but the only one that really is problematic is the pigmentation. Pseudotumors, lupus, and all the other side effects are rare.

**Dr. White:** Headaches and vertigo are also side effects.

**Dr. Robins:** Does the pigmentation occur whether or not there's sun exposure?

**Dr. Shalita:** It occurs in areas of trauma—when there's both acne and trauma.

**Dr. White:** *Without* sun exposure.

**Dr. Shalita:** Doxycycline is alleged to be phototoxic, but again that's a very rare phenomenon. Of course, if you're the one developing phototoxicity, it's no longer rare. And now they have all this low-dose doxycycline hydrate and doxycycline monohydrate treatments taken once a day or twice a day; they can make you crazy with all these different plans. I think they are both very valuable drugs, and I use trimethoprim sulfate when I need to go to the well. If those don't work, I go to Accutane.

**Dr. Shupack:** Don't forget, there's also oral clindamycin.

**Dr. Shalita:** Yes, but according to the work they did at Pennsylvania State University, the resistance pattern to clindamycin is virtually identical to the pattern with erythromycin. They crossed.

**Dr. Shupack:** Do you think there's any role for systemic cephalosporin in acne treatment?

**Dr. Shalita:** Yes, perhaps a bit of a role for the new generation cephalosporins. You know what is very simple? If you want to find out if a drug is going to work in acne, see if they use it in the prostate. That's true of some of the new quinolones, but I wouldn't want to use them with acne because they are very valuable drugs and you see what's happening to the resistance pattern of systemic drugs. Levaquin® for now is the drug of choice for prostatitis, and so is Bactrim.™

**Dr. White:** And Levaquin is once a day.

**Dr. Shalita:** So is trimethoprim sulfate. But I wouldn't want to see it widely used with acne.

**Dr. Robins:** Because then you won't have it when you really need it. What percentage of your patients do you put on oral antibiotics?

**Dr. Berson:** It depends on the variables, such as how they responded first to the topicals.

**Dr. White:** If they have a very deep nodular component, I'll immediately give them an oral antibiotic.

**Dr. Robins:** But you don't prescribe it routinely?

**Dr. Berson:** Not on a first visit, unless they have very inflamed acne.

**Dr. Brand:** What about prescribing isotretinoin?

**Dr. Shalita:** Let's do the antibiotics first.

**Dr. Robins:** I mean, Roche terminated their isotretinoin sales force, the reason being that the drug is off patent and will be available generically.

**Dr. Shalita:** They don't have a dermatology sales force, but they still have a sales force; they call on us periodically.

**Dr. Berson:** They call on us as well. They also give us the forms for filling out the yellow stickers and the qualifiers.

**Dr. Brand:** The generics are doing that as well.

**Dr. Berson:** Are you finding any differences with the generics?

**Dr. Brand:** I sometimes don't know what patients are getting.

**Dr. Shalita:** I don't either.

**Dr. Shupack:** Are the generic companies giving stickers, too?

**Dr. Shalita:** Yes.

**Dr. Berson:** I've been told that some of them don't get absorbed as well.

**Dr. Shalita:** I don't know. One was made in India, and someone claimed that the other one was made by Roche Pharmaceuticals, but I don't believe it.

**Dr. Berson:** But as we were discussing, they know exactly which prescription you've given anyway, because they put it in the computer. So it doesn't matter that it's not physician-specific.

**Dr. White:** Well, that depends on whether or not you write D.A.W. (dispense as written) on it.

---

*The population is  
increasing, and  
acne is increasing  
along with it.*

—Dr. Shalita

---

## Hormones

**Dr. Brand:** Hormones are an important category for a population that we often see—adult women with a lot of cyclic flares of their acne. Oral contraceptives can play a vital role for adult women who have not responded to topicals. It's a logical choice. I think that a higher percentage of women who tend to have very irregular cycles will have significant improvement when put on oral contraceptives than women who are of regular cycle. OCPs also take a few months to improve acne in these women.

**Dr. Shalita:** Do you think there are any differences among the oral contraceptives?

**Dr. White:** Yes, I think there are.

**Dr. Shalita:** Yet from a theoretical point of view, there shouldn't be. Because if you get enough estrogen to prevent ovulation, you decrease antigen-binding globulin and DHEA-S, etc. But I still think there's a difference clinically.

**Dr. Shupack:** The one that has the first labeling for it is Ortho Tri-Cyclen®.

**Dr. Shalita:** Right, and all the gynecologists are writing for it. Everybody comes in saying they're on birth control pills; it doesn't work for their acne.

**Dr. White:** For those people, which progestins do you look for?

**Dr. Berson:** Traditionally we talk about norgestimate and desogestrel as being the least androgenic progestins.

**Dr. Robins:** Norgestimate gets converted to norgestrel.

**Dr. Berson:** I'm not sure if the good progestin vs. bad progestin issue is relevant; the estrogen moiety is really responsible for the improvement that we see. Having said that, I do find that patients who are on the pills which contain norgestimate or desogestrel, such as Mircette®, Ortho-Cept®, and Desogen®, tend to do better with respect to acne. And Yasmin®, recently introduced, seems to be very helpful, possibly because its progestin has some anti-androgenic properties similar to Diane-35®.

**Dr. Shalita:** It's a spironolactone derivative.

**Dr. Berson:** Right, it's a low-dose drospirenone that someone can take and get the benefit of the closest thing to Diane-35 that we might have in the United States.

**Dr. Shalita:** And also get DVT —deep vein thrombosis. I saw recently in a medical letter that there is some concern about

whether DVT is going to be a problem.

**Dr. Berson:** One thing we should always remember is that while the patient is coming to us strictly for acne, if we prescribe an oral antibiotic, they also may need back-up birth control. Whether oral antibiotics can counteract the ovulatory properties of OCP is a controversial topic.

**Dr. Shalita:** ACOG (The American College of Obstetricians and Gynecologists) is supposed to have come out with a position paper saying that that's nonsense. It occurs only with a couple of antibiotics, not ones that we use. The original paper about those few antibiotics was published in the *British Medical Journal*, and then it got extrapolated to other antibiotics to the point where it actually was added to package inserts. The FDA wanted to take it out of the package insert, and now says that you have to do both pharmacodynamic and pharmacokinetic studies to prove it. As you know, that's very difficult to do when taking the two drugs, so nobody is willing to spend the money to do it.

**Dr. Berson:** But it is still on the package insert. If you want to be a purist, use back-up the first month.

**Dr. Shupack:** So, what is the current status of Diane-35? Are we ever going to see it in the United States?

**Dr. Shalita:** No, we'll never see it in this country. The patent has expired.

**Dr. White:** But they have Yasmin.

**Dr. Shalita:** Yes, they got one. But we'll never get Diane-35. Patients have to go to Mexico or Canada for it. The FDA can bother us if we get it for them, but when patients bring it in, the FDA can't do anything to them. If all else fails, I'll prescribe Accutane.

**Dr. Brand:** Accutane is the topic of a whole seminar by itself.

**Dr. White:** If you have severe acne and it's not responding to the orals and all your topicals, you go to Accutane.

*Hormones play a part in the irritation of acne at around the time of adolescence.*

—Dr. Berson

**Dr. Shalita:** They also used to use the combination of acetone and CO<sub>2</sub>. You'd put them together in a big piece of cheesecloth to do the treatment. Then the patients' faces would swell up so they'd look terrific for Saturday night. It didn't do anything for their acne otherwise.

**Dr. Berson:** A lot of people use a Q-tip with liquid nitrogen.

**Dr. Shalita:** We tested all of the freezing methods, including liquid CO<sub>2</sub> and liquid nitrous oxide. The results were similar to intralesional steroids.

## Office-Based Procedure

**Dr. Shalita:** I never do comedo extraction on the first visit.

**Dr. Berson:** Never. You want to loosen them up first with the topical retinoid.

**Dr. Shalita:** Unless you want to antagonize the patient—extraction hurts.

**Dr. Berson:** It's going to hurt, and you're going to have marks for a couple of days.

**Dr. Shalita:** Do that to yourself and see how it feels.

**Dr. Berson:** Extractions are very helpful for those with comedones, in their repeat visits to you after they've used a retinoid to loosen everything up. We know the value of intralesionals for inflamed cysts to decrease the pain and itching that some people get.

**Dr. Robins:** Does anyone do peels for acne patients?

**Dr. White:** I think salicylic and glycolic peels can be helpful.

**Dr. Berson:** I think of them as adjunctive treatments.

**Dr. White:** I'd put them in that category.

**Dr. Berson:** I do an occasional glycolic peel, but I don't do it weekly or as a regimen.

**Dr. Robins:** It's usually for somebody well into the teens or post-teens. You don't do it for someone who is only 13 or 14.

**Dr. Berson:** No, but it's usually an adjunct to decrease post-inflammatory pigmentation.

**Dr. Shalita:** What about microdermabrasion?

**Dr. Berson:** I don't do that.

**Dr. Shupack:** How about cryotherapy with CO<sub>2</sub> slush?

**Dr. Shalita:** There used to be a box of solid CO<sub>2</sub> sitting in a room at the Skin & Cancer Unit of NYU. We had to chop this stuff up with a hammer and chisel and put it in a big gauze bag.

**Dr. Robins:** Not gauze, cheesecloth.

**Dr. Berson:** You would have this steaming mixture.

**Dr. Shalita:** They also used to use the combination of acetone and CO<sub>2</sub>. You'd put them together in a big piece of cheesecloth to do the treatment. Then the patients' faces would swell up so they'd look terrific for Saturday night. It didn't do anything for their acne otherwise.

**Dr. Berson:** A lot of people use a Q-tip with liquid nitrogen.

**Dr. Shalita:** We tested all of the freezing methods, including liquid CO<sub>2</sub> and liquid nitrous oxide. The results were similar to intralesional steroids.



## Laser Treatment

**Dr. Robins:** How is the laser used with acne?

**Dr. Shalita:** Blue light, a visible light of 410-420 nm, activates the porphyrins in *P. acnes*. They have an action spectrum at a higher wavelength too, but the peak activity is there. We found first that blue light reduces the bacteria. Since then, clinical trials around the world have shown that it is about as effective as topical antibiotics, maybe a little bit more so. In patients who have tried everything else, it's useful, because they're looking for another form of therapy. On the other hand, it's a pain in the neck having to do 15-minute treatments twice a week. It's now claimed that you can do 20-25 minutes with the light, a little closer to the skin, once a week. So far, that hasn't worked as well for us, but we'll do more of it and see how that works. Some patients have done spectacularly well with it and others haven't. I had one patient with acne excoriée who improved, but then she relapsed. But Dr. Yoram Harth of the University of Haifa, who invented this thing, thinks that's where the beneficial effect is, because there's also an anti-inflammatory effect. The difference between this controlled form of blue light and the blue light that you are exposed to along with UV in the sun is that in the sun you're getting the carcinogenic effects. Plus, UV light thickens the walls of the follicles, so by the end of the summer their acne is worse. Under the blue light, there are absolutely no harmful effects.

**Dr. Shupack:** Is the manufacturing technology for this blue light so complex that a person couldn't just buy a blue light fixture?

**Dr. Shalita:** Yes, because it's a high-intensity bulb. Otherwise, you would be sitting there for an hour. That's where the technology is developing.

**Dr. Berson:** For which patients would you choose this option?

**Dr. Shalita:** It's for people with mild-to-moderate inflammatory acne who don't want to use conventional therapy.

**Dr. Berson:** Who don't want to use conventional therapy? In other words, it's not necessarily going to achieve better results than those other therapies.

**Dr. Shalita:** Right. Now the question is, what happens if you use it in conjunction with the conventional therapy? We're trying to do this now; it might turn out that it enhances the conventional therapy, but I can't tell you yet.

## Concluding Remarks

**Dr. Robins:** Does anyone have any concluding remarks?

**Dr. Shalita:** The population is increasing, and acne is increasing along with it.

**Dr. Robins:** Percentage-wise, do you see more and more acne today? Do people have more insurance that allows them to come to the doctor?

**Dr. Shupack:** As dermatologists, we see less, in a sense.

**Dr. Shalita:** More primary care doctors are taking care of it. There are more OTC products, and more primary care doctors are taking acne.

**Dr. White:** I also see patients who have never had insurance before but have it now; they come in and are happy to get treatment.

**Dr. Brand:** I think there are a great variety of treatments currently available for acne. They need to be tailored to the individual patient's skin type and lifestyle.

**Dr. Robins:** There are more products than ever in our armamentarium.

**Dr. Berson:** But nothing substitutes for the clinical dermatologist's expertise in evaluating the patient and deciding which treatments to use.

**JDDonline.com**