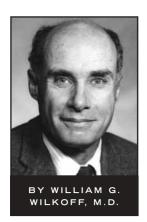
Opinion PEDIATRIC NEWS • May 2005



LETTERS FROM MAINE Time Well Spent

f e w weeks ago visited my favorite otolaryngologist. He's my favorite because he doesn't cut

first and ask questions later. He is also very good at explaining things to parents. Bob practice for a couple of years when I arrived in town in 1974.

My appointment was the first and last attempt to find a treatable cause for my dwindling hearing. I have long suspected that it is simply the result of years of auditory abuse, and reading the studies documenting that most pediatricians are exposed to noise levels deemed unsafe by the standards of the Occupational Safety and

is about my age and had already been in Health Administration only added to my suspicions. Although I feared that my difficulty catching every word in group conversations was the inevitable audiologic equivalent of presbyopia, I was in denial. I hoped that Bob could cure the problem by removing 35 years' worth of stethoscope-compacted cerumen.

After checking in with the receptionist, I spent a few minutes in his bare-bones waiting room catching up on Hollywood gossip and chatting with one of my teenage patients, who had just recovered from a bout of sinusitis-induced septicemia. When it was my turn, Bob ushered me into his small examining room and sat me down in what could have been an old barber chair. Since neither of us is a frequent attendee at hospital staff meetings, we had lots of catching up to do. The conversation ranged from children's weddings to our painful attempts at reacquiring tennis skills that had been allowed to atrophy over the last 2 decades.

After what seemed like less than 5 minutes of banter, he paused and said, "Well, the good news is that you don't have any wax in your ears. The bad news is that I bet you'll be wanting a hearing aid in a couple of years." He then spent 10 minutes explaining the physiologic process that was eroding my hearing and what I could do to remedy the situation. We parted with an agreement to get together for some doubles in a couple of weeks.

As I climbed back into my truck for the trip home, I wondered how Bob could sound so confident about the cause of my deafness without even looking in my ears. The examination portion of the visit had flown by so quickly that I didn't remember him using an otoscope.

As I turned onto the highway, I attempted to reconstruct our encounter. He had moved so smoothly and efficiently through the exam that my focus had been on our conversation and not his invasion into every orifice in my head. I began to recall that he had not only looked in my ears, but he had also removed a small bit of cerumen and insufflated my tympanic membranes. He had looked past my turbinates, sterilized a mirror with an alcohol lamp, and taken a peek at my vocal cords. His fingers had nimbly danced over my thyroid and all the nodes above my clavicles.

As I thought about it, I realized that Bob had done an extremely thorough head and neck exam. Because of his efficiency, which came from more than 30 years of experience and the familiar surroundings of an office where every instrument was exactly where it was supposed to be, the process had taken no more than 4 or 5 minutes. Thirty years of trial and error guided his hands to find my tympanic membranes on the first pass and locate my vocal cords without triggering my gag reflex.

In the hands of an experienced clinician, a good, focused physical exam doesn't take much time. The true test of our clinical ability is not the speed at which we have learned to perform a thorough examination but what we do with the time we have saved. Do we reinvest it in the patient we have just examined by conveying to them what we have discovered in a manner that says we care? Or do we use the time we have gained through our efficiency to rush on to the next patient? Fortunately for me, Bob has chosen to do the former, and that's another reason he's my favorite.

DR. WILKOFF practices general pediatrics in a multispecialty group practice in Brunswick, Maine. To respond to this column, write to Dr. Wilkoff at our editorial offices.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Rx Only

Duac Topical Gel has not been demonstrated to have any additional benefit when compared to benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne.

ic Topical Gel is contraindicated in those individuals who have shown by personsitivity to any of its components or to lincomycin. It is also contraindicated in those having a history of regional enteritis, ulcerative colitis, pseudomembranous colitis, or antibiotic-associated colitis.

WARNINGS
ORALLY AND PARENTERALLY ADMINISTERED CLINDAMYCIN HAS BEEN
ASSOCIATED WITH SEVERE COLITIS WHICH MAY RESULT IN PATIENT DEATH.
USE OF THE TOPICAL FORMULATION OF CLINDAMYCIN RESULTS IN
ABSORPTION OF THE ANTIBIOTIC FROM THE SKIN SURFACE. DIARRHEA, ABSORPTION OF THE ANTIBIOTIC FROM THE SKIN SURFACE. DIARRHEA, BLOODY DIARRHEA, AND COLITIS (INCLUDING PSEUDOMEMBRANOUS COLITIS) HAVE BEEN REPORTED WITH THE USE OF TOPICAL AND SYSTEMIC CLINDAMYCIN. STUDIES INDICATE A TOXIN(S) PRODUCED BY CLOSTRIDIA IS ONE PRIMARY CAUSE OF ANTIBIOTIC-ASSOCIATED COLITIS. THE COLITIS IS USUALLY CHARACTERIZED BY SEVERE PERSISTENT DIARRHEA AND SEVERE ABDOMINAL CRAMPS AND MAY BE ASSOCIATED WITH THE PASSAGE OF BLOOD AND MUCUS. ENDOSCOPIC EXAMINATION MAY REVEAL PSEUDOMEMBRANOUS COLITIS. STOOL CULTURE FOR Clostridium difficile AND STOOL ASSAY FOR AND MUCUS. ENDOSCOPIC EXAMINATION MAY REVEAL PSEUDOMEMBRANOUS COLITIS. STOOL CULTURE FOR Clostridium difficie AND STOOL ASSAY FOR Clostridium difficie TOXIN MAY BE HELPFUL DIAGNOSTICALLY. WHEN SIGNIFICANT DIARRHEA OCCURS, THE DRUG SHOULD BE DISCONTINUED. LARGE BOWLE ENDOSCOPY SHOULD BE CONSIDERED TO ESTABLISH A DEFINITIVE DIAGNOSIS IN CASES OF SEVERE DIARRHEA. ANTIPERISTALTIC AGENTS SUCH AS OPIATES AND DIPHEMOXYLATE WITH ATROPINE MAY PROLONG AND/OR WORSEN THE CONDITION. DIARRHEA, COLITIS AND PSEUDOMEMBRANOUS COLITIS HAVE BEEN OBSERVED TO BEGIN UP TO SEVERAL WEEKS FOLLOWING CESSATION OF ORAL AND PARENTERAL THERAPY WITH CLINDAMYCIN.

Mild cases of pseudomembranous colitis usually respond to drug discontinuatio alone. In moderate to severe cases, consideration should be given to manageme with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Reneral: For dermatological use only; not for ophthalmic use. Concomitant to acne therapy should be used with caution because a possible cumulative irrita effect may occur, especially with the use of peeling, desquamating, or abrasive

The use of antibiotic agents may be associated with the overgrowth or nonsusceptible organisms, including fungi. If this occurs, discontinue medication and take appropriate measures.

Avoid contact with eyes and mucous membranes

Clindamycin and erythromycin containing products should not be used in combination. *In vitro* studies have shown antagonism between these two antimicrobials. The clinical significance of this *in vitro* antagonism is not known

Information for Patients: Patients using Duac Topical Gel should receive the

- Duac Topical Gel is to be used as directed by the physician. It is for external use only. Avoid contact with eyes, and inside the nose, mouth, and all mucous use only. Avoid contact with eyes, and inside the membranes, as this product may be irritating.
- 2. This medication should not be used for any disorder other than that for which it
- 3. Patients should not use any other topical acne preparation unless otherwise directed by their physician.
- 4. Patients should report any signs of local adverse reactions to their physician
- 5. Duac Topical Gel may bleach hair or colored fabric.
- Duac Topical Gel can be stored at room temperature up to 25°C (77°F) for up to 2 months. Do not freeze. Keep tube tightly closed. Keep out of the reach of small children. Discard any unused product after 2 months.
- Before applying Duac Topical Gel to affected areas, wash the skin gently, rinse with warm water, and pat dry.

Benzoyl peroxide in acetone at doses of 5 and 10 mg administered twice per week induced squamous cell skin tumors in transgenic TgAC mice in a study using 20 weeks of topical treatment.

Genotoxicity studies were not conducted with Duac Topical Gel. Clindamycin Genotoxicity studies were not conducted with Duac Topical Gel. Clindamycin phosphate was not genotoxic in *Salmonella typhimurium* or in a rat micronucleus test. Benzoyl peroxide has been found to cause DNA strand breaks in a variety of mammalian cell types, to be mutagenic in *Salmonella typhimurium* tests by some but not all investigators, and to cause sister chromatid exchanges in Chinese hamster ovary cells. Studies have not been performed with Duac Topical Gel or benzoyl peroxide to evaluate the effect on fertility. Fertility studies in rats treated orally with up to 300 mg/kg/day of clindamycin (approximately 120 times the amount of clindamycin in the highest recommended adult human dose of 2.5 g Duac Topical Gel, based on mg/m²) revealed no effects on fertility or matting abilit

Pregnancy: Teratogenic Effects: Pregnancy Category C: Animal reproduction studies have not been conducted with Duac Topical Gel or benzoyl peroxide. It is also not known whether Duac Topical Gel can cause fetal harm when administered to a pregnant woman or an affect reproduction capacity. Duac Topical Gel should be given to a pregnant woman only if clearly needed.

Developmental toxicity studies performed in rats and mice using oral doses of clindamycin up to 600 mg/kg/day (240 and 120 times the amount of clindamyc the highest recommended adult human dose based on mg/m², respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (100 and 50 times th amount of clindamycin in the highest recommended adult human dose based on mg/m², respectively) revealed no evidence of teratogenicity.

Nursing Women: It is not known whether Duac Topical Gel is secreted into human milk after topical application. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness of this product in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS

During clinial trials, all patients were graded for facial erythema, peeling, burning, and dryness on the following scale: 0 = absent, 1 = mild, 2 = moderate, and 3 = severe. The percentage of patients that had symptoms present before treatment (at baseline) and during treatment were as follows:

Local reactions with use of Duac Topical Gel % of patients using Duac Topical Gel with symptom present Combined results from 5 studies (n = 397)						
	Before Treatment (Baseline)			During Treatment		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Erythema	28%	3%	0	26%	5%	0
Peeling	6%	<1%	0	17%	2%	0
Burning	3%	<1%	0	5%	<1%	0
Dryness	6%	<1%	0	15%	1%	0

(Percentages derived by # subjects with symptom score/# enrolled Duac subjects, n = 397).

HOW SUPPLIED

Duace (clindamycin, 1% - benzoyl peroxide, 5%) Topical Gel is available in a 45 gram tube - NDC 0145-2371-05.

Prior to Dispensing: Store in a cold place, preferably in a refrigerator, between 2°C and 8°C (36°F and 46°F). Do not freeze.

Dispensing Instructions for the Pharmacist: Dispense Duac Topical Gel with a 60 day expiration date and specify "Store at room temperature up to 25°C (77°F). Do

Keep tube tightly closed. Keep out of the reach of small children

U.S. Patent Nos. 5,466,446, 5,446,028, 5,767,098, and 6,013,637 Patents Pending

References: 1. Leyden 3J. A review of the use of combination therapies for the treatment of acne vulgaris. J Am Acad Dermatol. 2003;49:5200-5210. 2. Vernon P. Acne vulgaris: current treatment approaches. Adv N Pract. 2003;11:59-62. 3. Toyoda M. Morohashi M. An overview of topical antiblotics for acne treatment. Dermatology. 1998;196:130-134. 4. Tan H-H. Topical antibacterial treatments for acne vulgaris: comparative and guide to selection. Am J Clin Dermatol. 2004;57:97-84. 5. Lookinghill IPP, Chalker DK, Lindholm 135, et al. Treatment instantiant cindiamyrin/phezouple provide gel comparing/phezouple provide gel comparing/phezouple provide gel comparing/phezouple provide gel comparing with cindamyrin personal provided gel comparing with cindamyrin and verification potential and co acceptability of two combination topical acne gels—combined results of two comparative studies. Today's Ther Trends. 2003;21:269-275. 7. Tanghetti EA, Gold MH. A two-center patient preference study comparing benzoyl peroxide/clindamyrin gels in acne vulgaris patients. Poster presented at: 63rd Annual Meeting of the American Academy of Dermatology: February 18-22. 2005; New Orleans, La.