

## CLINICAL CAPSULES

## Chlamydia Climbs in Teen Girls

Overall rates of chlamydia in the United States increased by 6% in 2004 compared with 2003 levels, officials from the Centers for Disease Control and Prevention said in a telephone news conference. The highest rates of chlamydia continued to be among adolescent females aged 15-19 years old, with a reported rate of 2,761 per 100,000 persons. The increase in the chlamydia rate probably reflects improved screening and better tests, the CDC officials said. Efforts to increase chlamydia screening are a priority for CDC; the organization rec-

ommends annual screening of sexually active women younger than 25 years. Data from a recent CDC study conducted in conjunction with Kaiser Permanente showed that a program that prompted primary care physicians to tie chlamydia testing to Pap testing increased chlamydia screening by 30% among the health plan's younger female members.

## Missionary Imports Measles

A measles outbreak in Indiana in May-June 2005 has been attributed to an unvaccinated 17-year-old girl who had worked as

a missionary in an orphanage and hospital in Bucharest, Romania, according to the CDC (MMWR 2005;54;1073-5). The girl returned to the United States with symptoms including prodromal fever, cough, conjunctivitis, and acute rhinitis (coryza) on May 14, and a rash on May 16. She attended a church gathering that included people who had not been vaccinated. The outbreak included 34 patients, aged 9 months to 49 years, with a median age of 12 years. A total of 14 cases (41%) were laboratory confirmed, and the other 20 were epidemiologically linked to confirmed cases. Only two patients had been vaccinated; one had received a single

dose of vaccine and the other had received two doses.

Actions taken to control the outbreak included patient isolation; tracing patient contacts and administering vaccine and immunoglobulin to those who were susceptible; and voluntary quarantine for contacts who refused vaccination. In addition, local health officials reviewed the vaccine status of health care workers, alerted hospitals to the outbreak, and raised local media awareness of the need for vaccination. This measles outbreak represents the largest in the United States since 1996, and could have been prevented by adherence to the Advisory Committee on Immunization Practices recommendations, which include vaccination for all international travelers, people who work in medical facilities, and preschool and school-aged children.

Tx for Noncompliant *H. pylori* Patients

The clinical potency of metronidazole, despite evidence of in vitro resistance, may make it a more effective choice for children in areas with a high prevalence of *Helicobacter pylori*, said Bradford D. Gessner, M.D., of the Alaska Division of Public Health, Anchorage, and his colleagues (CID 2005;41;1261-8). Poor treatment compliance, crowded housing, and lower body mass index were among the risk factors for failed treatment of *H. pylori* infection in a randomized study of 219 children aged 7-11 years in rural Alaska. Those in the control group received 3 mg/kg iron sulfate twice daily, up to 60 mg/dose for 6 weeks. Those in the treatment group received iron sulfate plus a triple-barrelled therapy consisting of 40 mg/kg amoxicillin twice daily, up to 1.5 g/dose; 7.5 mg/kg clarithromycin twice daily, up to 500 mg/dose; and 30 mg lansoprazole twice daily. Children who were allergic to amoxicillin or macrolides received 10 mg/kg of metronidazole twice daily, up to 500 mg/dose. Compliance was a factor in the results; 8.3% of children who took their medications fewer than 10 times resolved their infections, compared with 19%, 40%, and 63% of children who took their medications 10-20 times, 20-27 times, and all 28 times, respectively. Posttreatment analyses showed a significant association between metronidazole and treatment success after controlling for multiple confounding variables.

## Genotypes Factor in Hepatitis C

Interferon therapy for chronic hepatitis C may be less effective in children with a hepatitis C virus (HCV) genotype 1 than in children with hepatitis C virus genotypes other than 1, based on a retrospective study of 50 children aged 3-15 years, said Raffaele Iorio, M.D., of the University of Naples (Italy) and his associates. The children had hypertransaminasemia with detectable HCV RNA. A sustained response to interferon was observed in 11 of 17 children (65%) infected with an HCV genotype other than 1, compared with 8 of 33 children (24%) infected with HCV genotype 1. In addition, eight of the children who did not have a favorable response received a second cycle at a mean age of 11 years, and only one child with an HCV genotype other than 1 sustained a response to the second cycle.

—Heidi Splete with staff reports

## BRIEF SUMMARY OF PRESCRIBING INFORMATION

## Duac® Topical Gel

(clindamycin, 1% - benzoyl peroxide, 5%)

For Dermatological Use Only.  
Not for Ophthalmic Use.

## Rx Only

## INDICATIONS AND USAGE

Duac Topical Gel is indicated for the topical treatment of inflammatory acne vulgaris.

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.

## CONTRAINDICATIONS

Duac Topical Gel is contraindicated in those individuals who have shown hypersensitivity 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, 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 *Clostridium difficile* TOXIN MAY BE HELPFUL DIAGNOSTICALLY. WHEN SIGNIFICANT DIARRHEA OCCURS, THE DRUG SHOULD BE DISCONTINUED. LARGE BOWEL ENDOSCOPY SHOULD BE CONSIDERED TO ESTABLISH A DEFINITIVE DIAGNOSIS IN CASES OF SEVERE DIARRHEA. ANTIPERISTALTIC AGENTS SUCH AS OPIATES AND DIPHENOXYLATE 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 discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

## PRECAUTIONS

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

The use of antibiotic agents may be associated with the overgrowth of nonsusceptible organisms, including fungi. If this occurs, discontinue use of this 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 following information and instructions:

1. 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 membranes, as this product may be irritating.
2. This medication should not be used for any disorder other than that for which it was prescribed.
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.
6. 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.
7. Before applying Duac Topical Gel to affected areas, wash the skin gently, rinse with warm water, and pat dry.
8. Excessive or prolonged exposure to sunlight should be limited. To minimize exposure to sunlight, a hat or other clothing should be worn.

**References:** 1. Leyden JJ. A review of the use of combination therapies for the treatment of acne vulgaris. *J Am Acad Dermatol.* 2003;49:S200-S210. 2. Vernon P. Acne vulgaris: current treatment approaches. *Adv Nurse Pract.* 2003;11:59-62. 3. Toyoda M, Maorohashi M. An overview of topical antibiotics for acne treatment. *Dermatology.* 1998;196:130-134. 4. Tan H-H. Topical antibacterial treatments for acne vulgaris: comparative review and guide to selection. *Am J Clin Dermatol.* 2004;5:79-84. 5. Lookingbill DP, Chalker DK, Lindholm JS, et al. Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: combined results of two double-blind investigations. *J Am Acad Dermatol.* 1997;37:590-595. 6. Fagundes DS, Fraser JM, Klauda HC. Difference in the irritation potential and cosmetic 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 two benzoyl peroxide/clindamycin gels in acne vulgaris patients. Poster presented at: 63rd Annual Meeting of the American Academy of Dermatology; February 18-22, 2005; New Orleans, La.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Benzoyl peroxide has been shown to be a tumor promoter and progression agent in a number of animal studies. The clinical significance of this is unknown.

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 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/m<sup>2</sup>) revealed no effects on fertility or mating ability.

**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 can 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 clindamycin in the highest recommended adult human dose based on mg/m<sup>2</sup>, respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (100 and 50 times the amount of clindamycin in the highest recommended adult human dose based on mg/m<sup>2</sup>, 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 clinical 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

Duac® (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 not freeze."

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



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