

Isolating *E. coli* O157 Cases May Halve Its Spread

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Contributing Writer

The immediate isolation of children with acute *Escherichia coli* O157 infection could potentially decrease the number of secondary cases by half, according to results of a retrospective study of 89 primary cases in a 2005 outbreak.

In particular, the researchers estimated that by quarantining patients who are at

the highest risk of transmitting the infection (those aged 10 years and younger who have a sibling), the number needed to be isolated to prevent one case of life-threatening hemolytic uremic syndrome (HUS) is only 47.

In comparison, the number of household contacts needed to be treated with prophylaxis to prevent one secondary case of meningococcal disease is 218, and the secondary attack rate for that disease is 10 times lower than the secondary attack

rate for HUS (4%), Dr. Dirk Werber and his associates reported (Clin. Infect. Dis. 2008;46:1189-96).

In an editorial comment accompanying this report, Dr. Christina K. Ahn and her associates said that if these findings are confirmed in further studies, “we should carefully consider the compelling empirical data from Werber et al. in favor of the commonsense practice of quarantine ... of all patients with plausible or definite *E. coli* O157:H7 infection during acute illness.”

Dr. Werber of the National Public Health Service of Wales, Cardiff, and his associates observed that in a 2005 outbreak of *E. coli* O157 infection primarily involving Welsh children who ate tainted meat in school meals, the source of infection was rapidly identified and removed. Yet many secondary infections occurred among household contacts of infected children.

Because the prevention of household transmission of this infection has not yet been investigated, the researchers conducted a retrospective cohort study to assess whether the immediate isolation of primary case patients would have prevented transmission.

There were 89 primary case patients in the study. All 25 cases of secondary infection developed in family members of the primary cases, the majority of them in younger siblings. HUS developed in four of these siblings, one of whom died.

A risk analysis showed that the presence of a sibling and young age (younger than 5 years) in the primary case patient were independent predictors that a secondary case would develop. Children aged 5-10 years also were liable to transmit the infection to family members.

Complete information was available for only 15 secondary cases. Seven of these were deemed to have been preventable, if the primary case patient had been isolated when diagnosed. All four secondary cases in which HUS developed were among these preventable cases.

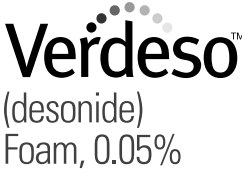
Dr. Werber and his associates estimated that in future outbreaks, the isolation of all primary case patients as soon as they are diagnosed would cut the rate of secondary cases by half. And in at-risk households, only 47 primary cases patients would need to be quarantined to prevent one case of HUS from developing in a family member.

The researchers added that hospitalizing these patients would be the easiest and most effective means of isolating them. A substantial portion of patients with *E. coli* O157 (20% in this outbreak) will require hospitalization anyway, and quicker access to IV fluids may mitigate the risk of HUS.

In their editorial comment, Dr. Ahn and her associates agreed that hospitalization is the best method of quarantine because medical professionals are better able to manage infection control than are parents (Clin. Infect. Dis. 2008;46:1197-9).

“It is unreasonable to expect families to implement measures that even begin to approximate [a hospital’s] hygienic standards at home. ... [Also,] caregiver fatigue must be considered, because infected children are often awake for much of the night, because they are in pain. Exhausted parents might be less able to adhere to sanitary practice,” Dr. Ahn and her associates said.

Moreover, preventing even one case of secondary infection leading to HUS “justifies hospitalizing many additional infected children while they are acutely ill. ... The vascular injury that presumably precedes and leads to renal injury following *E. coli* O157:H7 infection is already well underway by the time such patients present for medical attention,” they added.



BRIEF SUMMARY OF PRESCRIBING INFORMATION
Rx Only
FOR TOPICAL USE ONLY
NOT FOR OPHTHALMIC, ORAL OR INTRAVAGINAL USE
INDICATIONS AND USAGE
Verdeso Foam is indicated for the treatment of mild to moderate atopic dermatitis in patients 3 months of age and older. Patients should be instructed to use Verdeso Foam for the minimum amount of time necessary to achieve the desired results because of the potential for Verdeso Foam to suppress the hypothalamic-pituitary-adrenal (HPA) axis (see PRECAUTIONS). Treatment should not exceed 4 consecutive weeks.
CONTRAINDICATIONS
The use of Verdeso Foam is contraindicated in patients who are hypersensitive to desonide or to any ingredient in this preparation.
PRECAUTIONS
General: Systemic absorption of topical corticosteroids has produced reversible HPA axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients. Conditions which augment systemic absorption include the application of topical corticosteroids over large body surface areas, prolonged use, or the addition of occlusive dressings. Therefore, patients applying a topical corticosteroid to a large body surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression (see Laboratory Tests). If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur requiring supplemental systemic corticosteroids. For information on systemic corticosteroid supplementation, see prescribing information for those products. The effect of Verdeso Foam on HPA axis function was investigated in pediatric patients in one study. In this study, patients with atopic dermatitis covering at least 25% of their body applied Verdeso Foam twice daily for 4 weeks. Three out of 75 patients (4%) displayed adrenal suppression after 4 weeks of use based on the cosyntropin stimulation test. The laboratory suppression was transient; all subjects had returned to normal when tested 4 weeks post treatment. Pediatric patients may be more susceptible to systemic toxicity from equivalent doses because of their larger skin surface area to body mass ratios (See PRECAUTIONS - Pediatric Use). If irritation develops, Verdeso Foam should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a failure to heal rather than noticing a clinical exacerbation, as with most products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing. If concomitant skin infections are present or develop, the use of an appropriate antifungal, antibacterial or antiviral agent should be instituted. If a favorable response does not occur promptly, use of Verdeso Foam should be discontinued until the infection has been adequately controlled.
Information for Patients: Patients using topical corticosteroids should receive the following information and instructions:
1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes or other mucous membranes. The medication should not be dispensed directly onto the face. Dispense in hands and gently massage into affected areas of the face until the medication disappears. For areas other than the face, the medication may be dispensed directly on the affected area. Wash hands after use.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged, otherwise covered, or wrapped so as to be occlusive unless directed by the physician.
4. Patients should report any signs of local or systemic adverse reactions to the physician.
5. Patients should inform their physicians that they are using Verdeso Foam if surgery is contemplated.
6. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 4 weeks, contact the physician.
Laboratory Tests: The cosyntropin (ACTH₁₋₂₄) stimulation test may be helpful in evaluating patients for HPA axis suppression.
Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic or photoco-carcinogenic potential of Verdeso Foam or the effect on fertility of desonide. Desonide revealed no evidence of mutagenic potential based on the results of two in vitro genotoxicity tests (Ames assay, mouse lymphoma cell assay) and an in vivo genotoxicity test (mouse micronucleus assay).
Pregnancy: Teratogenic Effects: Pregnancy Category C: Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies of Verdeso Foam in pregnant women. Therefore, Verdeso Foam should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. No long-term reproductive studies in animals have been performed with Verdeso Foam. Dermal embryofetal development studies were conducted in rats and rabbits with a desonide cream, 0.05% formulation. Topical doses of 0.2, 0.6 and 2.0 g cream/kg/day of a desonide cream, 0.05% formulation or 2.0 g/kg of the cream base were administered topically to pregnant rats (gestational days 6-15) and pregnant rabbits (gestational days 6-18). Maternal body weight loss was noted at all dose levels of the desonide cream, 0.05% formulation in rats and rabbits. Teratogenic effects characteristic of corticosteroids were noted in both species. The desonide cream, 0.05% formulation was teratogenic in rats at topical doses of 0.6 and 2.0 g cream/kg/day and in rabbits at a topical dose of 2.0 g cream/kg/day. No teratogenic effects were noted for the desonide cream, 0.05% formulation at a topical dose of 0.2 g cream/kg/day in rats and at a topical dose of 0.6 g cream/kg/day in rabbits. These doses (0.2 g cream/kg/day in rats and 0.6 g cream/kg/day in rabbits) are similar to the maximum recommended human dose based on body surface area comparisons.
Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical

administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when Verdeso Foam is administered to a nursing woman.
Pediatric Use: Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children. HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema. Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children. The effect of Verdeso Foam on HPA axis function was investigated in pediatric patients, ages 6 months to 17 years, in one study. In this study, patients with atopic dermatitis covering at least 25% of their body applied Verdeso Foam twice daily for 4 weeks. Three out of 75 patients (4%) displayed adrenal suppression after 4 weeks of use based on the ACTH stimulation test. The suppression was transient; all subjects' cortisol levels had returned to normal when tested 4 weeks post treatment. Safety of Verdeso Foam has not been evaluated in pediatric patients below the age of 3 months.
Geriatric Use: Clinical studies of Verdeso Foam did not include any subjects aged 65 or over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.
ADVERSE REACTIONS
In a controlled clinical study of 581 patients 3 months to 17 years of age, adverse events occurred at the application site in 6% of subjects treated with Verdeso Foam and 14% of subjects treated with vehicle foam. Other commonly reported adverse events for Verdeso Foam and vehicle foam are noted in Table 1 (Commonly Occurring Adverse Events).

Adverse Event	Verdeso Foam (N=387)	Vehicle Foam (N=194)
System Organ Class		
General disorders and administration site conditions	32 (8%)	31 (16%)
Application site burning	11 (3%)	15 (8%)
Application site atrophy	5 (1%)	0 (0%)
Application site dermatitis	2 (1%)	1 (1%)
Application site reaction	3 (1%)	6 (3%)
Infections and infestations	79 (20%)	38 (20%)
Upper respiratory tract infection	37 (10%)	12 (6%)
Pharyngitis	2 (1%)	0 (0%)
Pharyngitis streptococcal	2 (1%)	1 (1%)
Viral infection	6 (2%)	0 (0%)
Nervous System Disorder	7 (2%)	1 (1%)
Headache	7 (2%)	1 (1%)
Psychiatric Disorder	3 (1%)	0 (0%)
Irritability	2 (1%)	0 (0%)
Respiratory, Thoracic and Mediastinal Disorders	27 (7%)	7 (4%)
Asthma	3 (1%)	0 (0%)
Cough	14 (4%)	3 (2%)
Skin and Subcutaneous Tissue Disorders	10 (3%)	6 (3%)
Dermatitis contact	3 (1%)	2 (1%)
Telangiectasia	3 (1%)	0 (0%)

Elevated blood pressure was observed in 6 (2%) subjects receiving Verdeso Foam and 1 (1%) subject receiving vehicle foam. Other local adverse events occurred at rates less than 1.0%. The majority of adverse reactions were transient and mild to moderate in severity, and they were not affected by age, race or gender. The following additional local adverse reactions have been reported with topical corticosteroids. They may occur more frequently with the use of occlusive dressings and higher potency corticosteroids. These reactions are listed in an approximate decreasing order of occurrence: folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae and milaria.

OVERDOSAGE
Topically applied Verdeso Foam can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS).

WARNING
FLAMMABLE. AVOID FIRE, FLAME OR SMOKING DURING AND IMMEDIATELY FOLLOWING APPLICATION.
Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperatures above 120°F (49°C). Avoid contact with eyes or other mucous membranes. Keep out of reach of children.

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Printed in USA September 2006 VER-13-2007-USA
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