# Skin Problems May Provide Clues to GI Disease

BY DOUG BRUNK
*San Diego Bureau*

LA JOLLA, CALIF. — Certain skin conditions may provide clues to the diagnosis of underlying gastrointestinal disease in children, ranging from epithelial defects, polyposis, or vascular syndromes to autoimmune and allergic disease.

"There are several areas of overlap between the skin and the GI tract," Dr. Magdalene A. Dohil said at a meeting sponsored by Rady Children's Hospital and the American Academy of Pediatrics. Diseases of the GI tract that commonly involve some form of cutaneous manifestation include:

**GI disease in epidermolysis bullosa is common, particularly in the recessive dystrophic type.**

DR. DOHIL

► **Epidermolysis bullosa.** This condition presents with different degrees of skin fragility and blister formation. The severity "really depends on the underlying molecular defect," said Dr. Dohil, who is a pediatric dermatologist at Rady Children's Hospital, San Diego. "GI disease in epidermolysis bullosa is extremely common, particularly in the recessive dystrophic type," [in which] almost 80% of children are affected [by dysphagia]."

Other symptoms may include lingual adhesions and microstomia; esophageal disease including strictures, webs, herniation, atony, and pseudodiverticula leading to feeding problems and ultimately protein-energy malnutrition; anemia; and vitamin and mineral deficiency.

► **Blue-rubber bleb nevus syndrome (BRBNS).** This disease causes multifocal venous malformations in the skin and GI tract. Most cases are sporadic, and histology demonstrates intact epithelium but insufficient smooth muscle. Dr. Dohil described the case of a child who presented with venous malformations on the bottom of the foot, which resembled common warts at first glance. "But when you palpate [them], they are soft and compressible."

Common complications of BRBNS include bleeding, chronic anemia, and the need for blood transfusion. Treatment often involves different degrees of surgical intervention including wedge resection, polypectomy, suture ligation, band ligation, and sometimes bowel resection.

"Medical treatment attempts haven't been very successful because these are not proliferative tumors, so we don't expect them to respond to corticosteroids or interferon," said Dr. Dohil, also of the University of California, San Diego. Capsule endoscopy "facilitates the diagnosis and follow-up of children who need endoscopic intervention and assessment."

► **Peutz-Jeghers syndrome.** The hallmark skin-related characteristics of this disease include mucocutaneous pigmentation due to melanin deposition. A GI work-up often reveals polyps that may reach into the antral part of the stomach or present throughout the duodenum. These polyps can cause significant morbidity including obstruction, intussusception, pain, hematochezia, and prolapse.

Children with Peutz-Jeghers also carry a high risk of developing invasive carcinoma. In fact, their cumulative risk of developing cancer is 93%, most commonly cancers of the breast, colon, and pancreas, noted Dr. Dohil.

► **Cowden's disease.** This condition, also known as multiple hamartoma–neoplasia syndrome, causes hamartomas that involve the skin, intestine, breast, and thyroid. It is autosomal dominant and has near complete penetrance by age 20 years. Only 40% of cases will have GI polyposis, but about 80% of cases will present with dermatologic tumors. Consider the diagnosis if you spot more than one trichilemmoma.

► **Henoch-Schöenlein purpura.** The most common skin presentation is a petechial rash that may develop into multiple raised purpuric lesions. GI symptoms occur in 50%-85% of cases and include abdominal pain, bleeding, vomiting, and bowel edema.

The GI effects include mucosal redness, as well as duodenal petechiae and hematomalike protrusions. Most of these changes can be detected with ultrasound.

► **Celiac disease.** Marked by a genetically determined intolerance to gluten, classic GI symptoms include abdominal distention, weight loss, failure to thrive, and diarrhea. Although serology has facilitated the diagnosis, small-bowel biopsy remains the preferred method.

"In these cases you will see villous atrophy, crypt hyperplasia, and lymphocytic infiltrate," Dr. Dohil said. "Such a blunted GI tract doesn't bode well for the absorptive functions that it's intended for."

Dermatitis herpetiformis (Duhring's disease) is considered a cutaneous manifestation of celiac disease. This condition affects about 25% of celiac disease patients and is marked by a pruritic eruption of lesions that may be symmetrical, erythematous, papular, vesicular, or bullous. It commonly occurs in the trunk area and on the back of the forearm and elbow. These lesions "are fairly uncommon in children, and when they do occur they may not be very distinct," she said. Recently a variety of skin conditions such as xerosis, urticaria, vitiligo, and alopecia areata have been linked to celiac disease. However, since they are fairly nonspecific, skin biopsies with direct immunofluorescence and antibody studies of gliadin, endomysium, and transglutaminase are often needed to confirm the diagnosis. Treatment includes dapsone and a gluten-free diet for life.

Dr. Dohil reported that she had no relevant disclosures to make. ■

# New Findings on Chronic Urticaria Refine Screening, Improve Outcomes

BY SHARON WORCESTER
*Southeast Bureau*

SAN ANTONIO — Treatment of chronic urticaria can be challenging, but recent findings on the condition may help improve outcomes, Dr. Aniko Kobza Black reported at the annual meeting of the American Academy of Dermatology.

One new advance is the usefulness of the autologous serum skin test (ASST) in screening for autoimmune urticaria, even though positivity can persist after clearing in autoimmune urticaria. With other types of urticaria, the test becomes negative as the condition improves and resolves.

Another recent finding is the association between a positive ASST and multiple drug sensitivities in patients with acute urticaria, said Dr. Black of St. John's Institute of Dermatology, St. Thomas Hospital, London.

Yet another new finding related to the ASST "may have practical implications." Dr. Black explained that by using plasma rather than serum in the test, the positive test rate can be increased from 55% to 86% in patients with chronic urticaria. "There is an additional factor in plasma that induces histamine release, and it's now been shown that in chronic urticaria, there is increased thrombin formation. Thrombin can activate mast cells, so the modulation of the coagulation system with anticoagulants may prove useful in therapy for urticaria."

The role of *Helicobacter pylori* in chronic urticaria is controversial. About 40% of patients have abdominal symptoms, but no evidence shows *H. pylori* infection causes the condition. It may be that it plays an indirect role in genetically predisposed individuals, but this remains unclear.

First-line treatment for chronic urticaria remains low-sedation antihistamines. The use of doses above recommended levels remains controversial—it seems to be clinically effective in some patients, but no trials have shown efficacy with the approach.

In rare cases, antihistamines may actually aggravate urticaria. Allergic reactions can occur in minutes but usually occur after 6 hours, and they have been seen with each type of antihistamine. No definite cause is known, but the reactions may be the result of a direct effect on mast cells.

When deciding on treatment, first consider possible side effects, then ease of administration, and then cost, she advised.

It is not possible to predict which treatments will be effective in a given patient. When first-line antihistamine treatments and combinations aren't adequate, it is important to reassess disease severity, patient history, and ASST status before trying the second- and third-line treatments because of the risk of side effects. All three types of treatments can be combined, however, "and indeed they usually have to be," Dr. Black said. ■

# *Ceftobiprole Rivals Vancomycin-Based Combination for Skin Infections*

BY BRUCE K. DIXON
*Chicago Bureau*

Monotherapy with ceftobiprole was found to be as effective as vancomycin plus ceftazidime for treating patients with a broad range of complicated skin and skin-structure infections caused by gram-positive and gram-negative bacteria.

The Food and Drug Administration granted ceftobiprole fast-track status for the treatment of complicated skin and skin-structure infections caused by methicillin-resistant staphylococci and hospital-acquired pneumonia. Ceftobiprole is a novel, broad-spectrum cephalosporin developed jointly by Basilea Pharmaceutica AG and Cilag AG International, a Johnson & Johnson company.

The randomized, double-blind, multicenter trial included 828 patients with diabetic foot infections, abscess, cellulitis, and wound infection, reported Gary J. Noel and his fellow researchers, all full-time employees of Johnson & Johnson Pharmaceutical Research and Development, Raritan, N.J., which funded the study (Clin. Infect. Dis. 2008;46:647-55).

Infecting pathogen types—identified in at least 10 patients at baseline—included coagulase-negative and coagulase-positive staphylococci, *Pseudomonas aeruginosa*, β-hemolytic streptococci, and enterobacteriaceae. The most prevalent pathogens were gram-positive bacteria, specifically methicillin-resistant *Staphylococcus aureus* (MRSA) in 123 patients and methicillin-susceptible *S. aureus* (MSSA) in 250 patients.

The patient cohort, accumulated over 129 international sites, was divided into two arms, with 547 patients receiving ceftobiprole and 281 receiving the glycopeptide antibiotic vancomycin plus the third-generation cephalosporin ceftazidime. Respectively, the two study arms consisted of 63% and 64% men and had mean ages of 53 years and 52 years. The proportion of patients completing the trial was 92% in the ceftobiprole arm and 90% in the comparator arm.

Patients in the ceftobiprole arm received 500 mg for 120 minutes every 8 hours. In the comparator group, the starting dose was 1,000 mg vancomycin infused over 60 minutes every 12 hours plus 1,000 mg ceftazidime infused over 120 minutes every 8 hours. The mean duration of treatment in the clinically evaluable population was about 9 days in both arms, the authors noted.

At the test-of-cure (TOC) visit (after 6-17 days of treatment) for the evaluable patients, clinical cure occurred for 439 of 485 (91%) ceftobiprole-treated patients and for 220 of 244 (90%) comparator-treated patients, the researchers noted. ■