gluten sensitivity compared with those with celiac disease ($P < .001$). Antigliadin antibody IgA was detected in 1 child with gluten sensitivity and in 11 children with celiac disease ($P < .001$). HLA-DQ2 was present in all children with celiac disease and in 7 (46%) of the 15 children with gluten sensitivity. Results of small bowel biopsies of gluten-sensitive children revealed 9 (82%) of 11 had normal mucosa, and 2 (18%) of 11 had Marsh stage 1 mucosa (increased intraepithelial lymphocytes).

CONCLUSIONS. Children with gluten sensitivity lack reliable serologic or genetic markers of the disease, as is the ease in adults with gluten sensitivity. However, similar to previous observations in adult gluten-sensitive patients, this study found that native antigliadin antibody IgG positivity and presence of HLA-DQ2 are more common in children with gluten sensitivity compared with control subjects.

REVIEWER COMMENTS. Antigliadin antibodies are commonly present in any patient with a disrupted gastrointestinal barrier, and they have actually fallen out of favor in the diagnosis of celiac disease. Thus, antigliadin antibody IgG positivity in nonceliac gluten-sensitive patients should be considered with caution. No biomarker for gluten sensitivity exists, and gluten sensitivity remains a clinical diagnosis. Other studies suggest that fermentable, oligo-, di, monosaccharides and polyols (FODMAPs) may be the symptom-inducing components of wheat, and not gluten itself. Carefully crafted prospective, double-blind studies are needed to further characterize gluten sensitivity and to clarify whether FODMAPs are involved.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2014–1817QQ

Matthew F. Feldman, MD
J. Andrew Bird, MD
Dallas, TX

Fructose Intolerance/Malabsorption and Recurrent Abdominal Pain in Children

PURPOSE OF THE STUDY. The goal of this study was to determine the incidence of fructose malabsorption in children who present with chronic or recurrent abdominal pain and whether a low-fructose diet improves their symptoms.

STUDY POPULATION. Study participants were recruited after retrospective chart review of consecutive patients from 2007 to 2009 without a specific etiology identified for chronic abdominal pain. A total of 222 children ages 2 to 19 years (64% female) who had been evaluated by a pediatric gastroenterologist for persistent abdominal pain completed the study.

METHODS. All enrolled participants underwent a breath hydrogen test (BHT) after a fructose ingestion dose of 1 g/kg (maximum: 25 g). A breath hydrogen value of $\geq 20$ ppm from baseline was considered positive for fructose malabsorption. These participants, with the aid of a dietitian, underwent a low-fructose diet with subjective follow-up assessment of clinical symptoms.

RESULTS. A total of 121 (55%) of 222 participants had a positive fructose BHT result. All 121 participants completed a 2-month low-fructose diet, with 77% ($P < .0001$) experiencing clinical improvement. Fifty-four percent of the fructose-negative BHT participants reported resolution of symptoms without a low-fructose diet although this finding did not reach statistical significance ($P = .37$).

CONCLUSIONS. Not only is fructose malabsorption a common underlying etiology for pediatric functional abdominal pain, but intervention with a low-fructose diet is highly successful.

REVIEWER COMMENTS. The approach to evaluate an “adverse food reaction” should be to determine whether it is immune or nonimmune mediated. Although the history for fructose malabsorption will undoubtedly be inconsistent for an IgE-mediated anaphylaxis food reaction, the labeling of a patient with “functional abdominal pain” is equally unsatisfying for the family. Of note, many of the “high-fructose” foods are also the same foods causing oral allergy syndrome, an IgE-mediated process occurring after ingestion of raw fruits that share similar proteins to pollen allergens. Although a fructose BHT many not be readily available, this article provides an excellent fructose food avoidance table that should be considered a valuable resource for both pediatricians and allergists who are evaluating children with adverse food reactions resulting in abdominal pain or underlying chronic functional abdominal pain.


Kirk H. Waibel, MD
Landstuhl, Germany

Challenge-Proven Nonsteroidal Anti-Inflammatory Drug Hypersensitivity in Children

PURPOSE OF THE STUDY. The goal of this study was to determine the frequency of true nonsteroidal antiinflammatory drug hypersensitivity (NSAID-H) and whether there were any factors in the history that could predict NSAID-H in children.

STUDY POPULATION. The study population included 58 children, aged 4 months through 17.8 years, with suspected NSAID-H based on a history of acute reactions, including urticaria/angioedema, bronchospasm, laryngeal edema,
rhinitis, and systemic reactions involving hypotension, laryngeal edema, bronchospasm, and/or shock.

METHODS. All subjects completed a questionnaire detailing the implicated NSAID, their reaction history, and any individual risk factors. Subjects were stratified into 2 separate groups: those who reacted to a single NSAID and those who reacted to multiple NSAIDs. Based on a diagnostic algorithm, those with a positive result on skin prick test (SPT) to a single NSAID (n = 1) were labeled as NSAID-H, and those with negative or no available SPT underwent an oral provocation test (OPT). Those with a confirmed history of anaphylaxis did not undergo OPT. Subjects with a history of reaction to ≥2 NSAIDs underwent OPT. Subjects received 4 to 5 escalating doses of the culprit NSAID at 60-minute intervals until they reached the maximum single dose. Patients were observed for 2 hours after the OPT to monitor for delayed reaction. All challenges were continued for 2 days at home, and subjects were contacted via telephone for follow-up. OPTs were performed in all children with confirmed NSAID-H in an attempt to find a safe alternative.

RESULTS. Sixty-five percent (n = 38) reported a reaction to a single NSAID. Thirty-five of these subjects underwent an OPT, and 5 had proven NSAID-H. Of the 20 patients who reported reactions to multiple NSAIDs, 8 had proven NSAID-H with OPT. Twelve patients were challenged to find a safe alternative, of whom 60% tolerated acetaminophen and 89% tolerated nimesulide. There was no association between gender, atopic status, presence of atopic disease, history of anaphylaxis, history of multiple reactions with the same NSAID, and safe use of a similar group of NSAD and OPT results. Family history of NSAID-H and having a reaction with multiple NSAIDs were associated with a positive result on OPT.

CONCLUSIONS. A history of reaction to both single and multiple NSAIDs was usually not indicative of true drug hypersensitivity. Therefore, diagnostic tests should be considered in all children with suspected NSAID-H.

REVIEWER COMMENTS. Although suspected allergic reactions to NSAIDs are very common, true allergy is uncommon in children compared with adults. This impression was confirmed in this study, with true allergy confirmed in only ~25% of those reporting a history of reaction. This study also confirms the value in performing provocation tests, and the lack of value in skin testing, in children presenting with a history of a suspected NSAID allergy.

Patterns of Clinical Management of Atopic Dermatitis in Infants and Toddlers: A Survey of Three Physician Specialties in the United States

PURPOSE OF THE STUDY. The goal of this study was to describe atopic dermatitis (AD) management patterns in children aged ≤36 months as reported by pediatricians, dermatologists, and allergists in the United States.

METHODS. A nationally representative survey was administered to pediatricians (n = 101), dermatologists (n = 26), and allergists (n = 26). Main outcomes included referrals to health care professionals, suggested/ordered laboratory tests, and management approaches (dietary, pharmacologic, or combination of both) according to age, AD location, and severity.

RESULTS. Significant differences were observed in referrals to health care professionals (P < .001). Pediatricians more frequently referred children to dermatologists than allergists in mild (52.4% vs 32.0%) and moderate/severe (60.6% vs 38.1%) cases. Dermatologists referred children to allergists less frequently for mild (9.1%) than moderate/severe (40.7%) AD cases. Pediatricians (59%), allergists (61.5%), and dermatologists (26.9%) reported treating at least some of their patients with AD by using dietary management (infant formula change) alone (with or without emollients). Soy-based formulas were often used. For mild AD, the most commonly reported first-line pharmacologic treatments included topical emollients, topical corticosteroids, and barrier repair topical therapy/medical devices. More than 80% of physicians used a dietary and pharmacologic combination approach. Dermatologists were most likely to manage AD symptoms with a pharmacologic-only approach. Location of the AD lesion influenced pharmacologic treatment in >80% of physicians.

CONCLUSIONS. Significant and distinct differences in AD treatment approach exist among the physicians surveyed. Most pediatricians and allergists use formula change as a management strategy in some patients, whereas dermatologists favor a pharmacologic approach.

REVIEWER COMMENTS. This survey highlights the need for a more unified approach to the diagnosis and treatment of this chronic disease, which affects 10% to 20% of children. The investigators concluded that pediatricians and allergists were more likely to use formula change as a management strategy, with allergists specifically more likely to use laboratory tests (eg, IgE, skin prick) or an elimination diet with a food challenge test, and that dermatologists favor a pharmacologic approach to treatment and are less likely to consider food allergy as a cause of AD. A unified approach should be based on the possible etiologies of AD in affected children. This approach requires an understanding of the mechanisms of hypersensitivity to food and some


Ashley Altman, DO
Robert Wood, MD
Baltimore, MD
Challenge-Proven Nonsteroidal Anti-Inflammatory Drug Hypersensitivity in Children
Ashley Altman and Robert Wood
Pediatrics 2014;134;S158
DOI: 10.1542/peds.2014-1817SS

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at: <a href="http://pediatrics.aappublications.org/content/134/Supplement_3/S158.2">http://pediatrics.aappublications.org/content/134/Supplement_3/S158.2</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="https://shop.aap.org/licensing-permissions/">https://shop.aap.org/licensing-permissions/</a></td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online: <a href="http://classic.pediatrics.aappublications.org/content/reprints">http://classic.pediatrics.aappublications.org/content/reprints</a></td>
</tr>
</tbody>
</table>
Challenge-Proven Nonsteroidal Anti-Inflammatory Drug Hypersensitivity in Children
Ashley Altman and Robert Wood
Pediatrics 2014;134;S158
DOI: 10.1542/peds.2014-1817SS

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/134/Supplement_3/S158.2