We found a significant association between susceptibility to childhood atopic asthma and the polymorphism regulating *ORMDL3* expression in a Japanese population. Our data strongly support the important role of *ORMDL3* in childhood asthma. Further investigation of the functional role of the variant during allergic events may provide additional targets for therapeutic interventions and would be helpful to clarify the etiology of childhood asthma.

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How readable are the American Academy of Allergy, Asthma & Immunology "Tips to Remember" leaflets?

To the Editor:

It has long been recognized that good communication has a beneficial effect on clinical outcomes,[1] and patient information leaflets can improve knowledge.[2] However, the information must not only be accurate but also written at an appropriate reading level to be helpful. National literacy surveys conducted since the 1970s have consistently shown that many adult Americans (about 20%) are functionally illiterate and that the average adult reading level is between the seventh and ninth grade levels.[3,4]

The American Academy of Allergy, Asthma & Immunology (AAAAI) "Tips to Remember" leaflets cover a wide range of topics for patients with asthma and allergic diseases, including diagnostic tests and the use of medication. To predict the level of educational attainment needed to understand and benefit from these, we analyzed the readability of the 29 English-language brochures by using the Simple Measure of Gobbledegook (SMOG).[5] This formula was selected because it is simple, quick, and widely used and has been shown to be reliable and valid in determining reading level.[6] The SMOG formula yields a high correlation (0.985) with the grades of readers who had 100% comprehension of the set material. A score of 8 equates with completion of junior high school. Completed high school is needed for reading material with a score of 12, and tertiary education is required for a score of 13 and above (Table I). Texts with a SMOG score of less than 5 will be understood by most persons, and it has therefore been recommended that health literature should ideally be written at a SMOG score of 5 or less.[7]

To obtain a SMOG score, 30 sentences were selected (10 from the start, 10 from the middle, and 10 from the end of the brochure) and pasted into the SMOG Calculator (http://www.wordscount.info). We found that the "Tips to Remember" brochures have SMOG scores ranging from 12.27 to 16.78 (ie, requiring successful completion of education between high school graduation and university degree; Table I). For comparison, we scored the readability of 6 editorial and review articles from the *Journal of Allergy and Clinical Immunology*. We randomly selected one article from volumes 113 to 118. Original research articles were excluded, so that the text was relatively free of abbreviations, gene sequences, or numeric data. These editorials and reviews had SMOG scores of between 15.37 and 17.46 (mean, 16.55; Table I).

Sometimes methods based on word length are criticized because they disregard patients' familiarity with the vocabulary that is associated with their illness, thereby overestimating the difficulty of the text. Because the word *allergy* and its many derivatives are polysyllabic, we assessed whether complexity of the text was reduced if familiar words such as *allergy*, *allergies*, *allergist(s)*, *allergic*, *allergenic*, and *allergen(s)* were excluded from the scoring. These exclusions had very little effect on the readability of the brochures. For example, the brochure showing the greatest shift in score ("What are allergy shots?") decreased from 15.08 to 13.20 after removing these words (Table II). We then went on to exclude from the scoring all the polysyllabic medical and technical terms defined within each brochure. The readability scores improved further, but the magnitude of shift makes very little

TABLE I. Distribution of SMOG scores of AAAAI leaflets in comparison with educational level, popular literature, and a sample of *Journal of Allergy and Clinical Immunology* editorial and review articles

SMOG grade*	No. of AAAAI leaflets	Educational level	Sample periodical	Sample JACI editorial [SMOG score]
0-6	0	Low-literate	*Soap Opera Weekly*	
7	0	Junior high school	*True Confessions*	
8	0	Junior high school	*Ladies' Home Journal*	
9	0	Some high school	*Reader's Digest*	
10	0	Some high school	*Newsweek*	
11	0	Some high school	*Sports Illustrated*	
12	4 (14%)	High school graduate	*Time Magazine*	
13-15	23 (79%)	Some college	*New York Times*	Colice GL. Small airway disease: a riddle wrapped in a mystery inside an enigma. 2006;118:337-9 [15.37]
				Casale TB. Status of immunotherapy: current and future. 2004;113:1036-9 [15.57]
16	2 (7%)	University degree	*Atlantic Monthly*	Bender BG, Leung DY. Sleep disorders in patients with asthma, atopic dermatitis, and allergic rhinitis. 2005;116: 1200-1 [16.23]
17-18	0	Postgraduate studies	*Harvard Business Review*	Galli SJ. Pathogenesis and management of anaphylaxis: current status and future challenges. 2005;115:571-4 [17.28]
				Moffitt JE, Golden DBK, Reisman RE, Lee R, Nicklas R, Freeman T, et al. Stinging insect hypersensitivity: a practice parameter update. 2004;114:869-86 [17.38]
				Gold DR. Allergy: the price paid for longevity and social wealth? 2006;117:148-50 [17.46]
19+	0	Postgraduate degree	IRS code	

JACI, Journal of Allergy and Clinical Immunology.
Adapted from McLaughlin GH. SMOG grading: a new readability formula. Journal of Reading 1969;12:639-46. Available at: http://harrymclaughlin.com/SMOG.htm. Accessed January 9, 2007.
*The SE of the estimated SMOG grade level is 1.52.

difference to the educational attainment required, and patients would still require successful completion of high school to understand most brochures. To our knowledge, this is the first time that anyone has objectively addressed this frequent criticism of readability scores disregarding patient's potential knowledge.

Full comprehension of these AAAAI brochures requires an educational level equivalent to completion of high school, and the most demanding leaflets have SMOG scores similar to the editorials and review articles in the *Journal of Allergy and Clinical Immunology*. To attain high levels of reader comprehension, all of these brochures would require revision. Alternatively, it might be more realistic to match readers with existing materials and to devise alternative literature for those with lower reading abilities. In addition, it would be worthwhile to strive for lower readability scores when revising brochures.

Readability formulae do have limitations. Ideally, testing should be done with patients because reading is a complex process, and the ability to comprehend a text is influenced by presentation (organization, print, and illustrations), situation (eg, stress), and reader characteristics (eg, motivation and maturity). Such testing is very resource intensive, but a pragmatic solution for clinicians is to use readability formulas, such as SMOG, which correlate well with the reader's comprehension.[5] The required grade level predicted by the SMOG formula does tend to be higher than other scoring methods because SMOG is based on 100% comprehension, whereas some other scores aim for lower levels of comprehension.

As educated health professionals, we might fail to realize just how much easier it is for us to read a text compared with many of our patients. Poor readability does not mean that the patient will obtain partial information: when texts exceed a person's literacy levels, he or she usually just stops reading altogether. Low levels of literacy are not confined only to immigrants, the elderly, or high school dropouts; the problem is ubiquitous and therefore very difficult to identify. The American Medical Association has recently developed an educational program to raise awareness of the health literacy problem.[8] To avoid giving out "Tips to Remember" brochures inappropriately, we need to be alert to the varying literacy skills of patients. For less-literate patients, we need to use texts written for people with more diverse reading skills (eg, AAAAI Pediatric Asthma Handouts). Where alternative brochures are not currently available, we might need to meet patients' information needs differently (discussion, video, and audiotapes). In the longer term, we should aim to develop a wider range of allergy and asthma patient information brochures enabling clinicians to provide the level and amount of information that best fits each patient's needs.[9]

In conclusion, "Tips to Remember" brochures currently have readability scores requiring successful completion of education between high school and a university degree. As a result, this range of brochures is not accessible or comprehensible to all patients, and therefore we must adopt strategies for recognizing patients with lower levels of literacy and meet their information

TABLE II. SMOG readability scores of AAAAI "Tips to Remember" brochures (listed alphabetically)

	SMOG score			
Brochure title	**No words excluded**	***Allergy* and related words excluded**	**Defined words excluded**	**Defined words**
Adverse reactions to medications	14.92	13.95	13.77	Anaphylaxis/actic, dehydrated, immunoglobulin
Allergic skin conditions	14.27	13.58	12.64	Urticaria, eczema, angioedema, atopic dermatitis, histamine, rhinitis, irritant, urushiol, neomycin
Asthma and allergy medications	16.11	15.49	15.12	Stabilizer, leukotriene, bronchodilator, β-agonist, rhinitis, theophylline, anticholinergic, antihistamine, histamine, decongestant, corticosteroid
Asthma and pregnancy	13.63	13.00	12.17	Pregnancy
Asthma medications and osteoporosis	13.15	13.00	12.10	Osteoporosis, glucocorticosteroid
Asthma triggers and management	16.78	16.11	15.00	Esophagus, irritants, infection, rhinitis, sinusitis, exercise-induced, gastroesophageal, bronchodilator, corticosteroid, cromolyn, nedocromil, leukotriene modifiers, beta2agonist, methylxanthines, omalizumab
Childhood asthma	13.54	13.34	13.34	Atopic dermatitis
Cough in children	12.38	12.06	11.83	Rhinitis, sinusitis esophagus, pollutants
Exercise-induced asthma	14.79	14.53	14.49	Rhinitis, exercise induced, expiratory, Spirometer
Food allergy	15.33	14.27	13.86	Immunoglobulin, intolerance, cross reactivity, coincidental, atopic dermatitis, eczema, anaphylaxis, additives, challenges
Guide to health care plans	15.00	14.66	14.00	Formulary, gatekeeper, pre-existing, primary care provider
Indoor allergens	13.39	12.11	11.94	Perennial
Latex allergy	13.82	12.80	12.70	Dermatitis, anaphylaxis, cross reactivity, spina bifida
Occupational asthma	15.04	14.83	14.27	Isocyanates, histamine, acetylcholine, occupational
Outdoor allergens	12.54	11.60	11.25	Rhinitis, seasonal
Prevention of allergies and asthma in children	14.36	13.44	13.44	
Recurrent and unusually severe infections	12.59	12.54	12.33	Exposure, susceptibility, respiratory tract infection, rhinitis, immunodeficiency, antibodies, intravenous immunoglobulins
Rhinitis	14.18	13.25	12.11	Rhinitis, antihistamine, corticosteroid, leukotriene, immunotherapy
Role of the allergist/immunologist	14.22	12.95	12.70	Immunoglobulin, mediator, rhinitis, sinusitis, atopic dermatitis, urticaria, angioedema, anaphylaxis
Sinusitis	14.49	14.00	13.00	Sinusitis, subacute, respiratory infection, immunotherapy, rhinitis, recurrent
Stinging insect allergy	13.77	12.70	12.59	Immunoglobulin antibody, anaphylaxis, Africanized honeybees
The importance of clinical research trials	13.63	13.58	13.58	Placebo, investigator, electrocardiogram
Traveling with allergies	14.49	13.39	13.39	Immunotherapy
Use of inhaled asthma medications	15.73	15.57	15.33	Bronchodilator, glucocorticosteroid, β_2-agonist, nonsteroidal anti-inflammatory medications
What are "allergy shots"?	15.08	13.20	13.00	Immunotherapy, sensitivity, anaphylaxis/actic
What is allergy testing?	15.73	13.34	13.05	Anaphylaxis, immunoglobulin, mediators, histamine, intradermal
What is an allergic reaction?	13.91	12.27	11.37	Immunoglobulin, mediator, histamine, conjunctivitis, rhinitis, urticaria, atopic dermatitis, anaphylaxis, sinusitis, otitis media, immunotherapy
What is anaphylaxis?	14.75	13.77	13.00	Anaphylaxis/actic, anaphylactoid, antihistamine, antibodies
What is a peak flowmeter?	12.27	12.22	12.17	Variability, expiratory
Mean	14.27	13.50	13.09	

needs differently. Looking to the future, the range of information available for patients with asthma and allergic conditions needs to be widened, ensuring that the needs of patients with low and moderate literacy are also met.

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Helminthic infection as a factor in new-onset coffee allergy in a father and daughter

To the Editor:

We report a father and daughter who experienced a new onset of food allergy to coffee occurring after helminth infection (*Clonorchis sinensis*) contracted in China. M.G. is a 55-year-old white Italian man without previous allergy, and V.G. is a 22-year-old woman with allergic rhinitis to grass pollens treated with antihistamines as needed. In May 2005 the father and daughter journeyed to rural areas of China for several weeks. When returning, they were laid over in the Beijing airport for 9 hours. During this period in the airport, they drank a large quantity of green coffee without any other food. A few days later, in Italy, they developed abdominal pain, diarrhea, and urticaria that worsened daily. The feces were initially pultaceous then liquid, accompanied by abdominal colic primarily in the morning. Fecal analyses (parasitologic, cultures, and chemical) and serum tests (*Salmonella-Shigellae*) were negative, as was abdominal sonography. The only abnormal laboratory values were blood eosinophil counts, 1200/mm^3 (father) and 1050/mm^3 (daughter), and serum eosinophil cationic protein (ECP), 44 ng/mL (father) and 84 ng/mL (daughter). Both were treated with oral antihistamine (cetirizine 10 mg/daily) with remission of itching, but without effect on diarrhea. In subsequent months their body weight diminished (10 and 8.5 kg, respectively, for the father and daughter).

Intestinal endoscopy was performed on the daughter, and the histology of the biopsy revealed the presence of *Clonorchis sinensis*. On the basis of this finding, both father and daughter were treated with mebendazole (300 mg twice a day $\times$ 10 days). Subsequent fecal analyses specifically performed to detect *Clonorchis sinensis* (Kato-Katz method and formalin-ether sedimentation technique) were negative in samples taken for 3 consecutive days; however, clinical symptoms of diarrhea and urticaria continued. Liver and bile duct ultrasounds performed monthly were negative. Two months after mebendazole therapy, blood eosinophils (1150/mm^3 [father] and 1100/mm^3 [daughter]) and serum ECP (52 ng/mL [father] and 73 ng/mL [daughter]) remained elevated, reducing the chance that these abnormalities were caused by ongoing parasite infection.

Importantly, they reported that diarrhea and urticaria were more evident after meals, in particular after breakfast when they usually drank only coffee. Thus, they eliminated coffee, and the urticaria and diarrhea completely resolved. Three successive coffee challenges consistently induced immediate symptoms. Skin prick testing for coffee was positive, and elevated coffee-specific serum IgE was documented (4.8 and 5.9 kU/L, respectively; CAP-FEIA; Phadia, Uppsala, Sweden). Total IgE were 599 (father) and 600 (daughter). Sensitization to coffee was further studied by *in vitro* methods. Lymphocyte proliferation and cytokine production by peripheral blood lymphocytes were evaluated in allergen-stimulated and unstimulated 5-day cultures (freeze-dried coffee allergen 5 μg, to be diluted in PBS; Lofarma, Milan, Italy). Results of lymphocyte proliferation and cytokine production are summarized in Table I. After a diet that eliminated coffee, the symptoms disappeared, but skin prick tests were still positive. After 3 months of this elimination diet, blood eosinophil counts were normal (300/mm^3 and 600/mm^3, respectively) as ECP levels, presumably reflecting the lack of coffee as a trigger of eosinophilia.

We hypothesize that the helminth infection facilitated the new onset of food allergy to coffee. One mechanism may be that the infection caused increased intestinal permeability of allergenic molecules through the enteric wall, altering antigen presentation/processing with consequent sensitization. In fact, these cases are similar to a previous case concerning a woman with pollen allergy who developed food allergy after cobalt (^{60}Co) therapy that induced damage of the enteric mucosa.[1] The precise mechanisms remain unknown, but Katz's theory[2] would indicate that *Clonorchis sinensis* may produce a transient disturbance of immune tolerance, resulting in an "allergic breakthrough." Considerable swelling of the small intestine occurs a few days after helminth infection. The intestines, as shown in mice, have an increase in mucosal permeability (studied with mannitol) because of an abundance of mast cells in the small intestine after infection.[3] Enterocytes from human beings, rat, and mouse constitutively express MHC class II molecules, with enhanced expression in states of inflammation. These cells are mostly restricted to the basolateral membrane, where the enterocytes contact the intraepithelial and lamina propria lymphocytes. Endocytosis in the polarized epithelial cells from the apical surface differs from uptake from the basolateral face. The processing of luminal antigens normally exposed only at the apical surface might orchestrate a different immunologic outcome when these antigens gain access to the basolateral surface of the enterocytes via leaky tight junctions. An antigen that normally elicits no significant responses, or a tolerogenic response when processed apically, may become immunogenic after processing from the basolateral membrane. Furthermore, during inflammation, the enterocytes express the costimulatory molecules CD80 (B7-1) or CD86 (B7-2).[4] Thus, under pathologic conditions, the enterocytes function as professional antigen-presenting cells and stimulate mucosal CD4$^+$ T-cell responses.

This altered response may lead to an allergy to food proteins in patients with helminth infection characterized by an evident IgE response and a low regulatory T-cell activity; however, other patients with high regulatory cell activity during helminth infections are protected from allergy.[5] Indeed, conflicting findings have been reported in the literature with regard to enhanced allergy compared with reduced allergy associated with helminth infection, with populations living in areas of low prevalence of helminth parasites having a greater risk of allergic responses to environmental allergens, and populations living in areas of high prevalence having a reduced risk of allergy.[6]