for identifying AD. Requiring a diagnosis of AD is problematic given the lack of use of the terminology AD by clinicians and patients during clinical encounters, health disparities, and poor access to specialty care in the United States. Had that study employed UKWP-like criteria alone, the prevalence would have likely been approximately 7%, which we posit is the true US prevalence of AD.

We confirmed previously observed associations of adult AD with female sex, higher education status, and household income, and inverse associations with black race, Hispanic ethnicity, birthplace outside the United States, and currently working.[1]

Adult AD was also associated with higher rates of divorce and separation. Atopic dermatitis is worsened by emotional factors, which may trigger or flare AD in aduilts. Indeed, early life stressful events, including parental divorce, were found to be associated with higher risk of childhood AD.[7] Similarly, US children from families with single or unmarried mothers and nonbiological fathers had increased odds of AD and poor health outcomes, even after controlling for parental history of AD.[8] Moreover, AD is associated with impaired quality of life, including vitality, social functioning, relationships, and mental health, and higher rates of sleep disturbances, fatigue, anxiety, and depression.[9,10] The negative life impacts of AD and comorbidities on social function and relationships may increase risk of separation and divorce. Parents with AD and concomitant psychosocial stressors may indirectly confer increased AD risk to their children through psychosocial stressors, in addition to established hereditary AD risk factors. Improved treatment of adult AD might reduce psychosocial stressors, quality of life impact, subsequent family impact, such as separation and depression, and possibly even rates of AD in their offspring. Future studies are needed to confirm these associations and determine whether AD treatment mitigates these effects.

In conclusion, AD occurs in 7% of US adults and is associated with higher odds of divorce or separation and previously demonstrated sociodemographic factors.

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Allergy to ginger with cysteine proteinase GP-I as the relevant allergen

Ginger (*Zingiber officinale*) belongs to the family Zingiberaceae, along with cardamom and turmeric. The edible portion is the horizontal rhizome, and it is valued for aroma and spicy flavor. The US Food and Drug Administration considers ginger to be a food additive that is "generally recognized as safe." Rare cases of immunoglobulin (Ig)E-mediated allergy to ginger have been reported,[1-3] but specific allergens have not been described.

We report 4 cases of IgE-mediated allergy to ginger. Patients were 52, 50, 45, and 40 years of age (patients 1, 2, 3, and 4, respectively), patients 1 and 2 presented with a history of vomiting, diarrhea, and dyspnea; patient 1 also presented with abdominal bloating and hypotension, whereas patient 3 presented with palpitations, profuse sweating, diarrhea, and loss of consciousness within minutes of consuming raw ginger. Patient 4 reported facial angioedema and conjunctival injection after handling ginger powder but tolerated ingestion of ginger. All patients tolerated ingestion of cardamom and turmeric. Patients 1, 2, and 4 had no atopic background, and patient 3 reported seasonal rhinoconjunctivitis caused by grass pollen. Skin prick tests (SPT) to commercial extracts of common aeroallergens (ALK Allergologisk Laboratorium A/S, Horsholm, Denmark), including pollens, dust mites, molds, danders, and pan-allergens such as palm pollen profilin (Pho d 2) and peach lipid transfer protein (Pru p3) were performed with negative results (wheal < 3 mm) to all of the 24 allergens tested for patients 1, 2, and 4. Patient 3 showed positive SPT to pollen (*Phleum pratense, Olea europaea, Platanus acerifolia, Cupressus arizonica*). Prick-by-prick skin test with raw ginger was positive in all patients (wheal diameter for: patient 1: 7 mm; patient 2: 8 mm; patient 3: 12 mm; patient 4: 6 mm). Three healthy control subjects had negative skin test with raw ginger, serum specific IgE (sIgE) to ginger (ThermoFisher Scientific Phadia AB, Uppsala, Sweden) was 2.2, 4, 5, and 2.5 kUA/L, respectively. A raw ginger extract (GE) was prepared by homogenization in phosphate-buffered saline (20% wt/vol), dialysis, and lyophilization (Roxall Laboratory, Bilbao, Spain). Protein content of GE was 21% (wt/wt) according to Bradford.[4] Skin prick test with GE was positive in all patients (wheal diameter for patient 1: 6 mm; patient 2: 7 mm; patient 3: 10 mm; patient 4: 6 mm). The GE was analyzed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) as described by Laemmli,[5] showing protein bands ranging from 90 kDa to 8 kDa (results not shown). The SDS-PAGE IgE immunoblotting assays with the individual patients' sera were performed and revealed

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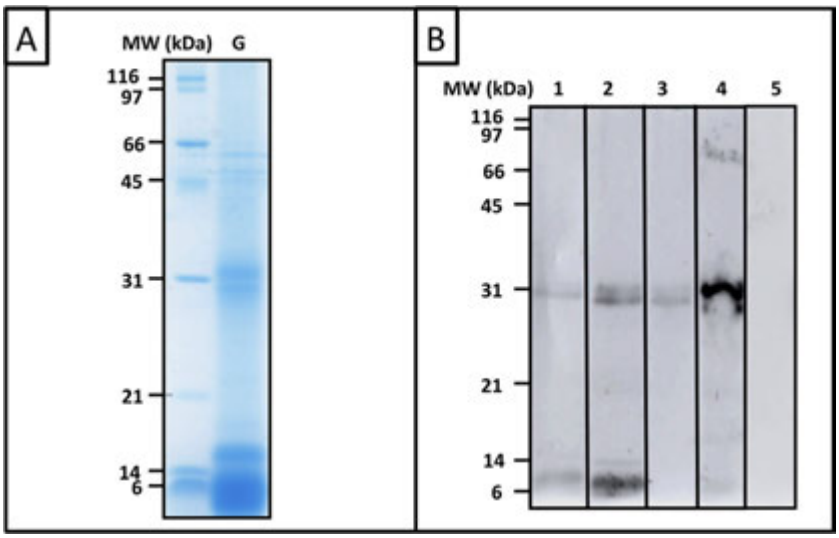

Figure 1. A: Lane G: Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) analysis of raw ginger extract (nonreducing conditions). B: SDS-PAGE immunoglobulin E (IgE) immunoblotting with patient's sera. Lanes P1-P4: Patient's sera; Lane P5: control serum (pool of sera from nonatopic subjects); MW: molecular weight marker; kDa, kilo-Dalton.

IgE-reactivity bands with molecular weights of approximately 30 and 32 kDa; furthermore patient 2's serum showed bands of 8 to 10 kDa, and patient 1 serum showed a band of 8 kDa (Fig 1). Immunoglobulin E–binding bands were selected using pooled sera from all patients. The 8-, 10-, 30-, 32-kDa protein bands of GE extract were manually excised from the gel, digested with trypsin, and analyzed by matrix-assisted laser desorption/ionization time of flight and liquid chromatography coupled to tandem mass spectrometry (MS/MS), following the methods of Pastor et al.[6] Protein identification was performed by searching a nonredundant protein sequence database (National Center for Biotechnology Information), using the Mascot program (http://www.matrixscience.com). When compared with the databases, the analysis of the resulting peptides by MS or MS/MS corresponded to the cysteine protease GP-I for the 30- and 32-kDa band. No matches were found for the 8- and 10-kDa bands. Cysteine proteases, also known as thiol proteases, are enzymes that degrade proteins. They share a common catalytic mechanism that involves a nucleophilic cysteine thiol in a catalytic triad or dyad. Twenty families of peptidases dependent on a cysteine residue at the active center are known.[7] They have been previously described as allergens in several allergenic sources and may behave as either ingested (kiwi Act d 1, pineapple Ana c 2, papaya Cari p chymopapain, Cari p papain, Fic c ficin, and soy Gly m Bd 30K) or inhaled allergens (ragweed Amb a 11, dust mite Blo t 1, and Der p 1).[8] Ginger proteases from ginger rhizome, *Zingiber officinale*, were first reported in 1973.[9] Two proteases, designated GP-I and GP-II, were isolated by chromatography on diethylaminoethyl cellulose and tentatively classified as cysteine proteases based on their inhibition by thiol reagents and their relative molecular masses.

In summary, we report 4 patients with IgE-mediated allergy to ginger. Three patients developed symptoms after ingesting raw ginger, and 1 patient developed symptoms after handling ginger powder. Our study identified cysteine protease GP-I and 8-, 10-kDa protein bands as potential ginger allergens. Physicians should recognize that in addition to dyspepsia or gastrointestinal intolerance symptoms,[10] ginger has the potential to also induce IgE-mediated allergic reactions.

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