

Subjective Health Complaints and Modern Health Worries in Patients with Subjective Food Hypersensitivity

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Perceived food hypersensitivity is much more common than food allergy as medically verified. Unexplained symptoms and wrong attribution are typical in subjective health complaints. We hypothesize that subjective health complaints and worries are abnormally prevalent among patients with subjective food hypersensitivity. Forty-six patients with subjective food hypersensitivity and two control groups, one formed by 50 health care workers and one by 70 sex- and age-matched volunteers from the general population, were included in our study. All filled in two questionnaires: Subjective Health Complaints Inventory and Modern Health Worries Scale. None of the patients had IgE-mediated food allergy. The patients scored significantly higher than the controls on sum scores for four domains of subjective health complaints, including gastrointestinal complaints ($P < 0.001$), musculoskeletal complaints ($P < 0.01$), “pseudoneurology” ($P < 0.001$), and allergy ($P < 0.001$). Sum scores on modern health worries did not differ significantly between groups. The results support our hypothesis of an association between subjective food hypersensitivity and subjective health complaints, corroborating the view that, in the absence of food allergy, the conditions are sharing pathogenetic mechanisms.

KEY WORDS: food hypersensitivity; food allergy; subjective health complaints; modern health worries.

Perceived food hypersensitivity is common. Surveys from England and the Netherlands showed that 15–20% of the general population claimed adverse reactions to food, even though food allergy could be confirmed in only 1–2% (1, 2). The pathogenesis of adverse reactions to food is poorly understood (3). The possibility of a correct diag-

nosis is also unsatisfactory and there is disagreement as to why this is the case (4, 5). The fact that perceived adverse reactions to food often remain unexplained (i.e., subjective) constitutes a continuous concern for many patients (6). The same is true for subjective health complaints in general. Subjective health complaints are defined as symptoms or complaints that, despite thorough examination, cannot be fully explained. They represent a significant health problem, as they are the most frequent sources of long-term sickness compensation and permanent inability to work (7). Whether there is an association between subjective food hypersensitivity and subjective health complaints has not been systematically examined previously.

Unexplained symptoms are typical in both conditions, and our hypothesis is that they are sharing pathogenetic mechanisms. According to Brosschot

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cognitive–emotional sensitization is considered an important pathogenetic mechanism in subjective health complaints (8). We therefore postulate that cognitive sensitization is similarly important in subjective food hypersensitivity. In fact, cognitive sensitization could be a much more prevalent cause of subjective food hypersensitivity than immunologic sensitization (i.e., allergy). Patients' cognitive bias is strengthened by worries about unexplained symptoms, which they more and more perceive as illness requiring medical explanation and intervention. Without sensitization of the cognitive–emotional networks, similar sensations may be considered normal. Why patients worry about and attribute their complaints to specific food items is not fully understood. Apparently, their concerns are specific and not due to a general anxiety.

In the present study we investigate the prevalence and severity of subjective health complaints and modern health worries among adult patients with subjective food hypersensitivity. According to our hypothesis, we anticipate that these subjective health complaints, but not modern health worries, are abnormally prevalent among patients with subjective food hypersensitivity.

MATERIALS AND METHODS

Patients. The sample consisted of 59 patients referred by general practitioners to the Centre for Occupational and Environmental Allergy at Haukeland University Hospital because of suspected food allergy. Thirteen patients were excluded, two because of Crohn's disease and eleven because of weak or no gastrointestinal symptoms. The patients were compared to 50 health care workers, mainly nurses from Haukeland University Hospital, and 70 persons randomly selected from the general population. The health care workers were healthy, without subjective food hypersensitivity. They are therefore denoted "healthy controls."

Persons with subjective food hypersensitivity were not excluded from the general population group. The participants were contacted after receiving permission from the Norwegian National Registry, using a randomized computer procedure. A sample of 323 was chosen from among persons living in the city of Bergen (225,000 inhabitants) and having the same age and sex distribution as the patients. They were mailed a letter explaining the study and asking whether they would like to participate. Forty-two envelopes were returned because of a change in address. Ninety-three (33%) of the 281 persons agreed to join the study. The questionnaire, with a stamped envelope for return mail, was then sent to the 93 persons and 75 (80%) of them completed it. Five of the 75 persons who answered were excluded, four because they delivered incomplete questionnaires and one because she was pregnant. None of the control groups were medically examined.

Examinations. In patients, the examinations included a complete medical history, routine biochemistry, skin prick tests using 22 common food items and inhalants (ALK Abello, Hørsholm, Denmark) and blood samples for determination of both total

serum IgE and food-specific IgE (CAP-FEIA-System; Pharmacia, Uppsala, Sweden). Trials with elimination diet, open provocation, and double-blind placebo-controlled food challenges (DBPCFC) were performed by a dietitian. An oral lactose tolerance test was performed to exclude lactose malabsorption. During upper gastrointestinal endoscopy, biopsies from the stomach and duodenum were taken to diagnose *Helicobacter pylori* infection and celiac disease, respectively. Inflammatory bowel disease was excluded by measuring intestinal permeability of ⁵¹Cr-labeled ethylenediaminetetraacetic acid (EDTA) and calprotectin in gut lavage fluid as previously described (9). Microscopy and culture of stool samples ruled out gastrointestinal infections. A screening questionnaire (Rome II criteria) was applied for the diagnosis of functional bowel disorders (10). Pregnant or lactating women and serious anaphylactic reactions were considered exclusion criteria. IgE-mediated food allergy was diagnosed according to history of immediate adverse reactions after ingestion of specific food items combined with a positive skin prick test and/or allergen-specific IgE and positive DBPCFC to the same food item (11).

The patients filled in validated questionnaires for subjective health complaints and modern health worries at first visit to the hospital. The Regional Ethical Research Committee approved the study and all participants gave written informed consent.

Subjective Health Complaint (SHC) Inventory. The SHC Inventory consists of 29 items concerning subjective, somatic, and psychological complaints experienced during the last 30 days. The questionnaire has been tested and has satisfactory validity and reliability (12). Severity of each complaint is rated on a 4-point graded Likert scale (0 = no complaints to 3 = severe complaints).

The questionnaire has five subscales: musculoskeletal pain (headache, neck pain, upper back pain, low back pain, arm pain, shoulder pain, migraine, and leg pain), "pseudoneurology" (tiredness, sleep problems, anxiety, sadness/depression, extra heartbeats, heat flushes, and dizziness), gastrointestinal problems (gas discomfort, stomach discomfort, diarrhea, constipation, gastritis/ulcer, heartburn, and stomach pain), allergy (allergies, breathing difficulties, eczema, and asthma) and flu (cold/flu and coughing).

The Modern Health Worries (MHW) Scale. This scale was developed to assess how concerned the respondents were about the effects of different aspects of modernity on their personal health (13). The MHW Scale has four subscales: "toxic interventions" including seven questions on both medical items and vaccination programs as well as dangers seen by individuals in toxic chemicals in household products; "environmental pollution" including eight questions about air pollution and depletion of the ozone layer; six questions about "tainted food" such as genetically modified food and hormones, additives, pesticides, and antibiotics in food; and finally, "radiation" including six items about topics such as radio or cell phone towers and high-tension power lines. The total score is the sum of all 27 questions in the scale.

Statistical Analysis. Results are given as individual values, medians with interquartile ranges. Differences between groups were evaluated using Kruskal–Wallis test and odds ratios (OR), with 95% confidence interval (95% CI) calculated for each item on the SHC questionnaire. Data were analyzed using the GraphPad Prism statistical software package (GraphPad Software Inc., San Diego, CA, USA). A *P* value < 0.05 was considered significant. Analyses were two-tailed.

TABLE 1. FOOD ITEMS SUSPECTED BY PATIENTS TO CAUSE FOOD HYPERSENSITIVITY

Food item	Number of patients	Percentage
Milk	32	69
Wheat flour	22	48
Egg	16	35
Paprika	14	30
Peanut	12	26
Sugar	11	24
Banana	10	22
Yeast	4	9

RESULTS

Demographic Profile. The median age for patients ($n = 46$) was 39 years (range, 19–80 years), a majority of women ($n = 41$; 89%). The healthy controls ($n = 50$) consisted of 44 women (88%) and 6 men (12%), with a median age of 45 (range, 22–61 years), and the volunteers from the general population ($n = 70$), 58 women (83%) and 12 men (17%), with a median age of 39 years (range, 20–81 years).

Somatic Findings. Table 1 lists the food items that were suspected of causing adverse gastrointestinal reactions. None of the patients had IgE-mediated food allergy, according to our definition. Two patients had non-IgE-mediated food hypersensitivity to egg and yeast/wheat flour, respectively, with a positive DBPCFC but a negative skin prick test and/or specific IgE. Another patient had parasitic infection (*Giardia lamblia*). All patients had a normal lactose tolerance test and normal upper gastrointestinal endoscopy. *Helicobacter pylori* were positive in four. Of the 28 patients who were scored according to Rome II criteria (13), 20 were diagnosed as having irritable bowel syndrome (IBS) and 5 as having functional dyspepsia (FD). The remaining patients ($n = 18$) either dropped out ($n = 9$) or refrained from further investigation, most often due to only minor gastrointestinal complaints ($n = 9$).

Subjective Health Complaints. The patients reported more frequent and severe health complaints (median score, 22.5; interquartile range, 15.5–32.0) than the healthy controls (median score, 5.0; interquartile range, 2.0–9.0) and the volunteers from the general population (median score, 9.5; interquartile range, 4.0–15.5; $P < 0.0001$). Ninety-six percent of the healthy controls had a sum score below 20. Considering a score below 20 as normal, 30 (65%) of the patients and 10 (14%) of the general population scored at or above this limit (Figure 1). Subscale scores of the SHC Inventory were highest for gastrointestinal and musculoskeletal complaints, but sum scores for all five domains were significantly higher than in healthy controls

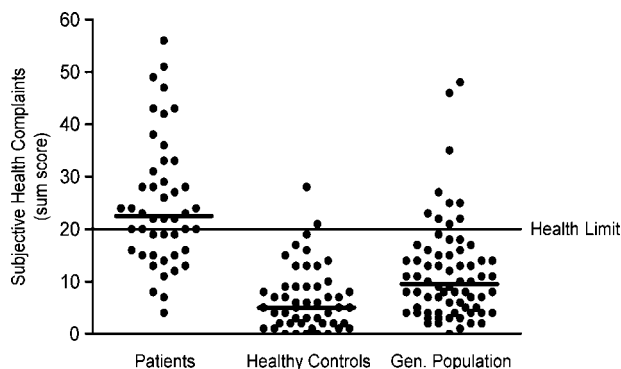


Fig 1. Subjective health complaints last 30 days in patients ($n = 46$) and two control groups, one formed by health care workers (healthy controls; $n = 50$) and one by volunteers from the general population ($n = 70$). Individual and median values indicated. Ninety-six percent of the healthy controls scored below 20. Considering a score below 20 as normal, 30 (65%) of the patients and 10 (14%) of the general population scored at or above this limit.

(Table 2). The differences between patients and controls were significant for several single items included in the SHC Inventory (Table 3).

The five most frequent complaints reported by the patients were tiredness (93%), followed by abdominal bloating (87%), headache (85%), diarrhea (83%), and low back pain (70%). Each patient reported at least four complaints during the last month. Five to 10 complaints were reported by 10 patients (22%) and 10–15 complaints by 17 patients (37%), whereas 18 patients (39%) reported more than 15 complaints during the last 30 days. The volunteers from the general population reported headache (54%), tiredness (51%), neck pain (46%), sleep problems (46%), low back pain (44%), and shoulder pain (36%) as their most frequent complaints.

Modern Health Worries. Sum scores on the MHW Scale did not differ significantly among groups: patients (median score, 66.5; interquartile range, 46.0–85.5), healthy controls (median score, 61.5; interquartile range, 44.0–75.5), and the group from the general population (median score, 57.0; interquartile range, 43.0–74.0; $P > 0.05$) (Figure 2). On the subscale “toxic interventions,” there was a significant difference between the patients and the controls from the general population ($P < 0.05$) (Table 4).

The patients were significantly more worried about overuse of antibiotics ($P < 0.001$), amalgam in dental fillings ($P < 0.01$), additives in food ($P < 0.05$), and genetically modified food ($P < 0.05$). Healthy controls (health care workers) were mostly worried about misuse of antibiotics and drug-resistant bacteria. All the participants were least worried about negative effects of vaccination

TABLE 2. COMPLAINT SCORES (MEDIAN WITH INTERQUARTILE RANGES) ON SUBSCALES OF THE SUBJECTIVE HEALTH COMPLAINTS INVENTORY

<i>Subscale</i>	<i>Patients (n = 46)</i>	<i>Healthy controls (n = 50)</i>	<i>General population (n = 70)</i>	<i>P: patients vs gen. pop.</i>	<i>P: patients vs healthy controls</i>
Gastrointestinal complaints	7.0 (4.0–9.0)	0.5 (0.0–2.0)	1.5 (0.0–3.0)	<0.001	<0.001
Musculoskeletal complaints	6.0 (3.5–10.0)	1.0 (0.0–4.0)	3.0 (1.0–7.0)	<0.01	<0.001
Pseudoneurology	5.0 (3.5–9.0)	1.0 (0.0–2.5)	2.5 (1.0–4.5)	<0.001	<0.001
Allergy	3.0 (1.0–6.0)	0.0 (0.0–1.0)	0.0 (0.0–2.0)	<0.001	<0.001
Flu	2.0 (0.0–3.0)	0.0 (0.0–1.0)	0.0 (0.0–2.0)	>0.05	<0.001

programs, medical and dental x-rays, and radio and cell phone towers (Figure 3).

DISCUSSION

Our study indicates that patients with nonallergic, subjective food hypersensitivity have considerably more subjective health complaints than healthy controls and people in the general population. Compared with our healthy controls, 65% of the patients and 14% of the sample from the general population scored abnormally high on subjective health complaints. Sum scores on the MHW Scale did not differ significantly between the groups, although the patients were significantly more worried about additives and genetically modified food, overuse of antibiotics, and amalgam in dental fillings. The results support our

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TABLE 3. NUMBERS (PERCENTAGES) OF INDIVIDUALS WITH COMPLAINTS FOR EACH ITEM OF THE SUBJECTIVE HEALTH COMPLAINTS INVENTORY. PATIENTS COMPARED WITH HEALTHY CONTROLS (HC) AND VOLUNTEERS FROM THE GENERAL POPULATION (GP) WITH ODDS RATIO (OR) AND 95% CONFIDENCE INTERVALS (95% CI)

	<i>Patients (n = 46)</i>	<i>HC (n = 50)</i>	<i>GP (n = 70)</i>	<i>OR (95% CI): Patients vs HC</i>	<i>OR (95% CI): Patients vs GP</i>
Musculoskeletal pain					
Headache	39 (85)	20 (40)	38 (54)	8.4 (3.1–22.4)	4.7 (1.9–11.9)
Low back pain	32 (70)	12 (24)	31 (44)	7.2 (2.9–17.9)	2.9 (1.3–6.3)
Neck pain	30 (65)	14 (28)	32 (46)	4.8 (2.0–11.5)	2.2 (1.0–4.8)
Shoulder pain	26 (56)	17 (34)	25 (36)	2.5 (1.1–5.8)	2.3 (1.0–5.0)
Arm pain	18 (39)	7 (14)	22 (31)	6.1 (2.2–17.2)	2.2 (1.0–5.0)
Upper back pain	21 (46)	7 (14)	16 (23)	5.2 (1.9–13.9)	2.8 (1.3–6.4)
Leg pain during physical activity	18 (39)	2 (4)	14 (14)	18.6 (4.0–86.0)	2.6 (1.1–5.9)
Migraine	8 (17)	4 (8)	8 (11)	3.0 (0.8–10.5)	1.6 (0.6–4.7)
Pseudoneurology					
Tiredness	43 (93)	23 (46)	36 (51)	16.8 (4.6–61.5)	13.5 (3.8–47.8)
Sleep problems	30 (65)	14 (28)	32 (46)	4.8 (2.0–11.5)	2.2 (1.0–4.8)
Anxiety	12 (26)	4 (8)	15 (21)	4.1 (1.2–13.7)	1.3 (0.5–3.1)
Sadness/depression	18 (39)	10 (20)	19 (27)	2.6 (1.0–6.4)	1.7 (0.8–3.8)
Extra heartbeats	9 (20)	5 (10)	8 (11)	2.2 (0.7–7.1)	1.9 (0.7–5.3)
Heath flushes	17 (37)	4 (8)	18 (26)	7.2 (2.2–23.8)	1.8 (0.8–4.1)
Dizziness	27 (59)	3 (6)	19 (27)	24.9 (6.7–92.7)	4.3 (1.9–9.5)
Gastrointestinal problems					
Gas discomfort	40 (87)	20 (40)	28 (40)	10.0 (3.6–28.0)	10.0 (3.7–26.7)
Stomach discomfort	4 (9)	3 (6)	3 (4)	1.5 (0.3–7.1)	2.1 (0.5–10.0)
Diarrhea	38 (83)	5 (10)	23 (33)	42.8 (12.9–141.6)	9.7 (3.9–24.2)
Obstipation	20 (43)	5 (10)	10 (14)	6.9 (2.3–20.6)	4.6 (1.9–11.2)
Gastritis, ulcer	18 (39)	5 (10)	8 (11)	5.8 (1.9–17.4)	5.0 (1.9–12.8)
Heartburn	19 (41)	0 (0)	19 (27)	—*	1.9 (0.9–4.2)
Stomach pain	39 (85)	7 (14)	18 (26)	34.2 (11.0–106.3)	16.1 (6.1–42.3)
Allergies					
Allergy	31 (67)	3 (6)	18 (26)	54.0 (13.5–215.2)	10.0 (4.0–24.9)
Breathing difficulties	17 (37)	2 (4)	10 (14)	14.0 (3.0–65.4)	3.5 (1.4–8.6)
Eczema	15 (33)	12 (24)	12 (17)	1.5 (0.6–3.7)	2.3 (1.0–5.6)
Asthma	12 (26)	1 (2)	9 (13)	17.3 (2.2–139.3)	2.4 (0.9–6.3)
Chest pain	16 (35)	0 (0)	5 (7)	—*	6.9 (2.3–20.7)
Flu					
Cold/flu	21 (46)	12 (24)	9 (27)	2.7 (1.1–6.4)	2.3 (1.0–4.9)
Coughing	27 (59)	8 (8)	11 (16)	7.5 (2.9–19.4)	7.6 (3.2–18.2)

*OR could not be calculated because of zero value in healthy controls.

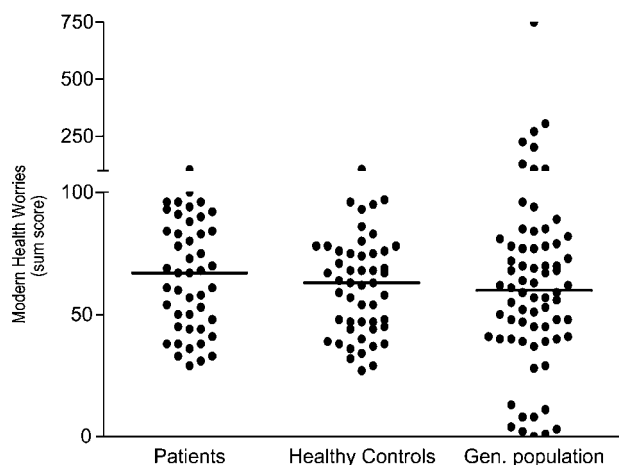


Fig 2. Modern health worries in patients ($n = 46$) and two control groups, one formed by health care workers (healthy controls; $n = 50$) and one by volunteers from the general population ($n = 70$). Individual and median values indicated.

hypothesis of an associated occurrence of subjective food hypersensitivity and subjective health complaints, corroborating the view that the conditions are sharing pathogenetic mechanisms.

The patients were remitted because they or their doctors suspected that the symptoms could be due to allergy. Consistent with the findings of others (14, 15), we rarely found indications of food hypersensitivity among these patients. None of the patients had IgE-mediated food allergy, and only two had non-IgE-mediated food hypersensitivity. Apart from one patient who was diagnosed as having parasitic infection (*Giardia lamblia*), none had evidence of organic disease. Hence, in most cases the patients' food hypersensitivity remained unexplained.

Subjective health complaints are common in the general population (12, 16, 17). However, in some persons these "normal" complaints may turn into intolerable conditions, making medical and psychological assistance necessary and creating great problems for the individual patients and society at large (7). When, why, and how these "normal" or common complaints become intolerable is not clear, but a sensitization phenomenon seems likely. The term sensitization is generally taken to mean an increased response

to a stimulus as a function of repeated presentations of that stimulus (18). Sensitization may occur at different levels in the organism, such as the peripheral, spinal, limbic, cognitive, and behavioral levels (8). Cognitive-emotional sensitization involves the central nervous system in complex neuronal networks. Most patients suffering from medically unexplained somatic complaints spend a lot of time worrying over their condition and this worrying may continuously activate the cognitive illness networks. Above a certain level of activation, these networks lead to more and more perception of illness. This can be compared with neuronal sensitization (at the spinal cord level); the main difference is that in cognitive sensitization, instead of one neuron being sensitized, complex neuronal networks are sensitized (8). Sensitization assumes some kind of specificity of the triggering mechanisms. Our patients with subjective food hypersensitivity were concerned about specific food items, not about food in general or, for instance, the influence of modern life on health. Hence, the finding of some specificity of the sensitization of our patients supports the cognitive sensitization theory.

Eriksen *et al.* (19) showed that subjective health complaints depended on interactions between demands and coping, more than demand and control. The combination of high demands and low coping was associated with most health problems, whereas low demand and high coping had the lowest level. It is well known that stress may exacerbate gastrointestinal symptoms and complaints (20, 21). Activation theories like the Cognitive Activation Theory of Stress (CATS) state that the stress response equals activation, a general alarm system operating whenever the organism notes that there is a discrepancy between what is expected and what really occurs (22). When expectancies are positive, high demands are no health risk in healthy organisms. Negative effects occur only when there is a lack of coping. This suggests that lack of coping with stress, meaning low expectancies of outcome, plays an important role in patients with subjective health complaints (19). However, whether demands and coping are disparate in our patients with subjective food hypersensitivity remains to be shown.

A number of studies have found that IBS is linked to adverse reactions to food (3, 5, 6). In one study 63% of

TABLE 4. SCORES (MEDIAN WITH INTERQUARTILE RANGES) ON SUBSCALES OF THE MODERN HEALTH WORRIES SCALE

Subscale	Patients ($n = 46$)	Healthy controls ($n = 50$)	General population ($n = 70$)	P: patients vs gen. popul.	P: patients vs healthy controls
Toxic interventions	18.5 (12.0–23.0)	15.0 (10.5–19.5)	13.0 (10.0–31.0)	<0.05	>0.05
Tainted food	17.5 (12.5–24.5)	16.0 (10.5–20.5)	15.0 (12.0–20.5)	>0.05	>0.05
Environmental pollution	20.0 (12.5–26.0)	20.0 (15.5–23.0)	18.5 (15.0–24.0)	>0.05	>0.05
Radiation	9.5 (7.0–14.5)	9.0 (7.0–13.0)	10.0 (7.0–14.0)	>0.05	>0.05

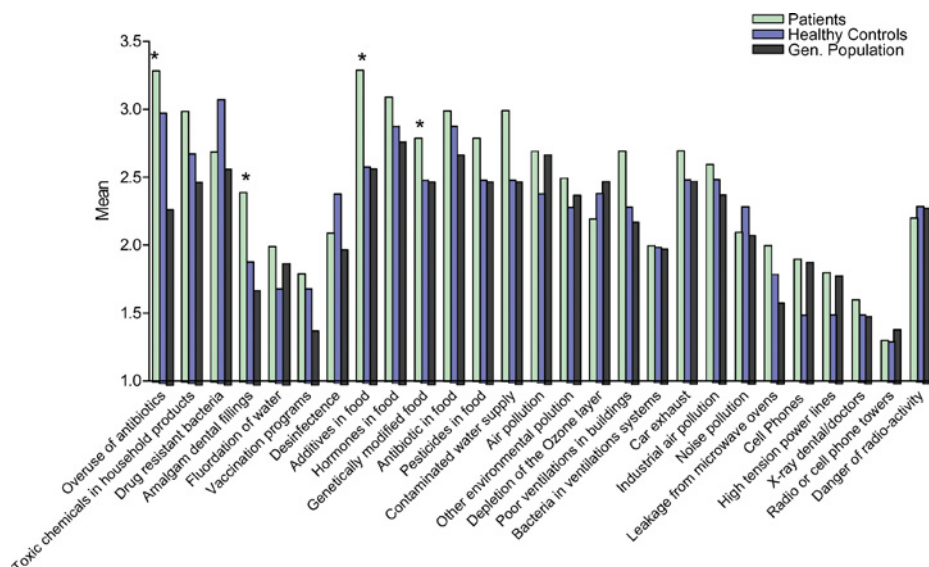


Fig 3. Mean scores on each item included in the Modern Health Worries Scale. *Significant difference ($P < 0.05$) between patients and controls.

the patients with IBS claimed such reactions (23). Dairy products and grains were the food items most commonly identified by the patients as the culprit (6). Nonabsorbable carbohydrates are fermented in the colon and the consequent production of gas may cause bloating and pain (24). Typically, patients with functional gastrointestinal disorders sensitive to distension by gas, and they are more anxious and depressed than healthy volunteers (4, 14, 25). Psychological factors are supposed to play an important role in the pathogenesis of IBS. Hence, there are similarities between IBS and subjective food hypersensitivity that should be investigated further.

There are several reasons why patients attribute their health complaints to food. It is, first of all, easier and more acceptable to present somatic complaints, rather than feelings of sadness or depression, and avoid being labeled psychologically disturbed. In fact, patients are often hostile to the idea that their symptoms have a psychological explanation and they seem to grasp any possible organic explanation for their symptom (14). Several meals during the day create many possibilities for random coincidence and wrong attribution between food intake and pain. Wrong attribution may also be ascribed to “associative learning” or influence (26, 27). Occasionally health care workers, friends, and therapists in the field of alternative medicine offer “good advice” that may be wrong. In our health region, patients with gastrointestinal problems are often told to avoid having milk and wheat in their diet. The high prevalence of suspected adverse reactions to these food items might be the result of this local

influence. Sometimes the patients’ own belief in their attribution is so strong that it in itself suggests some kind of psychopathology (14).

Our results suggest that attributing various subjective health complaints to food hypersensitivity might be a cognitive bias. However, patients are in some way right when they say they are hypersensitive; the crucial task for the physician is to distinguish cognitive from immunologic (allergic) sensitization. Unfortunately, these widely different conclusions rest on diagnostic methods that clearly need further improvement.

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