

Review article

Incorporating a gender dimension in food allergy research: a review

Sex and gender are the major determinants of health and disease in both men and women. The aim of this review paper was to examine differences in gender and sex in relation to the prevalence and effects of food allergy. There are still major gaps in our knowledge about the kinds of processes which shape men's and women's perceptions and experiences of food allergy. The expression and experience of health and illness may be moderated by variables such as biological vulnerability, exposure to health risks, perception of symptoms, evaluation of risk, information processing and role expectations. This review highlights the complex links between biological sex, gender, and health in general and offers a synthesis of how these may interact to produce sex and gender differences in biopsychosocial manifestations of food allergy. Implications for research and public health practice are discussed.

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The relationship of sex and gender to health and disease is complex, and varies across an individual's lifespan, and between cultures and different social contexts. Attention to sex and gender in biomedical and health sciences research is being actively promoted by the European Union Commission under their research policy of 'mainstreaming gender equality'(1). *Sex* denotes the differences attributed to biological origins alone, while *gender* refers to the social and cultural influences that lead to differences between women and men (2). One consequence of variables related to both sex and gender is that potentially differing patterns of disease prevalence, different degrees of severity, and different patterns of mortality and morbidity may be identifiable between men and women (e.g. 3, 4). With regard to asthma and allergy, some studies suggest both diseases have more adverse effects on female over male general emotional well-being (5, 6).

Allergic diseases and asthma pose an important and increasing problem for populations and health care

systems around the world (7). Allergy is a multifactorial disease that has a significant impact on society. An increase in the prevalence of asthma and allergy during the last two decades is documented for both children (8) and adults (9). The data for food allergy are less clear, in part because there is some confusion between the prevalence of diagnosed and perceived food allergy (10), although there appears to have been a real increase in rates of hospital discharge diagnosis of the condition (11). Many authors believe, however, that there has been a real increase in cases, possibly attributable to changes in the environment or human nutrition (12). Changes in eating habits and the appearance of novel foods (exotic foods and genetically modified organisms) and the increasing use of food proteins as ingredients may contribute to increased risk (13). There appears to be a correlation between the increased consumption of a novel food and a risk in allergic reactions. Although the exact rates of prevalence are unknown, recent estimates have reported a prevalence

of food allergies in the range of 5–8% in infants and 2–3% in adults (reviewed in Refs 14–16), an increase from the 1–2% adult incidence rate reported in the early 1990s (17).

The development of food and other allergies requires a complex interplay of host and environmental factors. A holistic approach to food allergy is informed by the biopsychosocial perspective on health (18). This perspective is now integral to research in many areas previously examined purely on a biological level. Sex and gender differences within the context of food allergy have not, to date, been systematically examined. Therefore, the objectives of this review are: to analyse what is currently known about sex and gender differences in relation to food allergy; to review the evidence on the biopsychosocial determinants of these gender differences; to offer a synthesis of how these interact to produce gender differences in psychosocial manifestations of food allergy, to identify the gaps in research on both sex and gender in food allergy, and to consider the implications for clinical and public health practice as well as for research.

Methods applied to literature search

The literature search was divided into four categories: sex, gender, sex and gender (general), sex and gender (food allergy). To begin with standard electronic databases were consulted. The main databanks concerned were Medline, PubMed, PubSoc. Literature searches in all databases were conducted for articles from 1990 to 2006 using the key words Sex and/or Gender; And (all the following terms separately and in combination) -

Primary search

definition/differences/prevalence/gender/research/health/disease/medicine/morbidity/mortality/diagnosis/biological determinants/socio-cultural determinants/interaction/social/psychology/psycho-social/science/bias/prejudice/physiological vulnerability/psychological vulnerability/immunology/atopy/asthma/food allergy/allergic disease/disease expression/influence of hormones/coping/pain/chronic conditions/management/health reporting/symptom reporting/health perception/health evaluation/parents/parental perception/parental influence/attitudes to health/quality of life/health related quality of life/health measurement/health risk/risk perception/research implications/health promotion/health policy/EU initiatives/International initiatives.

The research articles (primary and review) gathered as a result of the primary search – and filed according to the four categories above – allowed for a secondary search using more precise search terms and phrases.

Secondary search

Key words: Sex and/or Gender; Health and/or Disease; Food Allergy and/or Atopy; (as appropriate) And –

Pharmacodynamic sex influences/clinically relevant sex effects/gendered patterns of morbidity and mortality/gendered approach to health and illness/immune dimorphism/gender differences in perceived allergy/social construction of gender roles/perception, reporting and interpretation of symptoms/health beliefs influence on health behaviours/parent gender and reporting of child health/coping strategies for chronic illness/information processing on health and risk/self-assessment of health/EU research policy/multidisciplinary research/interdisciplinary research.

References containing information relevant to the objectives of this paper were examined further. The Web sites of relevant institutes, centres and offices such as the Society for Women's Health Research (<http://www.womens-health.research.org>) and the European Men's Health Forum (<http://www.emhf.org>) were also consulted, in addition to several national specialist medical societies.

Definitional problems. Problems and confusion with definition of the terms 'sex' and 'gender' quickly became apparent. In much of the published medical literature, many authors replace 'sex' with 'gender', using the term 'gender differences' to describe all or any observed differences between men and women, including relative rates of mortality and morbidity, as well as purely biological differences in sex organs and sex specific diseases (19). This lack of distinction in the interpretation of terminology provides a barrier to a greater understanding of the relative contribution of psychosocial, environmental and biological factors to a particular disease.

The term 'gender' in Medline was defined as 'sex', being the 'totality of characteristics of structures and functions differentiating the male from the female organism'. In the social sciences databases, the terms were, for the most part, used appropriately. For example, gender was defined as 'the characteristics of women and men that are socially and culturally determined' (i.e. not merely related to chromosomal sex). In the following review, the terms 'sex' and 'gender' are also defined in this way. Where findings can not clearly be attributed to either sex or gender, or there may be interaction, this is also noted.

Sex differences and food allergy

Sex differences in allergic diseases have been identified, and are well established (20). Attention to sex and gender effects may provide important clues to the prevention, diagnosis and treatment of atopic diseases such as food allergy.

In population-based studies sex differences in atopy (assessed as skin test reactivity to one or more of a panel of allergens) have been reported throughout childhood and into early adulthood, such that rates in girls are lower than in boys up to at least 15 years of age, in most studies

up to 25 years of age, but are not consistently observed thereafter (5). In contrast to the sex differences in atopy assessed as skin test positivity which vary and change direction across the human lifespan, sex differences in atopy assessed as total serum IgE levels are consistent across the lifespan, with levels in females being lower than those in males (21). With reference to asthma and food allergy, prevalence is higher in boys before puberty, while this sex ratio is reportedly reversed after puberty (22). Physiological pathways for these sex differences have been discussed with reference to 'immune dimorphism', the term given to differences in immune responses and regulation between the sexes.

The effects of sex steroids on autoimmunity have been known for many years; however, this knowledge has seldom been applied to allergy although there is evidence of their contribution to relevant underlying mechanisms (23). Women exhibit stronger antibody responses to immunization and infection and have higher levels of all antibody classes with the exception of IgG (24). Globally, estrogens depress T-cell-dependent immune function and diseases, but enhance antibody production and androgens suppress T-cell immune responses, resulting in the suppression of disease expression (25). It is plausible that proinflammatory properties of female sex steroids will increase susceptibility to atopy. Receptors for sex steroids have been identified on lymphocytes, monocytes and mast cells (26, 27). A recent study tested the hypothesis that female mice are more susceptible to the development of allergic asthma than male mice and studied allergic immune responses in the lung (28). The results demonstrated that female mice developed a more pronounced type of allergic airway inflammation than male mice after ovalbumin aerosol challenge. This might go some way towards explaining why the prevalence of asthma and atopy is higher among females than males after puberty, as reported by Osman (23).

Prenatal events appear to be crucial in programming the infant immune system. For example, programming of the fetal immune system by the mother could explain the greater effect of maternal vs paternal allergy that has been observed in the context of allergy and asthma in children (29). In a study of nearly 800 newborn infants in Detroit, an association between atopic mothers and an elevated cord blood IgE was shown for newborn girls but not for boys (30). A recent study has confirmed this finding (31).

Gender differences and food allergy

Biological sex differences are not the only factors influencing variations in male and female patterns of health and illness. It is also clear that more general, nonsex specific diseases and health problems may be experienced very differently by men and women, and have different implications in terms of lifestyle and health status (32, 33). The reasons for this sex-related divergence in disease

development are complex and thus, in order to understand the full range of influences on human health, it is necessary to take into consideration the various psychological and sociological explanations that have been advanced to explain observed gender differences in relation to disease. A 'gendered' approach to health attempts to examine, at a more holistic level, the causes and patterns, underpinning literature regarding sex differences (34).

A Norwegian study on severe allergic reactions to food (35) found that the sex distribution of severe reactions shows a 60/40 female over male dominance in adolescence and adulthood. Interestingly, this sex difference was not apparent at 18 months (36). This may be due to a female to male dominance in self-reported allergic disease (37, 38). Although female sex may serve as a biological gene modifier, it is gender that may affect disease outcome by determining the coping/management strategies used by males and females in their lived experience of the disease (e.g. Ref. 39).

Lovik et al. (35) noted that one would expect to see these gender differences predominantly for milder reactions to food because 'severe reactions are more likely to have clear physiological mechanisms and to make emergency medical care necessary regardless of differences in health-seeking behaviour ...' (p. 155). The authors hypothesized that either severe food allergy is more common in females than in males or females may have a different food allergen exposure than men. It is known that, in addition to genetic susceptibility as an important determinant of food allergy, sensitization to food proteins and subsequent allergic disease also depend on environmental and cultural factors (23, 40). These environmental factors may be modified by the effects of gender, but there is a paucity of studies that consider gender as either a confounding or explanatory variable. Writing on the higher susceptibility of 5- to 7-year-old girls to develop eczema compared with boys of the same age, Mohrenschrager et al. (41) noted that girls predominantly played indoors, whereas the majority of boys played outdoors. This is an area of research which has the potential to provide answers to questions relating to the developmental pathways of allergic diseases in males and females, and has preventative and therapeutic implications.

There has been little psychosocial research on the influence of gender in the context of food allergy. One area that has received attention is research investigating quality of life (QoL) of children and families, which can be severely impacted by food allergy (42, 43). An increasing concern about the need for critical evaluation of treatment programmes for chronic conditions has led to a rapidly growing theoretical interest and empirical research into QoL in relation to health and disease (44).

Marklund et al. (38) investigated the extent to which females and male adolescents experience allergy-like conditions and the impact of these on everyday life. They

found that adolescent females reported allergy-like conditions more frequently than adolescent males; a finding consistent with research looking at general health and gender (e.g. 45, 46). All adolescents with allergy-like conditions reported significantly lower health-related quality of life (HRQL) in seven of eight health scales that measured biopsychosocial functioning; however, females reported more severe HRQL-deterioration compared with males. This is consistent with research that shows an excess of psychological vulnerability in adolescent girls with chronic conditions when compared with boys suffering from the same conditions, including epilepsy and asthma (47), insulin dependent diabetes mellitus (48), and cerebral palsy (49). Of the allergy conditions reported by Marklund et al. (38), more than 50% of the adolescents stated they had food hypersensitivity with positive allergy tests. However, a sex and/or gender breakdown for confirmed food hypersensitivity or method of diagnosis was not included. Thus it is not possible to determine if there is a gender difference in perceived *vs* actual food allergy for these individuals. Work by Knibb et al. (50) has demonstrated a gender bias in reporting self-diagnosed food allergy and intolerance, with significantly more females self-reporting than males.

Research on *gender differences in processing information* for making self-assessments for health may also help to explain observed gender differences. Research has found that females are comprehensive information processors who consider both subjective and objective product attributes, and respond to subtle cues (51). Conversely, males selectively process information, tending to use heuristic shortcuts (cognitive 'rules of thumb') and missing subtle cues. Women with self-reported food allergy and intolerance have been shown to exhibit greater negative affect, such as depression and neuroticism (45), which in turn may affect self-assessment of their health. However, it is impossible to determine causality from studies such as this, and it is just as plausible that the negative affect was a consequence of the symptoms attributed to foods in these women and the concomitant effects on QoL associated with food allergy and intolerance. Prospective studies are needed to disentangle these issues.

Differences in self-reports of ill-health and psychological distress have also been observed in adolescent populations. Sweeting and West (52) found that self-reported general ill-health and physical symptoms, as well as psychological distress were significantly higher and increasing from age 11 for females compared with males. This increased with age and by age 15, there was a female excess in general ill-health, including psychological distress and 'malaise', limiting illness, poor self-rated health, headaches, stomach problems and dizziness. This may also explain possible gender differences in self-assessed health in the context of perceived food allergy.

There is clear evidence that *parental factors* influence child health outcomes. These include antenatal exposures

to teratogens, environmental and genetic determinants, socio-demographic factors and parental behaviours (53–55). The influence of parental perceptions of their own, and their child's health, remains relatively unknown. This is an important area of research because parents are frequently asked to assess and report on the health of their children in clinical care, population health surveys, health outcome and QoL research. Research has begun to examine whether a parent's perception of their own health affects their reporting of their child's health, yet uncertainty remains as to the influence of parental gender. Recent research found that parents self-reporting poor health had an increased chance of reporting that their children had poor health (odds ratio, 7 : 5), an effect which increased for mothers compared with fathers (56). In addition parental perceptions can have a profound impact on the way that children themselves perceive their own health and illness and on how they interpret risk with regard to possible and actual disease conditions (57, 58).

Within the food allergy literature, gender biases in parental assessments of their child's health have also been reported. King et al., assessed QoL in children with peanut allergy and their families (59). The results show that mothers had significantly poorer psychological QoL, and greater anxiety and stress than the fathers. In addition, mothers rated their peanut allergic child's QoL as significantly worse than the child's own ratings or the proxy ratings of an older sibling or father. These results provide an argument against only using the mother's proxy ratings when assessing allergic children's QoL. Parental attitudes have both positive and negative impacts on children's own perceptions and health (60, 61). Therefore, it is extremely important that maternal and paternal perceptions of their own and their children's QoL, in addition to the child's, are investigated in any research design.

Gender differences in *self-efficacy*, which is the general belief in one's own ability to respond to, and control, environmental demands and challenges (62), may play a part in the *perception, reporting and management of symptoms*. A study of how adolescents managed diabetes or asthma (63), found that girls incorporated asthma or diabetes into their social and personal identities and were prepared to inform others and treat themselves in public, although this strategy sometimes led to lowered self-efficacy and a sense of personal control. Boys tended to minimize their illness, particularly in public, thereby maintaining a sense of control, but leading to possible health-risk consequences. Self-efficacy makes a difference in how people think, feel and act. High self-efficacy for a particular situation allows one to deal better with uncertainty, distress and conflict (64), and, thus, should be investigated as a possible intervening variable in how food allergy is understood, reported and, in turn, managed by both males and females.

It is clear that food allergy has an impact on QoL, due in part to the constant vigilance required on the part of the allergic individual, or their caregiver, to ensure accidental ingestion of food allergens does not occur (65). The perception and management of the daily risk for these individuals is an area of concern (66, 67); however, to date no studies have investigated *gender differences in risk perception* in the area of food allergy. A study into food risk perception and responsibility in the eyes of consumers with allergic reactions to food was conducted in Norway; however, gender differences were not analysed (68). Psychological theories used to explain consumers' propensity to adopt self-protective behaviours assume that individuals are always rational decision-makers who routinely weigh the benefits of self-protection against the risks. Health belief models (69, 70) predict that the more vulnerable we feel ourselves to a disease that has severe personal health consequences, the more likely we are to take the action necessary to avoid the disease or, in terms of food allergy, its consequences. However, 'real life' is not that simple and affective or 'emotional' factors (as opposed to cognitive factors) may affect both the selection and evaluation of different aspects of a potentially risky situation (71–73). Therefore, although direct experience of the consequences of eating food to which an individual is allergic will have an influence on a person's perceptions and attitudes to risk taking behaviours, beliefs about risk are also influenced by demographic factors such as age and gender. For example, males, in particular young males, are more prone to exhibit 'optimistic bias', a phenomenon in which people believe they are less likely to experience negative effects, and more likely to experience positive ones, associated with a particular hazard compared with other people living in a particular society (74).

Research looking at the incidence of severe allergic reaction has supported the notion that adolescents and young adults are more at risk. In a Norwegian study on severe allergic reactions to food, the main risk group was comprised of young adults aged 20–35 years (35). A study from Britain on anaphylactic deaths (75) also reported similar findings. Several explanations have been suggested; adolescents and young adults frequently eat away from home, they may be unwilling to admit an allergy problem when eating out with friends, and alcohol consumption may be high (see also Ref. 17). The latter may both impair their ability to assess risk and augment the physiological effects of allergen encounter such as vasodilation.

In addition to peer group dynamics, other variables, including gender differences in coping strategies, information processing, risk perception and symptom evaluation should be explored to determine if these variables have an effect on the number of males *vs* females experiencing severe reactions to foods. Such research could inform the targeting and content of clinical and health promotional information.

Implications for research, clinical and public health practice

This review has highlighted the complex links between biological sex, gender, and health in general and has offered a synthesis of how these may interact to produce sex and gender differences in biopsychosocial manifestations of food allergy. Sex and gender are major determinants of health and disease in both men and women. The expression and experience may be moderated by variables such as biological vulnerability, exposure to health risks, perception of symptoms, evaluation of risk, information processing and role expectations. It is difficult to evaluate the relative contribution of each of these variables and each may have a cumulative and/or an interactive effect.

Building on the Platforms for Action developed at the UN conferences in Cairo (1994) and Beijing (1995), there has been a growing consensus towards putting both sex and gender at the heart of health research (1). It is now generally recognized that failure to incorporate sex and gender in research designs can result in failures of both effectiveness and efficiency (76). The new paradigm of evidenced-based medicine has underscored this awareness and, 'fuelled the debate on the limited generalizability of findings [that do not take sex and gender into account] in clinical research' (77).

In the context of atopy and food allergy, sex differences are of more than purely biologic interest. For example, 'elucidating the reasons for the switch in sex ratio [after puberty] should provide fresh insights into asthma and atopy with a real prospect of novel therapies for these troublesome diseases' (23). Building on recent studies that implicate immunosuppressant and proinflammatory properties of hormones, therapeutic implications include drug development leading to modification of sex steroids, sex specific treatment and organ specific therapy which would complement currently used glucocorticoid-derived steroids (23).

As discussed in this paper, there are still major gaps in our knowledge about the kinds of processes which shape men's and women's perceptions and experiences of food allergy. Key research areas identified include: what aspects of health beliefs and behaviours specific to gender mediate decision making processes with regard to risk perception; the moderating impact of gender on health and treatment outcomes; how gender roles play a part in the perception and, in turn, the reporting of symptoms of food allergy; how the interaction of biological determinants with environmental and psychosocial factors such as gender may moderate the manner in which men and women communicate, manage and cope with, the day-to-day experience of living with food allergy (Tables 1 and 2).

Several factors are key to developing a knowledge base for gendered research on food allergy. First, it is important for all involved in research and patient care to use the same terminology to define 'sex' and 'gender'.

Table 1. Key research areas in food allergy relating to sex and/or gender

Impact of gender on perception and reporting of symptoms
Gender differences in diagnosis, treatment, and follow-up at a clinical level
Independent /interactive impact of biopsychosocial variables on male and female quality of life
Impact of sex and gender on health and treatment outcomes
Impact of health beliefs and behaviours, specific to gender on decision making processes
Age, sex, and stressor effects in the use of different coping strategies in children with food allergy
Gender differences in perceived versus actual food allergy

Table 2. Recommendations for food allergy research and policy

The same terminology to define 'sex' and 'gender'
Gender and sex routinely identified in sampling
A strong emphasis on interdisciplinary and integrative research
Systems developed for monitoring gender differences in food allergy across the lifecycle
Stratification by sex and age in aetiological studies of the occurrence, risk factors and natural history of food allergy
Innovative qualitative and quantitative research methods to understand sex and gender differences
Link between policy and research on sex and gender made explicit
Training on the impact of sex and gender on health widely available across EU institutions and within Member States

This will allow researchers and clinicians from different countries and from different perspectives to communicate more effectively when compiling and evaluating data. Secondly, the Global Forum for Health Research (76) suggest that more work is needed to disentangle the links between biological sex and social gender and their

relationship with wider determinants of health. For example, many campaigns are targeted at women because of their perceived role as 'caregivers' (77), while ignoring women's specific concerns, and, as a byproduct, fostering the belief in men that health promotion messages are not relevant to them. Thirdly, if both sex and gender influences on health are to be properly understood, a new framework will be needed that can transcend traditional boundaries.

The value of integrated approaches (often using both qualitative and quantitative methods) has been clearly demonstrated in recent years in the fields of sexual and reproductive health and mental health (78). The new models of sex and gender research need to be developed through a series of research and methodological activities, to deal with the identified complex information and research needs, and incorporating the perspectives of a wide range of stakeholders. For example, recent research of the impact of the disease on QoL is to be welcomed; however, gender should be included as a specific variable in all studies on food allergy.

'A true integration of gender into research would profoundly affect the way in which scientific knowledge is defined, valued and produced, the methodologies that are invoked, and the theoretical reflections to which such new modes of knowledge give rise' (79).

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