



Government
of South Australia

Southern Adelaide
Health Service



FLINDERS
MEDICAL
CENTRE

Asthma, Allergy and Anaphylaxis - Interactions and Changing Prevalence

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Overview

- There are strong interactions between the various atopic disorders; some of these are likely to be causative
- Despite a levelling off or decrease in asthma prevalence in the young in high prevalence countries, there remain upward trends in atopic eczema in most countries
- Limited data suggests alarming increases in the frequency of hospital presentations with anaphylaxis
- Atopic eczema often leads to the “atopic march”; interventional studies on subjects at high risk for developing this condition may give insights into the “epidemic” of allergic disease



The Atopic Disorders

The “atopic foursome”:

- Atopic eczema/ dermatitis
 - Extrinsic asthma
 - Allergic rhinitis
 - Food anaphylaxis
- Loosely associated disorders
 - Increased intestinal permeability in infants with atopic eczema (Pike, Hedde et al, 1986)
 - Eosinophilic oesophagitis/gastro-enteritis



Determinants of These Disorders

- Non-allergic, often organ specific
 - For example
 - Asthma – genes favouring bronchial hyper-reactivity
 - Atopic eczema – genes favouring dry skin, lack of protease inhibitors
- Allergic
 - Atopy = inherited trend to make specific IgE responses to mucosal allergen exposure



“Allergic Links” Between Atopic Disorders

- Associations, not necessarily causative
 - Atopic eczema as a predictor of clinical IgE type food allergy (approx. 40%; Eigenmann, Sicherer et al, 1998) and/or asthma (approx. 50%; B-M Exl, 2001)
- Allergic rhinitis as a risk factor for future asthma (Guerra, Sherrill et al, 2002; Settupane, Hagy, Settupane, 1994)



Associations Likely to be Causative

- Aeroallergens and asthma
 - Allergy to perennial indoor allergens and bronchial hyper-reactivity (Peat, Tovey et al, 1994; Sporik, Chapman, Platts-Mills, 1992))
 - Allergy to pollens and thunderstorm related “asthma epidemics” (Girgis, Marks et al, 2000)
 - Severe or lethal asthma and mould allergy
 - Mid-west USA (O’Hollaren, Yunginger et al, 1991)
 - Chicago (Targonski, Persky, Ramekrishnan et al, 1995)
 - Europe (Neukirch, Henry et al, 1999; Zureik, Neukirch et al, 2002)



Associations Likely to be Causative

- Asthma, Food Allergy, Lethal Anaphylaxis I
 - Role of asthma in lethal food anaphylaxis (Bock, Munoz-Furlong, Sampson, 2001)
 - 32 cases of lethal food anaphylaxis
 - 31 known asthma
 - 30 peanut or tree nut trigger likely
 - 30 less than 30 years of age
 - Lethal (n=6) or near lethal (n=7) asthma (Sampson et al, 1992)
 - asthma a co-factor in 12 of 13 cases



Associations Likely to be Causative

- Asthma, Food Allergy, Lethal Anaphylaxis II
 - Bronchospasm the most common mechanism of death in food anaphylaxis (Pumphrey, 2000)
 - Insect sting anaphylaxis; cardiovascular collapse usually dominates, yet asthma/COPD remain adverse risk factors (Brown, Franks et al, 2003)



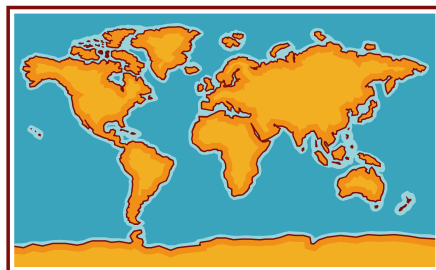
Associations Likely to be Causative

- Food Allergy and Severe Asthma (Roberts, Patel et al, 2003)
 - 10/19 children requiring ventilation food allergic
 - 4/38 ED presentations with non-life threatening asthma food allergic
 - Multiple regression analysis, only frequent admission with asthma and food allergy significant



Changes in Prevalence of Recent Wheezing to 2000

World



- Multiple questionnaire studies in many countries suggested prevalence of recent wheeze increasing by 50% or more over a generation, especially in children
- BUT
- Only 2 studies used objective measures (Burr and Butland, 1990; Peat, van den Berg et al, 1994)



Changes in Prevalence of Recent Wheezing to 2000

Australia



- At least 26 studies over 20 years suggested prevalence increasing in children at 1.4% per year
- The one study measuring airway function (Peat, van den Berg et al, 1994) showed 1.4 – 2.0 fold increase over 10 years



More Recent Data: ISAAC Three vs ISAAC One (Asher, Montefort et al, 2006)

“World” (37 Countries)

- Continued upward trend in prevalence atopic eczema and allergic rhinitis in most countries
- Heterogeneous trends with asthma, with many countries with high prevalence showing decrease in prevalence in the 13 – 14 year age group



More Recent Data: ISAAC Three vs ISAAC One (Robertson, Roberts, Kappers, 2004)

- Prevalence (%) of active conditions in 6 – 7 year olds

| | Recent Wheeze | Eczema | Rhinitis |
|-------------|-----------------------|-----------------------|-----------------------|
| 1993 | 27.2 (25.0 - 29.4) | 11.1 (10.0 - 12.3) | 9.7 (7.8 - 10.8) |
| 2002 | 20.0 (18.4 - 21.8) | 17.2 (15.7 - 18.8) | 12.7 (11.1 – 14.5) |



S A Branch AAI Launch 9/5/05

“Is the prevalence of food allergy and atopic disease increasing”

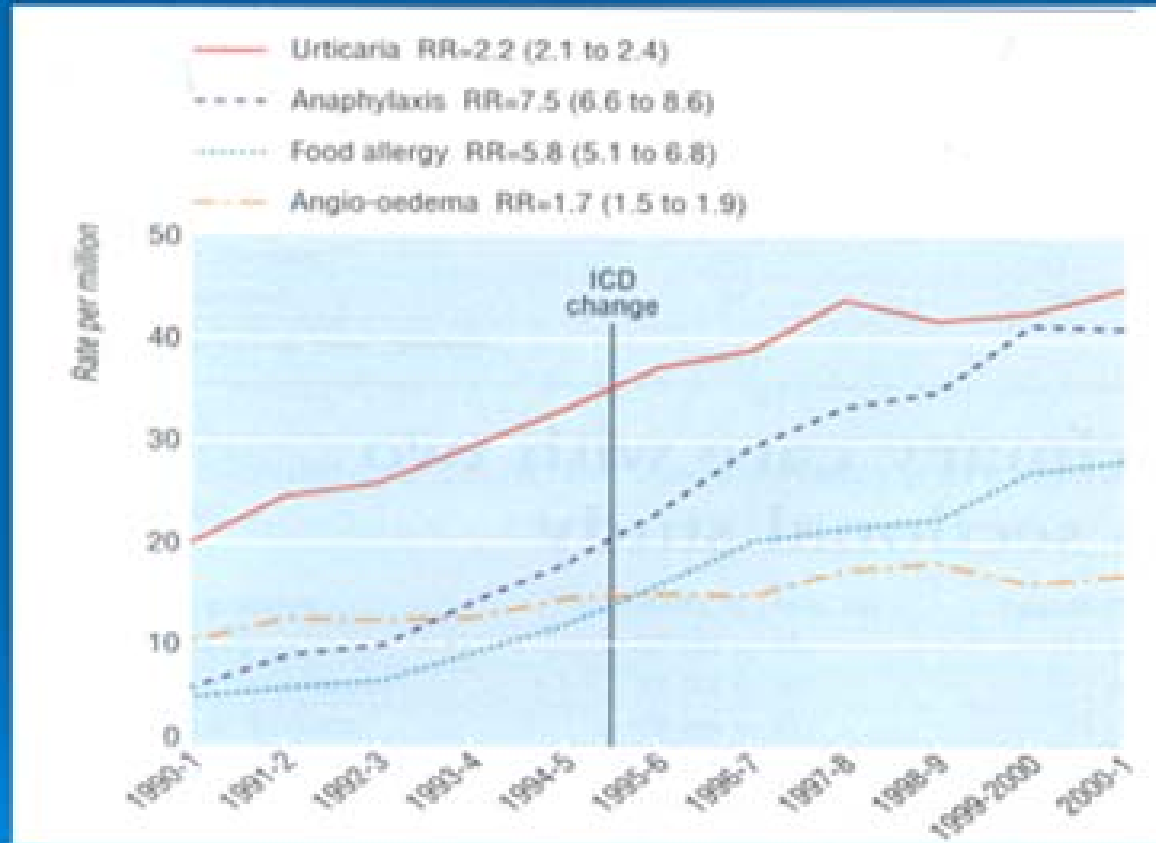


Figure from Gupta R, Sheikh, 2003



Factors to Consider in Explaining the Increasing Prevalence of Allergic Disorders

Genes

Not enough time

What we do

Diet

Modern Lifestyles

What we breathe

Airborne allergens

Outdoor pollution

Indoor pollution

What we live with – the “Hygiene Hypothesis”

Gut microbe

Patterns of infection

Immunisation, antibiotics



What We Live With

- 1976 - Original observation
 - Higher prevalence of allergic disorders in the white vs Metis communities of Saskatchewan (Gerrard, Geddes et al, 1976)
 - Higher prevalence of untreated worm, bacterial and viral infection in Metis community
- 1989
 - British study demonstrated “protection” from eczema and hay fever increased according to number of older or (weaker effect and for hay fever only) younger siblings (Strachan, 1989)



What We Live With

Further observations supporting hygiene hypothesis

- Early life contact with cattle in stable is “protective” against allergic disease and asthma (3 studies)
- 2002 – Italian study of US health survey data (34,000 subjects): hay fever and asthma far less common in subjects whose blood tests show past exposure to infections that mark poor oro-faecal hygiene (Matricardi, Rosmini et al, 2002)



Requirements for Candidate Extrinsic Protective Factors

1. Present throughout evolution of mammalian immune system
2. Depleted from environment of developed countries over last 2 – 3 decades

CANDIDATES: indigenous biota of gut and parasites



Evidence that Human Gut Flora Plays a Role in Allergic/ Non-Allergic Orientation of the Immune System

Different patterns of gut flora in babies appear to predict which babies have a higher chance of developing an allergic disorder (Bjorksten, Sepp et al, 2001)

Level 1 Evidence (randomised, double-blind, placebo controlled trial)

- Lacto bacillus GG fed prenatally to high risk mothers and postnatally to their babies for 6 months, at 2 and 4 years prevalence of atopic eczema approx. halved (Kalliomaki, Salminen et al, 2003)



Further Studies on Use of Pro-biotics in Early Childhood

5/6 studies show benefit on atopic eczema

BUT

1. Although atopic eczema is a critical marker for future development of other atopic disorders, it is particularly susceptible to dietary and gut influences
2. Study populations highly selected
3. Pro-biotic effects are strain specific and many commercial pro-biotics do not contain viable forms of what is claimed



Conclusions

- **Atopic disorders are systemic conditions**
- There are **heterogeneous changes in prevalence** including **increase in prevalence of atopic eczema**, a condition of high morbidity and with high positive predictive value for future respiratory and/or anaphylactic problems
- We have reached a stage where rather than speculating about causes for changes in prevalence, hypotheses can be supported or rejected by intervention studies

