The potential link between asthma, allergy, and obesity

Øresund Food Network, Winther School 2008-09

1st seminar: Allergy and Obesity

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Agenda

- **Background**
- **Obesity and asthma**
- **Obesity, insulin resistance, and asthma in the Inter99-study**
- **Obesity and allergy**

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What happens when a population adopts a westernized, urban, and affluent lifestyle?

Westernization →

Urbanization →

Affluence →

- **Obesity**
- **Diabetes**
- **CVD**
- **Allergy!**
- **Asthma!**

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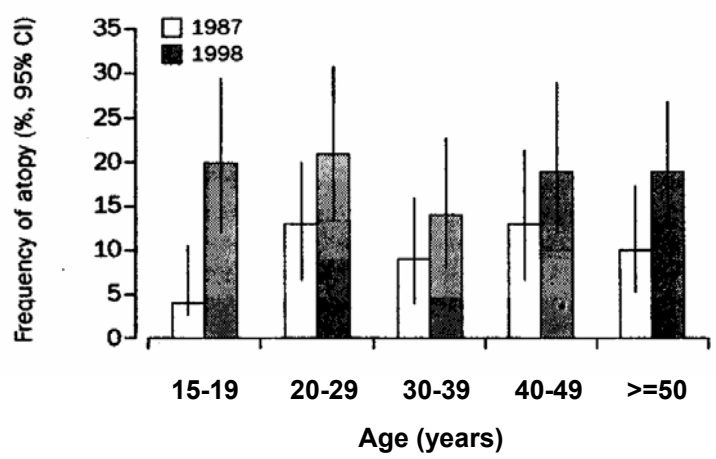
Prevalence of allergy (specific IgE in serum) in Greenland between 1987 and 1998



Krause, Lancet 2003

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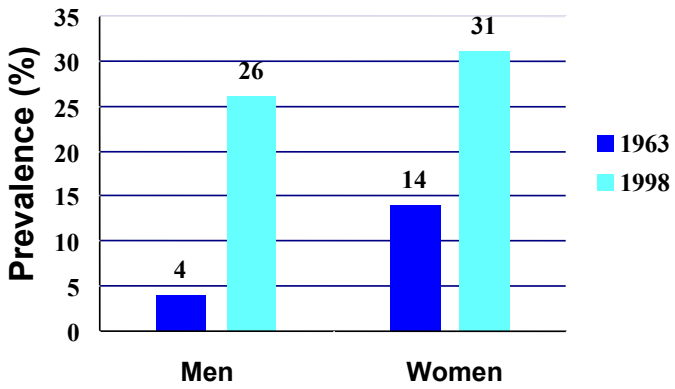
Overweight among 50-69 year-olds in Greenland



Andersen et al., Eur J Endocrinol 2004

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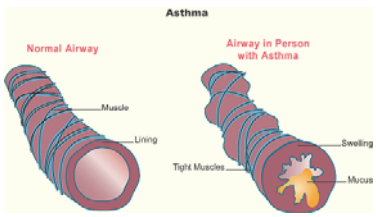
Asthma - definition

- A chronic respiratory disease with airways obstruction
- Characterized by episodes/ attacks of inflammation and constriction of the airways
- The airway constriction responds to bronchodilators
- Symptoms: wheezing, shortness of breath, chest tightness, and coughing
- Allergic and non-allergic asthma



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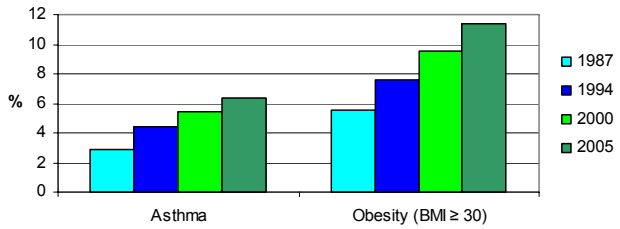
Prevalence of asthma and obesity in Denmark

(1987-2005)



National Institute of Public Health

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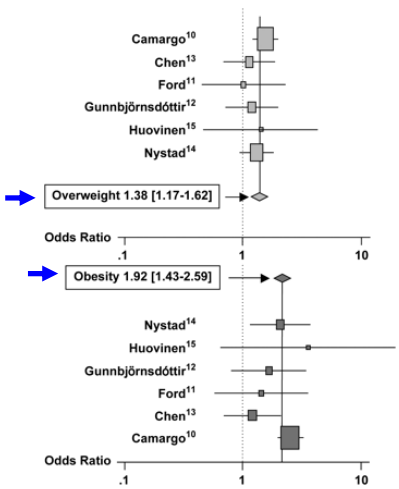
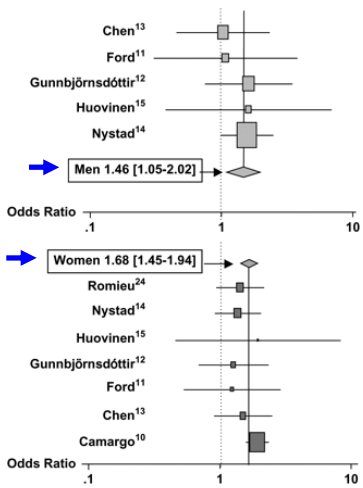
Incident asthma and obesity





Beuther et al., Am J Respir Crit Care Med 2007

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Asthma and weight changes

- Observational studies indicate that weight gain is associated with increased risk of asthma
- Weight loss induced by bariatric surgery in obese asthmatics → decreased asthma severity
- A small randomized study: Weight loss induced by low calorie diet and physical training in obese asthmatic adults → significantly reduced asthma symptoms and medication scores and improved lung function

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Potential mechanisms

A causal relationship between obesity and asthma is indicated by the consistency of the association, the temporal relationship, and the dose-response curve - however, the specific biological mechanisms underlying the link are not known.

Hypotheses:

- **mechanical effects on the lungs**
- **alterations in immune or inflammatory responses**
- **genetic factors common to both asthma and obesity**
  (ADRB2, IGF1, TNF, etc. - gene-environment interactions)
- **hormonal influences** (oestrogen)
- **influence of maternal diet on foetal programming** (low birth weight)

Mechanical effects?

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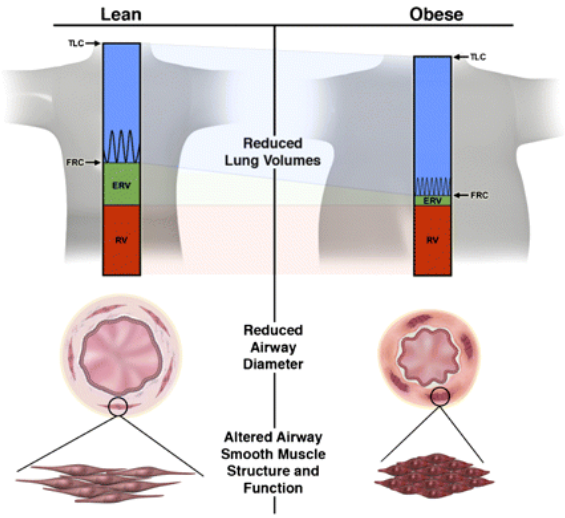

Beuther et al., Am J Respir Crit Care Med 2006

Immunmodulatory effects?

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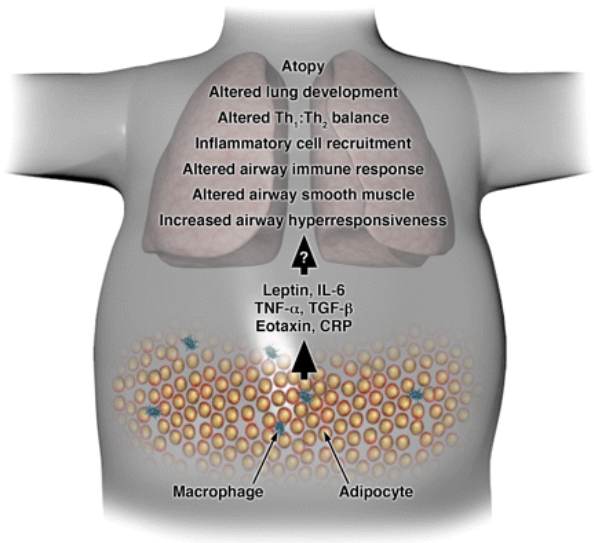

Beuther et al., Am J Respir Crit Care Med 2006

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Aim of study:

- to examine the association of obesity and insulin resistance with incident asthma symptoms in a prospective population-based study of danish adults

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Insulin resistance

- ”The subnormal biological response to a given concentration of insulin”
- Precedes the development of type 2 diabetes
- Associated with increased levels of inflammatory cytokines such as TNF-α, IL-6, and IL-1β and alterations in circulating levels of adipokines (adiponectin, leptin and resistin) seen in obesity

Hypothesis:

-the systemic low-grade inflammatory processes mediating insulin resistance may also cause asthma

-insulin resistance may be an even stronger risk factor for asthma than obesity itself

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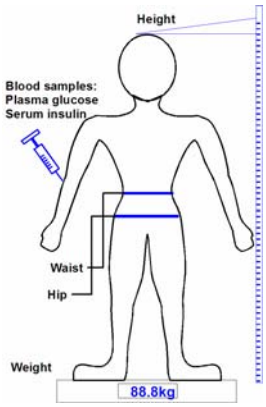
The Inter99-study

- A prospective population-based study with 5 years follow-up
- Participants were residents of Copenhagen County, Denmark and aged 30-60 years at baseline
- Questionnaires for information on asthma symptoms and confounders at baseline and follow-up
- Physical examination and blood samples at baseline
- 3,441 men and women defined as non-asthmatic at baseline and with complete information on all variables were included in the analyses
- Analyses were controlled for confounding by sex, age, social status, and smoking



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Obesity and increased risk of incident asthma symptoms

BMI Class	OR (95% CI)*	Adjusted for insulin resistance OR (95% CI)
Underweight BMI<18.5	*Data confidential*	*Data confidential*
Normal 18.5≤BMI<25	1.00 (reference)	1.00 (reference)
Overweight 25≤BMI<30	*Data confidential*	*Data confidential*
Obese BMI≥30	*Data confidential*	*Data confidential*
	P_{trend}=0.001	P_{trend}=0.057

*OR: Odds Ratio, CI: Confidence Interval

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Insulin resistance – a independent predictor for incident asthma symptoms in adults

Adjusted for:	BMI	WC	WHR
HOMA-IR	OR (95% CI)	OR (95% CI)	OR (95% CI)
Non-insulin resistant	*Data confidential*	*Data confidential*	*Data confidential*
Insulin resistant	*Data confidential*	*Data confidential*	*Data confidential*

Only normal weight subjects (18.5≤BMI<25)

(N=1,522)

HOMA-IR	OR (95% CI)
Non-insulin resistant	*Data confidential*
Insulin resistant	*Data confidential*

Results

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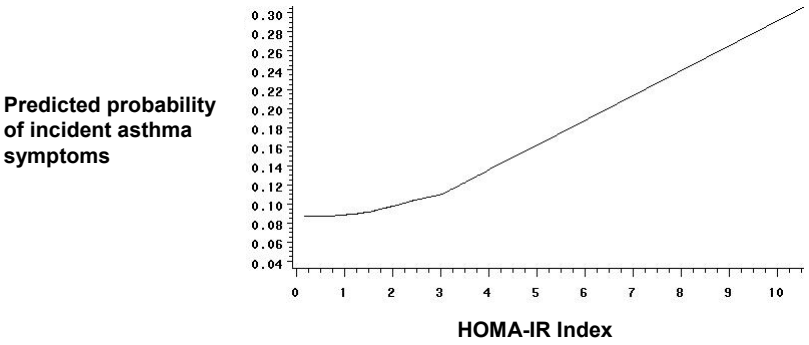
HOMA-IR index as continuous variable – dose-response relationship between degree of insulin resistance and incident asthma



Conclusions

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- All considered obesity measures were associated with incident asthma in adults
- Insulin resistance is a risk factor for incident asthma symptoms in adults – the effect is independent of obesity
- Inflammatory pathways involved in insulin resistance may also contribute to the pathogenesis of asthma
- These inflammatory processes may be part of the underlying biological mechanism linking obesity to asthma

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Obesity and the prevalence of allergy

BMI Class	OR (95% CI)*	Adjusted for insulin resistance OR (95% CI)
Underweight BMI<18.5	0.90 (0.39-2.11)	0.92 (0.39-2.15)
Normal 18.5≤BMI<25	1.00 (reference)	1.00 (reference)
Overweight 25≤BMI<30	1.18 (0.95-1.42)	1.13 (0.93-1.36)
Obese BMI≥30	1.33 (1.05-1.68)	1.11 (0.86-1.44)
	P_{trend}=0.01	P_{trend}=0.28

*OR: Odds Ratio, CI: Confidence Interval

Husemoen et al., Allergy 2008

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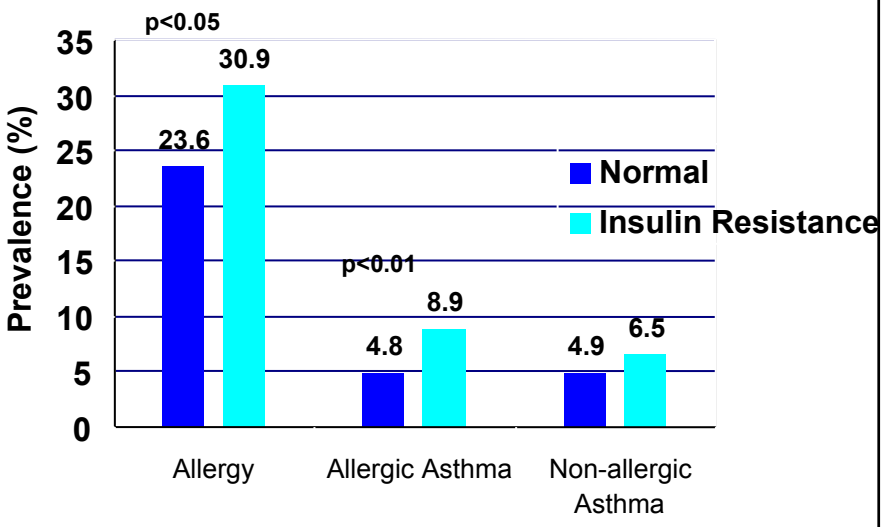
Insulin resistance and allergy



Husemoen et al., Allergy 2008

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Future studies

- The potential association between obesity and allergy
- Randomized studies of the effect of weight loss on asthma and allergy
- Studies including measurements of inflammatory and metabolic markers (e.g. cytokines, leptin and adiponectin) as well as genetic variations in these pathways to identify the specific pathways linking obesity to asthma development
- Asthma definitions!

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Betydelig gevinst ved at bekæmpe fedme

Fedme årsag til

- Øget mortalitet og nedsat livskvalitet
- Type 2 diabetes
- Hjertekarsygdom
- Apopleksi
- Kræft (fx i bryst, prostata)
- Slidgigt
- Søvnapnø syndrom
- **Astma & Allergi**

Kilde: Forslag til National Handlingsplan mod svær overvægt, Sundhedsstyrelsen 2003 (www.sst.dk)

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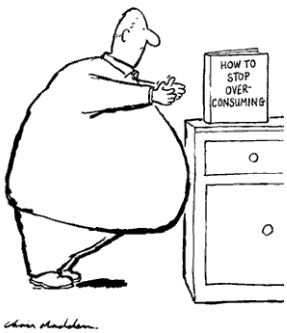

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