

Obesity and Atopy: What Is the Relationship?

‘Thou seest I have more flesh than another man, and
therefore more frailty.’
William Shakespeare
History of Henry IV, Part I, Act III, Scene 3
Falstaff to Prince Henry

There is overwhelming evidence that obesity is a threat to health. ‘The prevalence of obesity has risen up to three-fold in the last two decades. Half of all adults and one in five children in the WHO European Region are overweight. Of these, one third are already obese, and numbers are increasing fast. Overweight and obesity contribute to a large proportion of noncommunicable diseases, shortening life expectancy and adversely affecting the quality of life. More than one million deaths in the Region annually are due to diseases related to excess body weight’ [1]. While in developed countries obesity is more common among socially disadvantaged groups, the reverse is the case in low-income countries [2].

To the long list of diseases that are related to overweight and obesity, evidence obtained during the last decade suggests that also asthma and allergic diseases in general should be added [3–7]. The rise in the incidence of individuals with atopy might at least partly be due to the epidemic of obesity. Another piece of evidence is provided in this issue of *International Archives of Allergy and Immunology* [8]. In a comprehensive investigation including almost 2,000 adult residents of the town of Humboldt, Saskatchewan, Canada, the authors assessed atopy by skin prick tests and found a 50% increased risk in obese adults with a more pronounced effect in females.

Earlier reports relating asthma and other allergic diseases to overweight and obesity were welcomed with skepticism and it was speculated that these relationships could be due to bias and confounding [9]. However, as new studies with better control of confounders as well as findings from prospective studies diminished the likelihood of the relationship being spurious [10], the time was ripe to discuss potential mechanisms responsible for the increased risk of asthma and atopy in obese children and adults [11–14].

Over the last 150 years a continuous change of lifestyle and population composition has taken place in industrialized countries. There has been a transition from a mainly rural condition focusing on agricultural production to urban conditions and industrial production, followed by developmental, administrative work and services. In parallel, hygiene and affluence have improved, leading to a continuous increase in life expectancy. This increase in life expectancy is to a large degree due to the reduction of fatal communicable diseases. As a consequence, non-communicable chronic diseases such as cardiovascular diseases, cancer and chronic pulmonary diseases became the leading causes of death. This process was accompanied by a change of lifestyle characterized by consumption of high-energy food and inactivity. In recent decades this process has accelerated due to an increase of industrialized food production. Furthermore, urban environments have changed to mainly car-focused conditions with low attractiveness to pedestrians and children in particular. Together these trends have led to the vast increase in the fraction of overweight adults and children. How could these processes be related to the sec-

ular trend of an increasing prevalence of asthma and allergies?

First of all, there is an etiologic pathway relating obesity to exacerbation of asthma. In the obese, elastic properties of the chest wall are changed leading to a reduced functional residual capacity. This may lead to shortening of airway smooth muscles (ASM) – the major cause of airway narrowing in asthma [12, 13]. Furthermore, tidal volume is reduced in obese persons leading to less frequent stretching of ASM contributing to airway stiffness by a vicious circle where reduced strain to the ASM increases ASM stiffness that in turn leads to even less strain.

Adiposity is a state of chronic inflammation. White adipose tissue has an important regulatory immunological function. There is evidence that increasing body weight leads to an increase in the levels of IL-6, leptin, and TNF- α . IL-6 increases the release of acute-phase proteins and modulates the activity of regulatory T cells. At an increased volume of white adipose tissue, reduced amounts of adiponectin are released, downregulating the secretion of IL-10 from macrophages and adipocytes. These changes lead to a Th2 bias and may cause a decreased tolerance to antigens [11].

However, it is also possible that obesity and asthma are not directly causally related but share a common etiology,

and that increases in the prevalence and incidence of asthma in the obese are due to common predispositions. These include common genetic predictors, prenatal exposure to specific nutrients and maternal nutrition, as well as colonization of the neonatal and infant gut. Some of these factors relate the hypotheses mentioned above to the hygiene hypothesis since results of experimental studies suggest that deviations in gut microbiota composition (e.g. due to changed exposure condition in developed societies) predispose to excessive energy storage and obesity [14].

Common features of these hypotheses are the proposition that obesity, a 'side-condition' of the Western lifestyle, is associated either as a causal or cofactor with immunological changes resulting in decreased immunological tolerance to antigens. More studies are definitely needed to further substantiate and discriminate the proposed hypotheses. Furthermore, details of the immunological mechanisms underlying the possible decreased immune tolerance need to be explored in greater detail.

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References

- 1 WHO European Ministerial Conference on Counteracting Obesity: Diet and physical activity for health. EUR/06/5062700/8, November 16, 2006.
- 2 Friel S, Chopra M, Satcher D: Unequal weight: equity-oriented policy responses to the global obesity epidemic. *BMJ* 2007;335: 1241–1243.
- 3 Tantsira KG, Weiss ST: Complex interactions in complex traits; obesity and asthma. *Thorax* 2001;56(suppl II):ii64–ii74.
- 4 Chinn S: Obesity and asthma: evidence for and against a causal relation. *J Asthma* 2003; 40:1–16.
- 5 Beuther DA, Sutherland ER: Overweight, obesity and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med* 2007;175:661–666.
- 6 Kilpelainen M, Terho EO, Helenius H, Koskenvuo M: Body mass index and physical activity in relation to asthma and atopic diseases in young adults. *Respir Med* 2006;100: 1518–1525.
- 7 Visness CM, London SJ, Daniels JL, Kaufman JS, Yeatts KB, Siega-Riz AM, Liu AH, Calatroni A, Zeldin DC: Association of obesity with IgE levels and allergy symptoms in children and adolescents: results from the National Health and Nutrition Examination Survey 2005–2006. *J Allergy Clin Immunol* 2009;123:1163–1169.
- 8 Chen Y, Rennie D, Cormier Y, Dosman J: Association between obesity and atopy in adults. *Int Arch Allergy Immunol* 2010; 153:372–377.
- 9 Wilson MM: The association of asthma and obesity. Is it real or a matter of definition, Presbyterian ministers' salaries and earlobe creases? *Arch Intern Med* 1999;159:2513–2514.
- 10 Chinn S: Asthma and obesity: where are we now? *Thorax* 2003;58:1008–1010.
- 11 Hersoug LG, Linneberg A: The link between the epidemics of obesity and allergic diseases: Does obesity induce decreased immune tolerance? *Allergy* 2007;62:1205–1213.
- 12 Shore SA: Obesity and asthma: possible mechanisms. *J Allergy Clin Immunol* 2008; 121:1087–1093; quiz 1094–1095.
- 13 Shore SA: Obesity, airway hyperresponsiveness, and inflammation. *J Appl Physiol* 2010; 108:735–743.
- 14 Penders J, Stobberingh EE, van den Brandt PA, Thijs C: The role of the intestinal microbiota in the development of atopic disorders. *Allergy* 2007;62:1223–1236.