Obesity, allergy and immunology

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Asthma, allergy, and obesity are common health problems, and their prevalence is increasing (Fig 1).[1] Obesity is defined by a body mass index of greater than 30. Over the last few years, a number of studies have described an association between obesity and asthma (Fig 2).[2-7] In a large population of white Australian girls, a higher body mass index was reported to be a risk factor for atopy and wheeze.[8] As a corollary, weight loss, as after bariatric surgery, has consistently been shown to improve asthma severity and control (Fig 3).[9]

Changes in airway structure and function have been associated with obesity. For example, it is common to observe an atypical obese airway pattern in morbidly obese persons at bronchoscopy (Fig 4). This pattern is believed to be attributed to fat infiltration and might be responsible for airway narrowing. In regard to physiologic changes, Boulet et al[10] recently reported that obese subjects had lost the protective effect of deep inhalation to methacholine-induced bronchoconstriction that was observed in nonobese individuals (Fig 5).

Fat tissue in obese persons is a source of inflammatory mediators (Table I)[11] that might be implicated in asthma pathophysiology. Leptin is of particular interest because it has been found to be present in higher

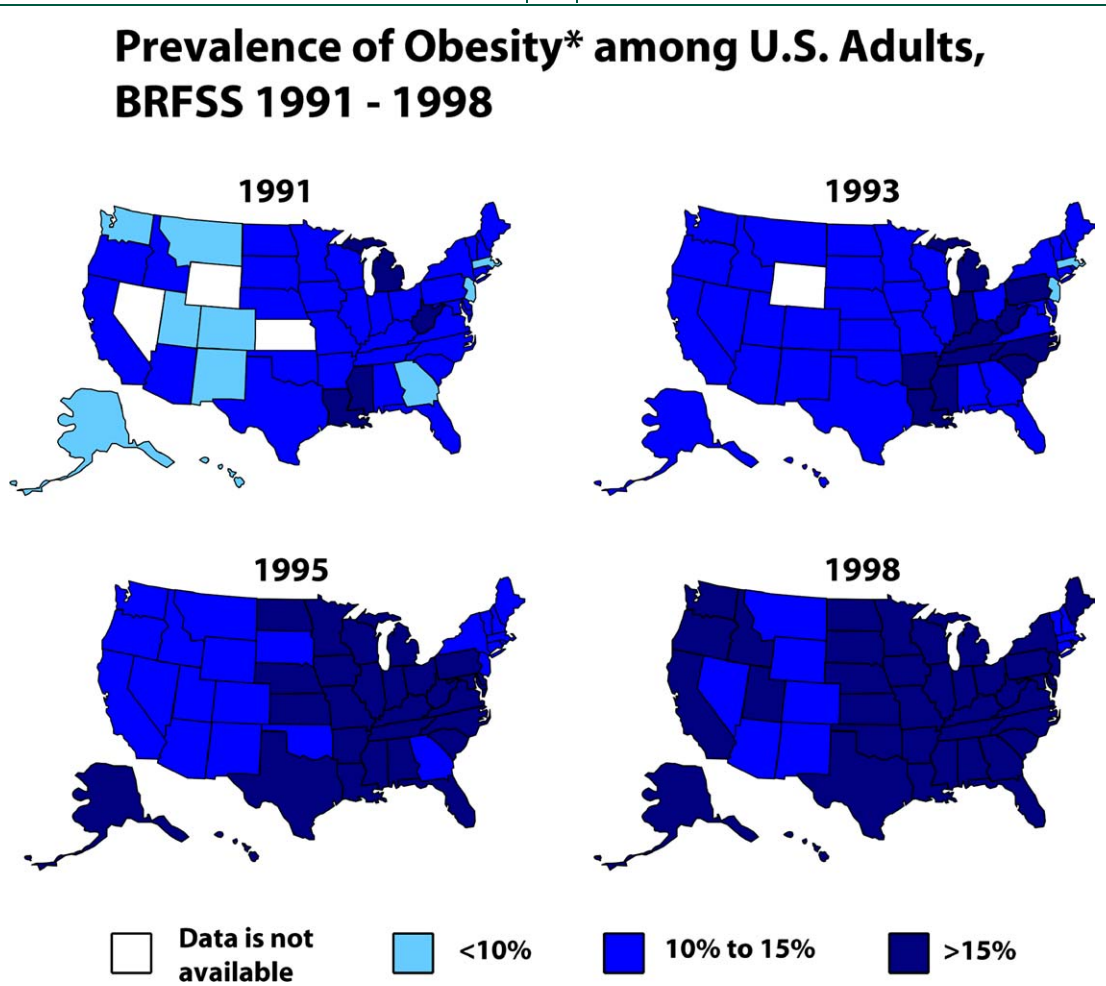

FIG 1. Prevalence of obesity in the United States. A significant increase was observed in the 1990s throughout the United States. Mokdad AH, Serdula MK, Dietz WH, Bowman BA, Marks JS, Koplan JP. The spread of the obesity epidemic in the United States, 1991-1998. JAMA 1999;282:1519-22.

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TABLE I. Inflammatory mediators produced by fat tissue

Mediators release	Visceral fat	Subcutaneous fat
Leptin	+	++
TNF-α	+	+
IL-6	++	+
Plasminogen activator inhibitor 1	++	+
Insulin-like growth factor 1	+	+

Modified with permission from Wajchenberg.[12]

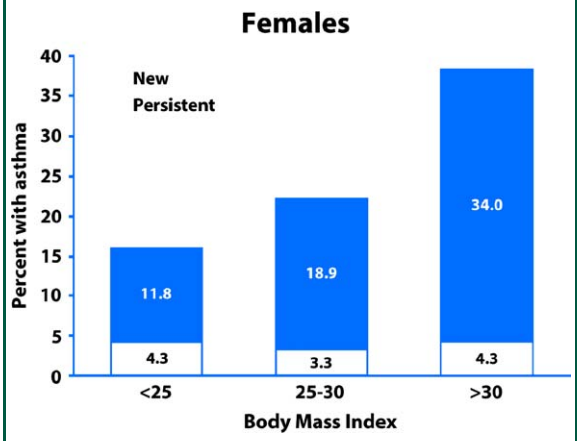

FIG 2. Association of high body mass index with asthma. In female subjects asthma is more prevalent in overweight and obese individuals. Reproduced with permission from Hancox et al.[2]

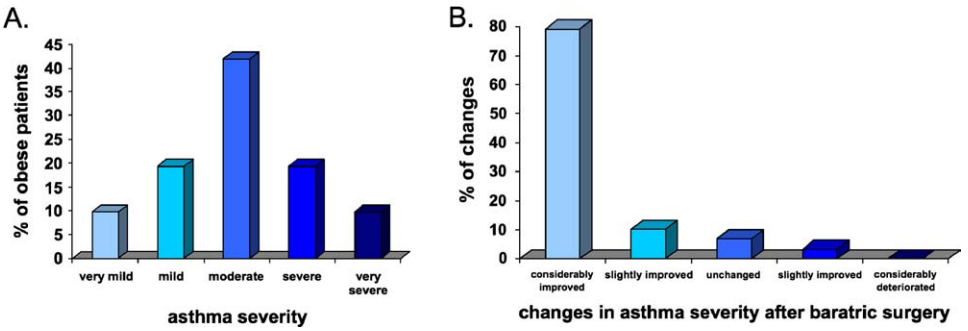

FIG 3. A, Asthma severity among morbidly obese asthmatic subjects before bariatric surgery. **B**, Changes in asthma severity after bariatric surgery. Close to 70% of obese asthmatic subjects have moderate-to-severe asthma. Two years after the bariatric surgery, 80% of obese asthmatic subjects have considerably improved their asthma symptoms and control. Reproduced with permission from Obesity Surgery 2004;14:1381-8.

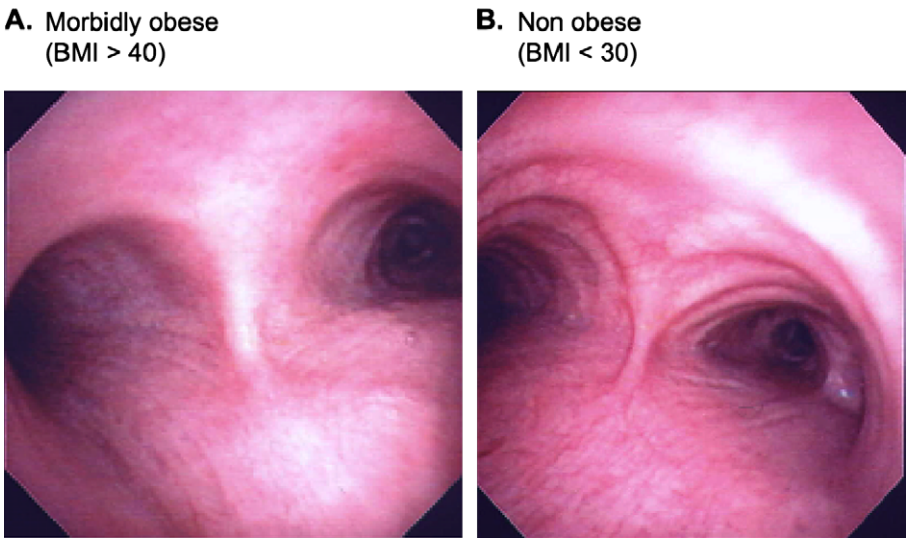

FIG 4. Airways of a morbidly obese person **(A)** and of a nonobese person **(B)**. In morbidly obese individuals it is common to observe widening of the bifurcation and a less-defined cartilage ring. *BMI*, Body mass index.

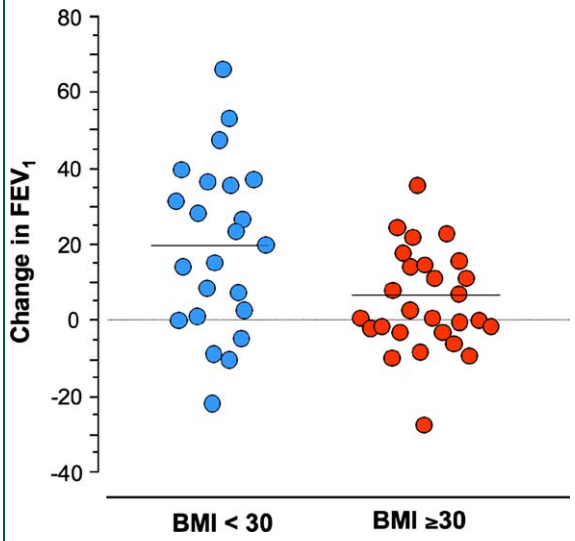

FIG 5. Absence of a protective effect of deep inhalation to methacholine-induced bronchoconstriction in obese subjects. For a similar dose of methacholine, avoidance of deep inspiration for a 20-minute period before methacholine challenge increased the decrease in FEV_1 compared with nonavoidance in nonobese subjects (*blue circles*, body mass index *[BMI]* <30; $P = .0003$), whereas no difference was observed in obese subjects (*red circles*, body mass index ≥30; $P > .05$).

levels in obese asthmatic subjects compared with in obese nonasthmatic subjects (Fig 6).[12] Leptin, an adipocyte-derived hormone, has been suggested to upregulate the inflammatory immune response. In an animal model of asthma, Shore et al[13] recently showed that the allergen airway response is increased in the presence of leptin. They found that airway hyperresponsiveness, the number of BAL eosinophils and lymphocytes, and IL-4, IL-5, and IL-13 levels are all increased in leptin-treated animals compared with control animals.

However, despite the animal, epidemiologic, and physiologic evidence to date, there have been no reports yet of a comprehensive study that shows a substantial difference in the pathology of asthma in obese compared with nonobese patients.

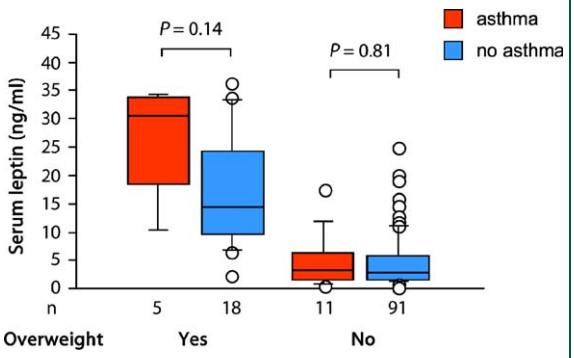

FIG 6. High levels of leptin in overweight children with asthma. High levels of serum leptin are present in overweight children, and even higher levels are found in asthmatic overweight children. Reproduced with the permission of Blackwell Publishing from Mai XM, Bottcher MF, Leijon I. Leptin and asthma in overweight children at 12 years of age. Pediatr Allergy Immunol 2004;15:523-30.

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