Obesity and Asthma

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Definitions

• Adults
  • Obesity  >30 kg/m²*
  • Overweight >25 kg/m²

• Children
  • Obesity >95th percentile for age and gender⁺
  • Overweight >85th percentile for age and gender

*40% of US population
⁺19 % of US population
Prevalence of obesity*, ages 20+, age standardized
Both sexes, 2008

Prevalence of obesity (%)
- <10
- 10–19.9
- 20–29.9
- ≥30
- Data not available
- Not applicable

* BMI ≥30kg/m²

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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization
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The prevalence of childhood obesity is increasing worldwide.

By 2020, an estimated 60 million children worldwide will be overweight or obese.
They banned soda pop in Los Angeles schools 'cuz they say it makes kids fat! What's next... Nintendo?
Current Asthma Prevalence Percents by Age, Sex, and Race/Ethnicity, United States, 2017

Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention
Figure 2. Current asthma prevalence among adults aged 20 and over, by weight status and race and Hispanic origin: United States, 2011—2014

1Significantly higher than normal weight ($p < 0.05$).
2Significantly higher than overweight ($p < 0.05$).
NOTES: Age adjusted by the direct method to the 2000 U.S. Census population using age groups 20–39, 40–59, and 60 and over.
Access data table for Figure 2 at: http://www.cdc.gov/nchs/data/databriefs/db239_table.pdf#2.
Risks Associated with Obesity

- Atherosclerosis
- Dyslipidemia
- Kidney Disease
- Hypertension
- Metabolic Syndrome
- Type 2 diabetes
- Asthma
- Increased hospitalizations
- Isolation and depression
Effects of Obesity

• Sedentary lifestyle and behavior leads to poor conditioning.
• Increased intake of processed and high-fat foods leads to reduced antioxidants, diabetes, and cardiovascular diseases.
• Increased work of breathing at any level of effort including resting.
• Increased risk of sleep disordered breathing and GERD.
• Abnormalities of pulmonary function at rest and with exercise.
Does obesity lead to higher incidence of asthma or vice versa?
Does obesity lead to a higher incidence of asthma (or vice versa)?

- Prevalence studies
  - Difficult to determine causation because of confounding variables (inactivity, effects of systemic steroids, etc.) or confounding conditions (OSAS, GERD, etc.).

- Prospective studies
  - Require a strict definition of asthma.
  - Control of confounding variables including conditions.
  - Ideally have a control or well-defined comparison group.
Obesity Leads to Increased Incidence of Asthma

• Adults
  • Obesity is a risk factor for development of a new diagnosis of asthma 1.1 and 3.0 X non-obese subjects.
  • Increasing BMI leads to increasing risk.
  • The relationship appears to be stronger for women than men.

• Children
  • A similar relationship to adults with some studies showing a greater risk for girls and some showing a greater risk for boys.
  • Stage of lung development and prepubertal sex hormone differences in children at various ages probably account for these inconsistencies.
Asthma and Obesity?

- How does obesity predispose to a higher prevalence of asthma and asthma symptoms?
  - Anatomic and physiologic effects.
  - Comorbidities (GERD, SDB).
- What are the differences between allergic asthma and asthma associated with obesity?
- Is there a difference in response to asthma medications in obese individuals?
- What are the effects of weight reduction on asthma symptoms and QOL in obese individuals with asthma?
Pulmonary Physiology
Why does obesity predispose to air flow limitation?
Obesity is a state of chronic inflammation.
T Cells

TH Helper (CD4+)

TH1
Helps macrophages produce an inflammatory response

TH2
Helps B cells produce antibodies
Adipose Tissue

• An important endocrine organ that produces and secretes two hormones, adipokines, important in energy regulation.

• The two most studied-leptin, adiponectin.

• Adiponectin-anti-inflammatory
  • Decreases inflammatory and increases anti-inflammatory cytokines.
  • Decreased synthesis in obesity.

  • “starvation” hormone.
Leptin

- Proinflammatory
- Favors chemotaxis, phagocytosis, and a TH1 cellular response.
- Elevated in obesity.
- Favors a higher TH1/TH2 cellular ratio leading to nonatopic inflammation.

- Other effects
  - Increases metabolism
  - Involved in surfactant production
  - Increases airway hyperresponsiveness
  - Affects cholinergic airway tone
  - Regulates ventilatory drive
Leptin levels rise with increasing BMI
## Difference Between Atopic Asthma and Obesity and Asthma

<table>
<thead>
<tr>
<th>Atopic Asthma</th>
<th>Non-Atopic Asthma and Obesity</th>
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<tbody>
<tr>
<td>• TH2/TH1 ratio leads to allergic phenotype with eosinophils in airways.</td>
<td>• TH1/TH2 ratio leads to airway inflammation due to neutrophils in the airway.</td>
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<td>• Potentially normal PFTs when well.</td>
<td>• PFTs often not normal even with optimal therapy and environmental control due to mechanical factors.</td>
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<td>• FeNO increases with increasing eosinophil inflammation.</td>
<td>• FeNO not reliable indicator of airway inflammation.</td>
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<td>• Expected response to asthma medications with step wise therapy.</td>
<td>• Response to asthma medications suboptimal.</td>
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Mechanical Factors That Affect Airways
Android Obesity  Gynoid Obesity

Dixon, Peters  2018
Pulmonary Function Abnormalities in Obesity

- Reduction in lung volumes
  - (F)V C, TLC, FRC, ERV, IC, Vt
- Abnormalities of respiratory mechanics
  - Decreased respiratory compliance
  - Increased work of breathing
- Flow limitation
  - Decreased FEV1, FEF25-75
  - Increased airway resistance and decrease airway conductance
- Increased oxygen consumption and CO2 production
Functional Residual Capacity

• FRC is the resting volume of the lung after a normal quiet expiration.
• Sum of the expiratory reserve volume and residual volume.
• It is reduced in obesity.
• Leads to
  • Airway narrowing and early airway closure
  • Ventilation and perfusion mismatching
  • Increased ventilatory rate due to shallow breathing
  • Smooth muscle dysfunction and increased airway hyperresponsiveness
Comorbidities
Aggravating Asthma Control in Obesity
Gastroesophageal Reflux

- Higher prevalence in obese individuals and an independent risk factor for asthma symptoms and poor asthma control.
- Reflux or Reflex or both is the underlying mechanism.
- Micro aspiration leads to TH1 mediated inflammation in the airways.
- Asthma medications that relax smooth muscle can aggravate reflux.
- PPI’s probably play some role in helping this.
- Weight loss and diet control are important.
Sleep Disordered Breathing

- Decreased resting lung volumes and intermittent hypoxemia can cause airway and systemic TH1 mediated inflammation.
- Like obesity, airway smooth muscle is affected leading to increased AHR.
- Vagal stimulation during upper airway collapse leads to reflex increased AHR.
- Treatment for SDB ranges from CPAP to surgery but weight loss is optimal.
- CPAP improves asthma symptoms and PEFRs and decreases use of rescue medications.
Does weight reduction lead to better asthma control and quality of life?
• Children 8-18 years with mod-severe overweight followed a healthy diet for 6 weeks.

• Outcome measures: exercise challenge with cold air before and after, FeNO, PAQLQ, and ACQ.

• Results: Decrease in BMI 2.6%, decrease in fall in FEV1 from 30% to 21%, and improvements in PAQLQ.

• Conclusions: Weight reduction in children leads to reduced exercise associated airways obstruction and better quality of life.
• 14 obese adults with very low-calorie diet for 8 weeks.
• Outcome measures: PEF variability, FEV1, lung volumes, Raw, Gaw, and minute ventilation.
• Results: BMI decreased from 37 to 32 kg/m², diurnal and day to day PEF variability declined, FEV1 and FVC increased, Raw decreased, and resting minute ventilation decreased.
• Conclusions: weight loss reduces airways obstruction and PEF variability in obese adults.
• 23 obese adult asthmatics undergoing bariatric surgery.
• Outcome measures included comparison to a non asthmatic group of obese patients also undergoing bariatric surgery: ACQ, response to methacholine, serum and BAL leptin and adiponectin levels, CD4+ lymphocyte cytokine levels, serum IgE at baseline and at 12 months after surgery.
• BMI decreased from 51.4 to 37.5 at 12 months.
• AHR improved significantly in those with normal IgE serum levels but not in those with elevated levels.
• Paradoxical increase in CD4+ derived cytokines at 12 months.
  • Related to changes in medication use.
• Trend to decrease in leptin levels and a significant increase in adiponectin levels at 12 months.
• ACQ scores went down and patients reported less use of rescue medications.
• Conclusions
  • Weight reduction more effective in non allergic obese patients.
  • As lymphocyte numbers were not affected after surgery, medications directed at lymphocyte derived cytokines may be less effective in obese patients.
  • Increased AHR in obese patients may be due to other factors including breathing at low lung volumes, decreased adiponectin levels and increased leptin levels.
  • Non allergic obese patients may represent a unique asthma phenotype.
Treatment

- Medications
- Weight reduction
- Exercise
- Diet and nutrition
Obese asthmatics have a suboptimal response to standard asthma therapies

- Lower lung volumes lead to smaller airways that may affect distribution of inhaled medications.
- Altered cellular responses to corticosteroids in some obese individuals.
- Fixed airway obstruction due to abnormally linked smooth muscle and airway remodeling.
- Corticosteroids work better than leukotriene modifiers.
- Responses to beta-agonists are usually normal.
High fat diets including synthetic trans fats lead to increased inflammatory mediators and reactive oxygen species.
  • Also associated with airway neutrophilia.

Diets high in antioxidants and vitamins may lead to lower inflammation.

Vitamin D deficiency is common in obesity and vitamin D may have a role in enhancing immunity.

Diets high in omega-3 may have benefit in asthma.
  • Asthma prevention in children
  • Decrease FeNO and airway reactivity in children
  • Reduce EIB and response to allergen challenge
Mediterranean Diet

- Fresh fruits and vegetables are high in antioxidants which may be beneficial in airway inflammation.
- A trend to improvement in asthma symptoms (Sexton et al., 2013).
- 1,125 Greek children had lower risk of asthma (Grigoropoulou et. Al., 2011).
- 158 asthmatic and 50 non-asthmatic Mexican children had better lung function (Romieu et al., 2009).
- No protective effect on development of asthma in 7000 Spanish children (Gonzalez et al., 2010).
Pre/Probiotics

- Microbiome
- Obesity alters the gut microbiome.
- Gut microbiome plays a role in the regulation and maintenance of hyperglycemia, insulin resistance, and systemic inflammation.
- The gut microbiome altered early in life by antibiotic exposure, formula feeding, c-section delivery, and early exposure to pets and/or farm animals may influence the development of allergy.
- In obese mice, the microbiome determines an asthmatic response to a non-allergic trigger (ozone) with a neutrophilic response.
Pre/Probiotics

- There are sex differences in the gut microbiome in humans,
- And this may regulate differences in immune function and may account for a female predominance in late onset non-allergic asthma in obesity.
- Evidence in small studies for beneficial effects of pre/probiotics in asthma and obesity with asthma:
  - Inulin+probiotics reduces FeNO and inflammation in stable asthmatics.
  - Probiotics may help promote weight loss along with diet control in obesity.
  - Probiotics reduce airway inflammation in mice.
  - Probiotics improve lung function and symptom scores in children with asthma.
Exercise

- Exercise as part of a comprehensive program of asthma management leads to better asthma control and improvement in lung function.
- May reduce allergic airway inflammation.
- Best in combination with diet to achieve weight reduction and better asthma control.
There appears to be 3 distinct phenotypes in asthma and obesity:

- Asthma complicated by obesity (earlier onset, high IgE, very poor asthma control).
- Asthma consequent to obesity (later onset, women, increased oxidative stress)
- Irritant induced airway disease (aggravates above phenotypes and may cause de nova disease)
Conclusions

• Asthma incidence increases with increasing BMI.

• It is important to evaluate atopy and potential comorbidities in obese patients with asthma.

• Obese patients with asthma may have suboptimal response to controller medications and require higher doses and combinations.

• Weight loss is the most effective therapy for improvement of asthma symptoms and control.

• Diet high in antioxidants may be important adjunctive therapy.
Thank you