

# Obesity and Infection

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# Obesity & Infection

- The role of obesity in infections has not been well appreciated
  - Does obesity influence:
    - The susceptibility for the development of infections?
    - The outcome of infections (once developed)?
  - If yes, what are the factors mediating these associations?

# Obesity & Likelihood of Development of Infection

- Perioperative infections
  - Surgical site infections
    - Case-control study
    - Setting: 130-bed tertiary-care teaching hospital for adult patients with cancer
    - Study followed 3372 surgeries
    - Obesity was independently associated with the development of surgical site infection
    - OR = 1.76, 95% CI = 1.14-2.7

# Coronary Artery Bypass Grafting

1 <sup>st</sup> Author	Number of patients/ procedures	Comparison groups (BMI)	Type of infection	Odds ratio (95% CI)
Crabtree	4004	Obese vs non-obese	Superficial sternal wound infection	1.09 (1.06–1.12)
			Deep sternal wound infection	1.08 (1.04–1.11)
Lilienfeld	1204	Obese vs non-obese	Sternal wound infection and/or endocarditis	6.2 (p<0.05)
Potapov	22 666	26–26.9	Infection following coronary artery bypass grafting	1.0
		28–28.9		1.2 (1.1–1.7)
		34–34.9		1.8 (1.1–2.6)
		≥36		3.7 (2.7–4.8)
Harrington	4474	Obese vs non-obese	Surgical-site infection	1.8 (1.4–2.3)

Adapted from: Falagas ME, Kompoti M. Lancet Infect Dis. 2006;6(7):438-46.

# Obstetric & Gynecologic Surgery

- 574 women undergoing both elective and non-elective caesarian delivery
  - Higher BMI associated with greater infectious morbidity
    - Endomyometritis, wound infection, urinary tract infection, septic pelvic thrombophlebitis, pneumonia

# Obesity & Higher Incidence of Infection in Surgical Patients

- Orthopedic & spinal surgery
- Vascular surgery
- Bariatric surgery
- Vascular surgery
- Liver transplantation
- Burn patients

Davenport DL, et al. J Vasc Surg. 2009;49(1):140-7.

Schaeffer DF, et al. Ann Hepatol. 2009;8(1):38-40.

# Obesity-Related Factors that can Increase the Risk for SSI

- Adipose tissue has relatively low blood supply
  - Impaired oxygenation during laparoscopic surgery
  - Delayed wound healing
- Local tissue trauma due to retraction
- Longer operative time
- Higher likelihood of nasal carriage of *Staphylococcus aureus*

Flancbaum L, Choban PS. Annu Rev Med. 1998;49:215-34.

Herwaldt LA, et al. Infect Control Hosp Epidemiol. 2004;25(6):481-4.

Fleischmann E, et al. Obes Surg. 2005;15(6):813-9.

# Obesity & Infection in Intensive Care Unit Patients

- Matched case-control study, medical-surgical ICU
- 170 Obese patients under mechanical ventilation were matched with 170 normal-weight patients
- During ICU stay, obesity was associated with:
  - Higher rate of septic shock (8% vs. 3%)
  - Higher rate of acquisition of infection (24% vs. 15%)
    - Ventilator-associated pneumonia, bloodstream infection, deep surgical site infection

# Factors that can Increase the Risk of Infection in Obese Inpatients

- Medical and nursing care of obese patients
  - Delay in diagnostic evaluation due to difficulty in patient transfer and accommodation
  - Difficulty in mobilization and physical therapy
- Breaches in skin integrity
- Increased duration of mechanical ventilation

El-Solh A, et al. Chest. 2001;120(6):1989-97.

Yaegashi M, et al. J Intensive Care Med. 2005;20(3):147-54.

# Factors that can Increase the Risk of Infection in Obese Inpatients - II

- Difficulty in obtaining vascular access
  - More punctures for insertion of central venous catheters (CVCs)
    - Increased rate of complications
  - Higher duration of use of CVCs
- Higher duration of use of bladder catheters
  - Increase in the rate of urinary tract infections

El-Solh A, et al. Chest. 2001;120(6):1989-97.

Bochicchio GV, et al. Surg Infect (Larchmt). 2003;4(4):379-85.

# Does BMI Influence the Outcome of Infections?

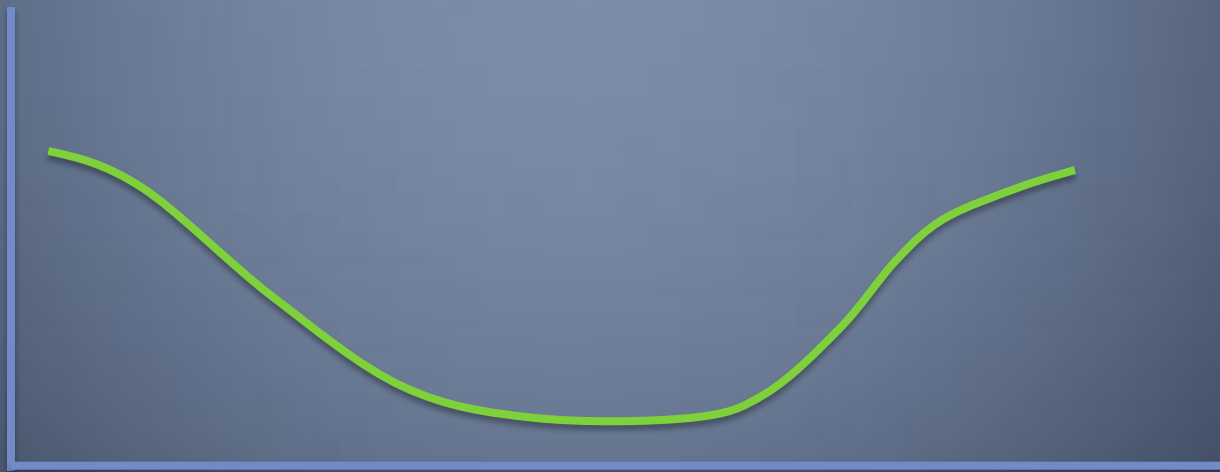
- Systematic review of the literature
- 11 relevant studies identified
  - 9/11 studies involved hospitalized patients (3/9 studies involved ICU patients)
  - 6/11 studies referred to the outcome of lower respiratory tract infections
  - Mortality was the outcome assessed in 9/11 studies
  - Various body weight groups were compared

# Data Synthesis

- 7/11 studies showed significant associations between body weight category and outcome of infections
  - Obese or morbidly obese patients had worse outcome than the rest of patients or normal weight ones in 4/7 studies
  - Patients with the lowest BMI had worse outcome than the rest of the patients in 3/5 studies

# Data Interpretation

- A U-shape or J-shape association between BMI and the outcome of infections might exist, although findings are not always consistent



# Obesity and Respiratory Tract Infections

- Obese patients have increased risk for respiratory comorbid diseases
  - Asthma, chronic bronchitis, obstructive sleep apnea, pulmonary embolism
  - Obstructive sleep apnea increases risk for aspiration
- Direct effect of obesity on lung mechanics
- Decreased respiratory reserve function

Beuther DA, et al. Am J Respir Crit Care Med. 2007;175(7):661-6.

Guerra S, et al. Chest. 2002;122(4):1256-63.

McClellan KM, et al. Thorax. 2008;63(7):649-54.

# Obesity & the Immune System

- Adipose tissue is not metabolically inert
- Adipose tissue matrix (non-fat) cells produce a variety of cytokines, chemokines, proteins, growth factors
  - IL-6
  - TNF-alpha
  - Monocyte chemoattractant protein 1
  - Plasminogen activator inhibitor 1
  - Vascular endothelial growth factor

Fain JN, et al. *Endocrinology*. 2004;145(5):2273-82.

Fantuzzi G. 2005;115(5):911-9.

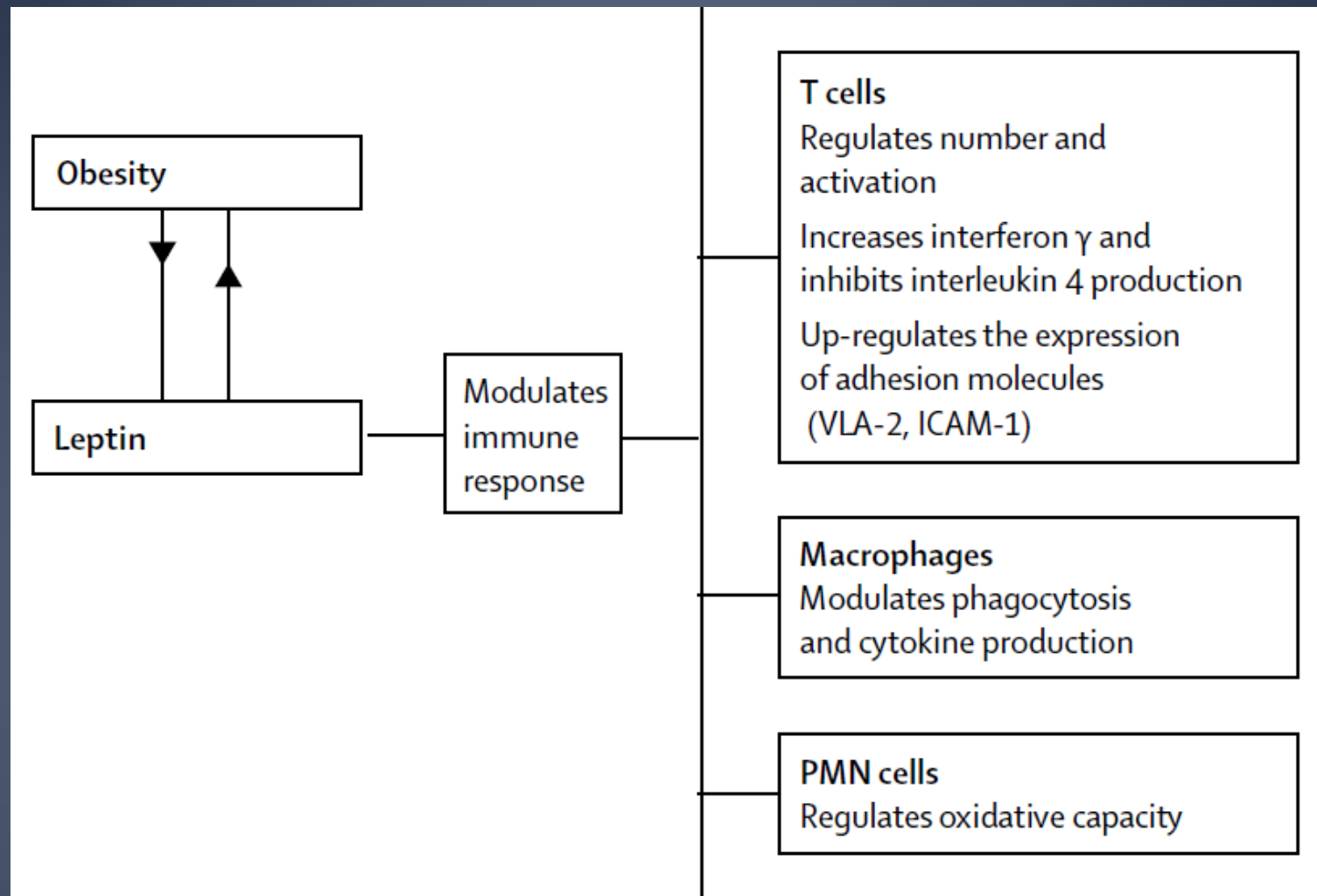
# Obesity & the Immune System – II

- Adipocytes produce hormones that act on the immune system
  - Leptin
    - Production increased in obesity
    - Pro-inflammatory effects
  - Adiponectin
    - Production decreased in obesity
    - Anti-inflammatory effects

Faggioni R, et al. FASEB J. 2001;15(14):2565-71.

Ukkola O, et al. J Mol Med. 2002;80(11):696-702.

Arita Y, et al. Biochem Biophys Res Commun. 1999;257(1):79-83.

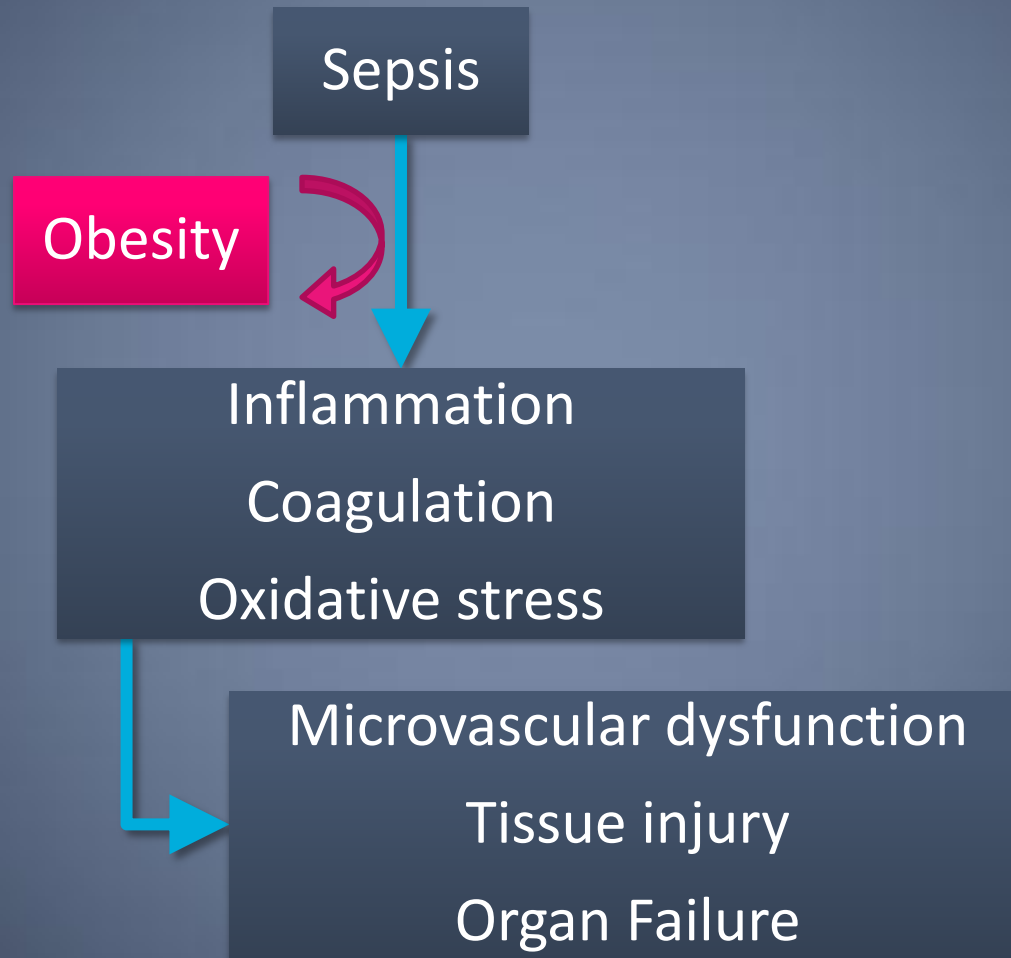


**Leptin has a key role in linking nutritional state to the immune response**

Leptin deficiency has been associated with susceptibility to infections in animals as well as in human beings

Adapted from: Falagas ME, Kompoti M. Lancet Infect Dis. 2006;6(7):438-46.

# Obesity & Sepsis: a Linking Hypothesis



# Factors that can Influence the Association of Obesity & Infection

- Obesity comorbidities
  - Diabetes mellitus
    - Impaired neutrophil and monocyte/macrophage function
      - Chemotaxis, phagocytosis, bactericidal capacity
  - Cardiovascular disease
- Inappropriate dosage of antibiotics
  - Decreased effectiveness, higher toxicity, emergence of antimicrobial drug resistance

Geerlings SE, et al. FEMS Immunol Med Microbiol. 1999;26(3-4):259-65.

Falagas ME, et al. Obes Rev. 2009;10(3):280-9.

# Dosing of Antibiotics for Obese Patients

- Specific pharmacokinetic studies in obese patients are not required during new drug development
- The physiological alterations of obesity can affect the distribution, protein-binding, metabolism, and clearance of antimicrobial agents

# Dosing of Antibiotics for Obese Patients

- Data indicate need for increase in the dosage of several  $\beta$ -lactams, vancomycin, fluoroquinolones, macrolides, linezolid, sulphonamides, and fluconazole in obesity
- Exact body weight measure that must be used for each agent requires further study

## Hydrophilic

- $\beta$ -lactams
  - Penicillins
  - Cephalosporins
  - Monobactams
  - Carbapenems
- Glycopeptides
- Aminoglycosides
- Polymyxins
- Fosfomycin

## Lipophilic

- Fluoroquinolones
- Macrolides
- Lincosamides
- Tetracyclines
- Tigecycline
- Co-trimoxazole
- Rifampicin
- Chloramphenicol

## Hydrophilic and lipophilic classes of antibiotics

Degree of hydrophilicity/lipophilicity can differ between agents of each class

# Obesity and 2009 Pandemic Influenza

- Obesity highlighted as an important risk factor
- We systematically reviewed 15 studies reporting the experience with pandemic influenza in the Southern Hemisphere during the 2009 winter season

Louie JK, et al. JAMA. 2009;302(17):1896-902.

Falagas ME, et al. Submitted for publication

# Obesity and 2009 Pandemic Influenza

- The prevalence of obesity among the influenza cases increased as the severity of cases increased
  - 1.8% in unselected cases
  - 1.6-13.3% in hospitalized cases
  - 28.5-44% in ICU admitted cases

# Can infection be the cause of obesity?

- Animal and human viruses have been shown experimentally to cause obesity
- Viruses potentially related to human obesity
  - SMAM-1 (avian adenovirus)
  - 3 human adenoviruses (Ad-36, Ad-37, Ad-5)
- Ad-36 present in 30% of obese humans vs. 11% of non-obese humans