The Epidemic of Obesity

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I am a consultant, speaker, advisor, or receive research support from:

Abbott
Allergan
Amylin,
Arena
Ethicon-Endosurgery
GI Dynamics
Novo Nordisk
Orexigen
Sanofi
Vivus

I have stock ownership in *BMIQ* and Atlas Therapeutics
The Epidemic of Obesity is Worldwide

Reproduced from the Organisation for Economic Co-operation and Development.7

More Than 2/3 of Adults are Overweight or Obese

- Overweight (BMI = 25-29.9)
- Obese (BMI = ≥ 30)
- Extremely Obese (BMI = 40)

NHANES I 1960-1962
NHANES II 1971-1974
NHANES III 1988-1994
NHANES 1999-2000
NHANES 2001-2002
NHANES 2003-2004
NHANES 2005-2006
NHANES 2007-2008

13.4%
31.5%
0.9%
34.3%
33.6%
6.0%

NHLBI. Obes Res. 1998;6(suppl 2):51S-209S.
www.cdc.gov/nchs/data/hestat/obesity_adult_07_08/obesity_adult_07_08.htm

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NHLBI. Obes Res. 1998;6(suppl 2):S1-S209S.
www.cdc.gov/nchs/data/hestat/obesity_adult_07_08/obesity_adult_07_08.htm
Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2009

The Biggest Increases are in Clinically Severe Obesity, US 1987-2005

- BMI ≥50: Increased 75% in 5 years
- BMI ≥40: Increased 52%
- BMI ≥30: Increased 24%

Figure 1 Percentage increase in BMI categories since 1986 (source: Behavioral Risk Factor Surveillance Survey; results adjusted for changes in population demographics to be comparable to 2005 demographics).

1972 – 2011 Football Linemen Are 68 Lbs Heavier

N.F.L. Heavyweights
Offensive linemen have been putting on the pounds over the past 30 years, as exemplified by players in various Super Bowls and by the startling size of Aaron Gibson, who now plays for Dallas.

Super Bowl VI
1972
AVG: 248.2 lbs.

Super Bowl XVI
1982
262.3 lbs.

Super Bowl XXVI
1992
281.2 lbs.

Super Bowl XXXVI
2002
303.9 lbs.

Chad Clifton
T, 6-5, 320

XLV
2011
316.3

Larry Little
Miami
G, 6-1, 265

Anthony Muñoz
Cincinnati
T, 6-6, 278

Kent Hull
Buffalo
C, 6-5, 275

Joe Andruzzi
New England
G, 6-3, 315

Chad Clifton
T, 6-5, 320
What’s Causing the Epidemic of Obesity?
Contributors to the Obesity Epidemic

The usual suspects
• Too much fattening food
• Not enough physical activity

Some new ideas
• Sleep debt
• Endocrine disruptors
• Pharmaceutical iatrogenesis
• Reduction in variability of ambient temperature
• Microorganisms
• Epigenetics-heritable changes in gene expression like DNA methylation, chromatin folding
• Increasing maternal age
• Greater fecundity among people with higher adiposity
• Assortive mating
• Intrauterine and intergenerational effects

Every One Trends UP!
Once Weight Is Gained
Tolerance to Leptin, Inflammation, New Neuronal Connections
Appear to Cause a “Ratcheting” Phenomenon

Afferent Signals

Ghrelin
GLP-1
CCK
Vagus

Amylin
Insulin

Leptin

Adrenal Steroids

Adrenal Cortex

Gut and Liver

Pancreas

Adipose Tissue

Meal Size

Energy Balance and Adipose Stores

Energy Expenditure

Efferent Signals

Stimulate

Inhibit

NPY
Orexin-A
α-MSH
CART

AGRP
Dynorphin
CRH/UCN
NE

Galantin
Endocannab
GLP-I
5-HT

External Factors
Food Availability, Palatability

Autonomic Nervous System

Food Intake

Obesity Causes Disease – It IS a Disease

Increased Expression of Some Hormones, Suppression of Others, Leads to Inflammation and Disease

INFLAMMATION

HYPERTENSION

Fat Stores

↑ LPL
↑ Lactate
↑ Angiotensinogen

ARTHURIS

↑ IL-6
↑ Leptin

DYSLIPIDEMIA

↑ FFA → ↑ Insulin
↑ Resistin

ASTHMA

↑ TNFα
↑ Adipsin (Complement D)
↑ PAI-1
↑ C-C L2
↑ Estrogen

T2DM

ASCVD

↓ Adiponectin

THROMBOSIS

ASCVD=atherosclerotic cardiovascular disease; C-C L2=chemokine (C-C motif) ligand 2; FFA=free fatty acid; IL-6=interleukin 6; LPL=lipoprotein lipase; PAI-1=plasminogen activator inhibitor-1; TNFα=tumor necrosis factor alpha.

Source: Louis J. Aronne, MD, after Dr. G Bray. ©2007
Excess Adipose Tissue Attracts and Activates Macrophages, Leading to Chronic Inflammation and Adipocyte Insulin Resistance

- When adiposity reaches a certain threshold, factors derived from adipocytes induce macrophage activation and infiltration.
- Activated macrophages secrete cytokines that impair adipocyte insulin sensitivity and stimulate further activation and infiltration of peripheral monocytes and macrophages into fat.
- Preadipocytes can also secrete chemokines under the stimulation of TNF-α, which contributes to macrophage infiltration and eventually causes systemic insulin resistance.

Diseases Caused by Obesity

More than 70 illnesses are caused by excess body weight
Obese Patients are at substantial risk to develop Type II Diabetes
Which increases with BMI

Relationship between obesity and risk of developing Type II Diabetes

Prevalence of T2DM vs. BMI

Source: Center for Disease Control, NHANES III
The Growing Burden of Obesity: Over the Next 20 Years In the US and UK, the Increase in Obesity Will Add

- 6–8 million cases of diabetes
- 5–7 million cases of cardiovascular diseases,
- More than half a million new cancers
- Negative effects on longevity, disability-free life-years, quality-of-life, and productivity
- By 2030, these increases in health-care costs by $48–66 billion a year in the USA and by 1-2 billion a year in the UK.

The Cost of Obesity

- 27% of the growth in health-care expenditure between 1987 and 2001 is attributable to the increase in obesity and increased spending on obesity-related diseases.
- A loss of 1.7–3 million productive person-years in working US adults, representing an economic cost as high as $390–580 billion over the next 20 years.

Do the 4 M’s of Obesity’s Comorbidities Improve with Weight Loss?

- Metabolic
- Mechanical
- Mental
- Monetary

The 4 M’s: Dr. Arya Sharma

There are other comorbidities besides metabolic
Do the 4 M’s of Obesity’s Comorbidities Improve with Weight Loss?

- Metabolic - Yes
- Mechanical - Yes
- Mental – Usually, depends
- Monetary – Possibly, depends

The 4 M’s: Dr. Arya Sharma

There are other comorbidities besides metabolic
## What-if scenarios
Yang CY et al., Lancet, Aug 2011

<table>
<thead>
<tr>
<th>Scenario 1. BMI reduced by 1% across entire population</th>
<th>2010 – 2030</th>
<th>2010-2050</th>
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<tbody>
<tr>
<td></td>
<td>US</td>
<td>UK</td>
</tr>
<tr>
<td>Disease avoided</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>2,391,000</td>
<td>116,000</td>
</tr>
<tr>
<td>CHD &amp; Stroke</td>
<td>1,544,000</td>
<td>68,000</td>
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<tr>
<td>Cancer</td>
<td>149,000</td>
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<td>Medical cost avoided (in billions)</td>
<td>$227</td>
<td>£3.10</td>
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<thead>
<tr>
<th>Scenario 2. Reducing proportion obese to 5% in youths and 15% in adults</th>
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<th>2010-2050</th>
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<tbody>
<tr>
<td></td>
<td>US</td>
<td>UK</td>
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<tr>
<td>Disease avoided</td>
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<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>7,436,000</td>
<td>615,000</td>
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<tr>
<td>CHD &amp; Stroke</td>
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<tr>
<td>Cancer</td>
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<td>Medical cost avoided (in billions)</td>
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<tr>
<th>Scenario 3. Obesity rates cease to rise from 2008</th>
<th>2010 – 2030</th>
<th>2010-2050</th>
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<tbody>
<tr>
<td></td>
<td>US</td>
<td>UK</td>
</tr>
<tr>
<td>Disease avoided</td>
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<tr>
<td>Diabetes</td>
<td>6,999,000</td>
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<td>CHD &amp; Stroke</td>
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<tr>
<td>Cancer</td>
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<td>Medical cost avoided (in billions)</td>
<td>$573</td>
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