Big Fat Myths: What You Didn't Know about Adipose Tissue and Obesity

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Classic Function

Adipocyte

Capillary

TG, glucose, glycerol, FFA
Little attention given to Adipose tissue (as of Jan 2019)
Obesity Trends* Among U.S. Adults
BRFSS, 1985

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1986

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1987

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1988

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1989

(*BMI ≥30, or ~ 30 lbs. overweight for 5’4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1990

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1991

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1992

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1993

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1994

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1995

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1996

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1997

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1998

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1999

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2000

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2001

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2002

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2003

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2004

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2005

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2006

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2007

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2008

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2009

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2010

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1990, 2000, 2010

(*BMI ≥30, or about 30 lbs. overweight for 5’ 4” person)
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory

BRFSS Methodological Changes Started in 2011

- New sampling frame that included both landline and cell phone households.
- New weighting methodology used to provide a closer match between the sample and the population.
- Excluded records with the following:
  - Height: <3 feet or ≥8 feet
  - Weight: <50 pounds or ≥650 pounds
  - BMI: <12 kg/m2 or ≥100 kg/m2
  - Pregnant women
Prevalence\textsuperscript{\dag} of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2011

\textsuperscript{\dag} Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2012

† Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2013

† Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2014

¹ Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2015

Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2016

*Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
The less fat, the better.

Myth or fact?
Lipodystrophy

• “lipo-" = "fat“
• “-dystrophy" = “abnormal or degenerative condition“
• defective lipid metabolism
• Loss of fat tissue or altered fat deposition
Figure 2. The role of adipocytes in triglyceride metabolism. [A] Under normal conditions, there is ample room within adipocytes to store excess dietary triglycerides (TGs); therefore, fewer TGs are directed to liver and skeletal muscles. Under states of energy deprivation (e.g., fasting, starvation), stored TGs are released from adipocytes to deliver free fatty acids (FFAs) to the liver, skeletal muscle, and other organs. [B] In individuals with generalized or regional obesity, adipocytes become enlarged, resulting in a limitation in adipocyte storage capacity and, potentially, a relative block in the disposal of excess dietary TGs to adipocytes. TGs may then be directed for storage to ectopic sites, such as the liver and skeletal muscles. Lipolysis of excess TGs may also contribute to increased FFA flux, further contributing to TG storage in ectopic sites. [C] In individuals with generalized or partial lipodystrophies, there is an absolute or relative lack of available adipocytes to store TGs; therefore, disposal of excess dietary TGs into adipocytes is limited, and TGs are directed for storage to ectopic sites, such as the liver and skeletal muscles. FFA flux from adipocytes may not be increased, particularly in patients with generalized lipodystrophies. N = normal; ↑ = increase; ↓ = decrease.
# Obesity versus Lipodystrophy

<table>
<thead>
<tr>
<th><strong>Obesity</strong></th>
<th><strong>Lipodystrophy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Marked increase in fat mass</td>
<td>• Markedly reduced adipose tissue</td>
</tr>
<tr>
<td>• Insulin resistance/DM</td>
<td>• Insulin resistance/DM</td>
</tr>
<tr>
<td>• Metabolic syndrome (T2DM,</td>
<td>• Metabolic Syndrome (T2DM, impaired GT, hypertriglyceridemia, low HDL-C,</td>
</tr>
<tr>
<td>impaired GT, hypertriglyceridemia, low HDL-C, hepatic steatosis, acanthosis nigricans, polycystic ovary syndrome, agdominal obesity, HTN)</td>
<td>hepatic steatosis, acanthosis nigricans, polycystic ovary syndrome, adiponectin obesity, HTN rare)</td>
</tr>
<tr>
<td>• More excess fat mass greater</td>
<td>• Greater the reduction in fat mass</td>
</tr>
<tr>
<td>the insulin resistance/metabolic syndrome phenotype</td>
<td>the greater the insulin resistance/metabolic syndrome phenotype</td>
</tr>
<tr>
<td>• Lipotoxic</td>
<td>• Lipotoxic</td>
</tr>
</tbody>
</table>

*Note: The terms 'adiponectin obesity' and 'HTN rare' are placeholders and should be replaced with appropriate terms.*
**Mesenchymal Stem Cell**
- Preadipocyte
  - Adipogenic factors (Insulin, IGF-1)
    - PPAR-γ*, C/EBP*
    - AKT2*
  - Activation of adipocyte specific expression
    - Mediates hormonal regulation in adipose tissue
- Adipocyte
  - PTRF (Caveolin-1)*
  - AGPAT-2*, GPAT*
  - Caveolin formation
  - Triglyceride Synthesis
- Mature Adipocyte
  - LMNA*
  - ZMPSTE24*
  - Nuclear structure/function

*Defects in these Genes/Protein activators leads to lipodystrophy
### Inherited Lipodystrophies

<table>
<thead>
<tr>
<th>Type</th>
<th>Salient features</th>
<th>Mode of inheritance</th>
<th>Genetic defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital generalized lipodystrophy</td>
<td>Generalized deficiency of subcutaneous fat from birth</td>
<td>Autosomal recessive</td>
<td>AGPAT2, BSCL2, CAV1, PTRF, FBN1, BANF1</td>
</tr>
<tr>
<td>Familial partial lipodystrophy</td>
<td>Loss of subcutaneous fat from extremities with variable loss/excess of fat from trunk and face</td>
<td>Autosomal dominant (usually)</td>
<td>LMNA, PPARG, AKT2, PLIN1, CIDEC*</td>
</tr>
<tr>
<td>Lipodystrophy in association with other rare syndromes</td>
<td>Variable degree of fat loss in association with features of other syndromes such as MAD, SHORT, progeria and autoinflammatory syndromes</td>
<td>Both autosomal recessive and autosomal dominant</td>
<td>LMNA, ZMPSTE24, PSMB8, PIK3R1</td>
</tr>
</tbody>
</table>

### Acquired Lipodystrophies

<table>
<thead>
<tr>
<th>Type</th>
<th>Salient features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquired generalized lipodystrophy</td>
<td>Development of generalized loss of subcutaneous fat, with normal fat distribution at birth</td>
</tr>
<tr>
<td>Acquired partial lipodystrophy</td>
<td>Loss of subcutaneous fat from face, upper extremities and trunk, but not from lower extremities</td>
</tr>
<tr>
<td>HIV-associated lipodystrophy</td>
<td>Loss of fat from face and limbs with variable loss/excess from trunk and associated with antiretroviral therapy</td>
</tr>
<tr>
<td>Localized lipodystrophy</td>
<td>Patchy loss of subcutaneous fat usually following trauma or injections</td>
</tr>
</tbody>
</table>

Abbreviations in the table: MAD, mandibuloacral dysplasia; SHORT, short stature, hyperextensibility, hernia, ocular depression, Rieger anomaly and teething delay.

*CIDEC reported in a single patient with autosomal recessive inheritance.
Adipose tissue is an endocrine organ.

Myth or fact?
Endocrine Function

- Leptin
- Adiponectin
NORMAL

LEPTIN DEFICIENT
How did they lose weight?
Ate less and expended more energy

Leptin deficient
+ Leptin
Leptin deficient
Normal
Leptin negatively regulates the hypothalamus (ARC, LHA, VMH), mesolimbic dopamine system (VTA), and hindbrain (NTS). This leads to a decrease in neuroendocrine function, including reproductive hormones, thyroid hormone, and IGF-1, resulting in energy deficiency (leaniness, fasting). Conversely, leptin positively regulates the hindbrain, increasing food intake and energy expenditure, leading to energy excess (obesity, overfeeding).
Leptin in Humans

Are there examples of leptin deficiency in humans?
Patients Before Treatment
After Ten Months of Treatment
Body Weight Over the 10 Months of Treatment
LEPTIN

- Helps regulate the synthesis of thyroid hormones
- Decreases glucose-stimulated insulin secretion
- Increases heart rate
- Regulate bone mass
- Regulating the menstrual cycle
- Regulate appetite. Control of metabolism and energy homeostasis
- Activation of immune cells
- High blood pressure
Too many enlarged adipocytes are the problem with obesity!

Myth or fact?
Macrophages in epididymal WAT

Cinti et al. J. Lipid Res. 2005

Lymphocytes in epididymal WAT

Cinti et al. J. Lipid Res. 2005
Fat expands and shrinks but you never really lose it.

Myth or fact?
Hypertrophy

Adipocyte death
Hypoxia
Inflammation
Insulin resistance

Adipocyte

Macrophages, other inflammatory immune cells
Adult humans have ‘brown fat’.

Myth or fact?
Two Types of Adipose Tissue

The above image of adipose tissue is from Duke University's page at [pathology.mc.duke.edu/research/PTH225.html](http://pathology.mc.duke.edu/research/PTH225.html).
Basic Function of Brown Adipose Tissue

• Dissipate heat
• Thermoregulation
• Uncoupling proteins
• Endocrine?

[Image: Diagram of electron transport chain and ATP synthesis.]

All fat is in your body is ‘created equal’.

Myth or fact?
Intraabdominal vs. Subcutaneous

- subQ healthy
- Intraabdominal or visceral and health
- Body mass index a good gauge?
- Waist circumference
Transplantation Studies

<table>
<thead>
<tr>
<th>Donor</th>
<th>Recipient</th>
<th>Body Fat</th>
<th>Glucose Homeostasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-abdominal</td>
<td>subcutaneous</td>
<td></td>
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Tran et al., *Cell Metab*, 2008
Harris & Leibel, *Cell Metab*. 2008
All adipocytes in a depot are created equal.

Myth or fact?
The lipid droplet is an inert organelle storing lipid.

Myth or Fact
Vishu Puri, PhD.
My research...
Mice with Altered GH

GHR signaling
IGF-1
High
High
Normal
Normal
Low
Low
Absent
Very Low

Glucose
Normal
Normal
Normal
Low Normal

Insulin
Very High
Normal
Low Normal

Lifespan
Short
Normal
Normal
Long