




**Welcome to
COGS163**



The science behind metabolic disorders

EXPLORE THE SCIENCE associated with Metabolic Disorders

For example:

What is the science of obesity?

Is obesity a disease?

What is the health impact of obesity?

What is the genetic component of obesity?

How does diet and exercise impact obesity?

Is obesity a neurodevelopmental disorder?

What are effective treatments?



Hormones and Behaviors

Hormones

How do they control behaviors?

When and how do they wire your brain?

How can they change your metabolism?

What is their role in neurodegenerative diseases?

Insulin

Leptin

Ghrelin

FGF21

Orexin

Oxytocin



1. Understanding Obesity

A brief tour of the class



Obesity

evolutionary perspective



**I THINK
THAT...**



**Is it fair to
hold the
morbidly
obese
responsible
for their
condition?**

↑ yes!

↓ no



Obesity

OBESITY AND DISEASE RISK

Health Consequences of Obesity

- Type 2 Diabetes
- Hypertension
- Coronary Heart Disease
- Fatty Liver Disease

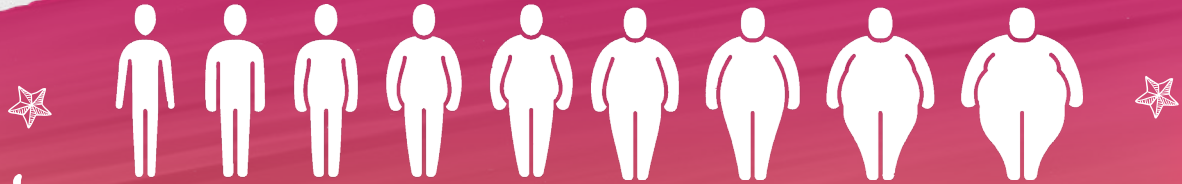


Metabolic Syndrome

Metabolic Syndrome:
the principal cause
of mortality in the
developed world.



How is obesity defined and measured



obesity:

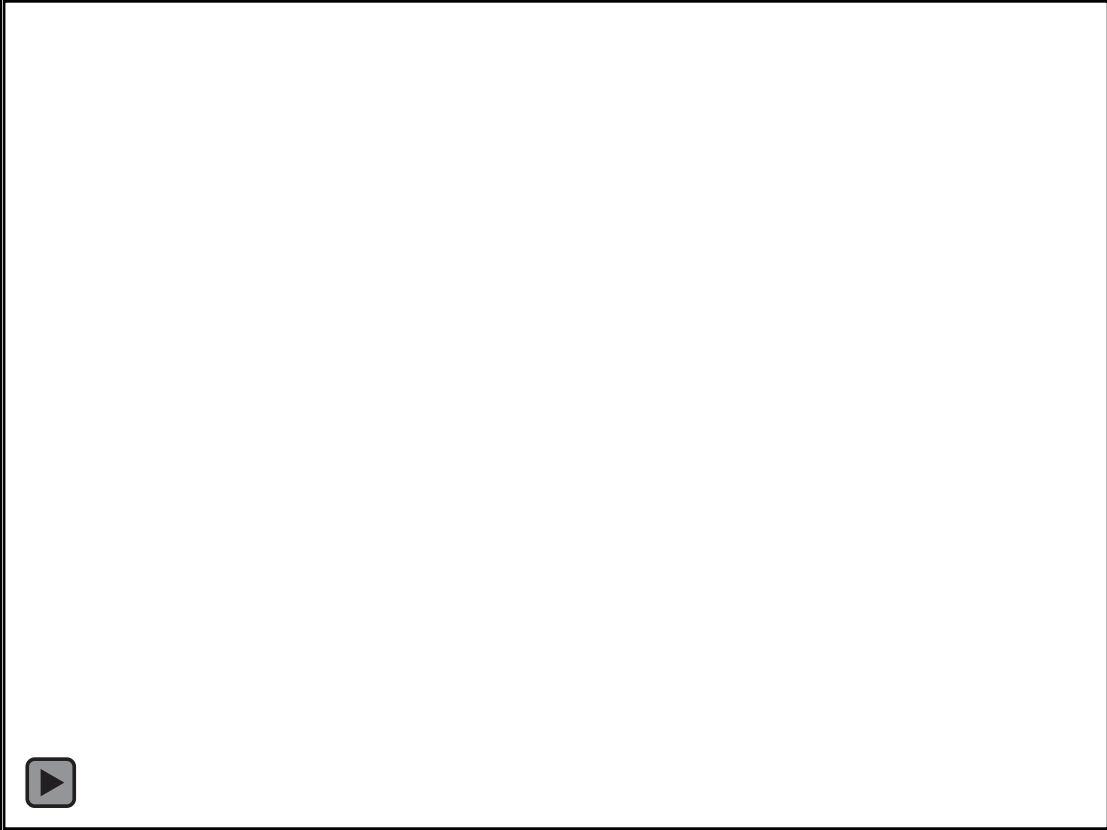
① excessive amount of body fat
in relation to lean body mass

② DISTRIBUTION OF FAT
MATTERS



BMI: BODY MASS INDEX

$$\text{BMI} = \frac{\text{Weight (kg)}}{(\text{Height (m)})^2}$$



This guy is borderline **OBESE**
according to the B.M.I. (Body Mass Index)

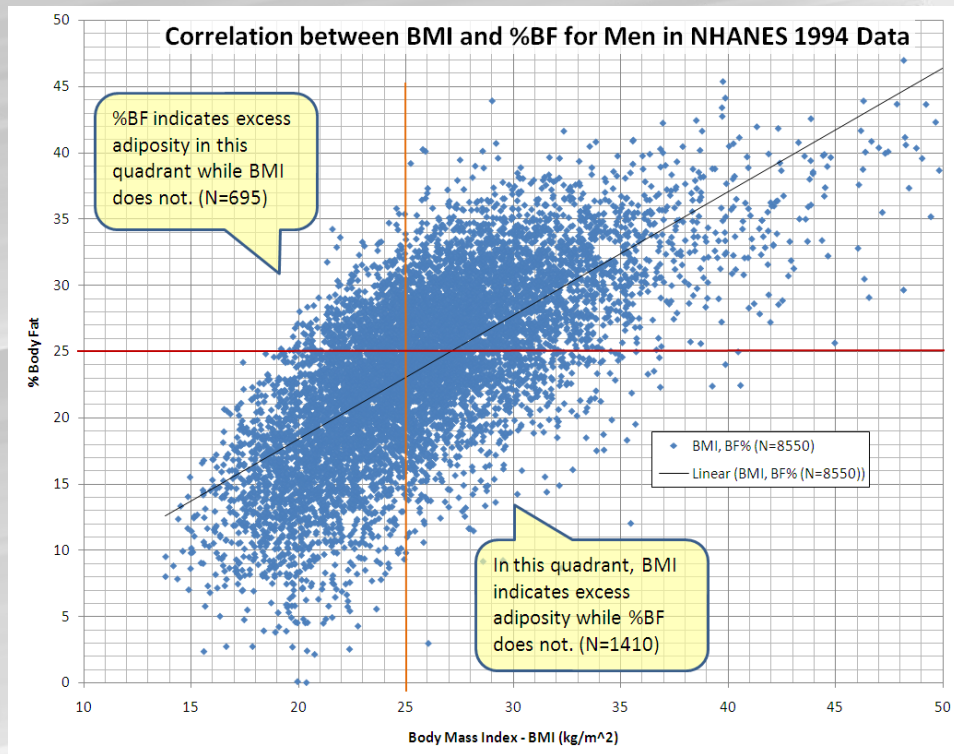
LOL!

There's more to measuring fitness than height and weight. We don't buy into gimmicks or labels. We just want you to be FIT, no matter where you're at in life. The Fitness Town team is committed to helping you identify what equipment will fit your budget, goals, and lifestyle.

<< Dai Manuel
 COO Fitness Town
 6'1", 210 lbs.

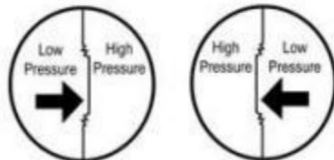
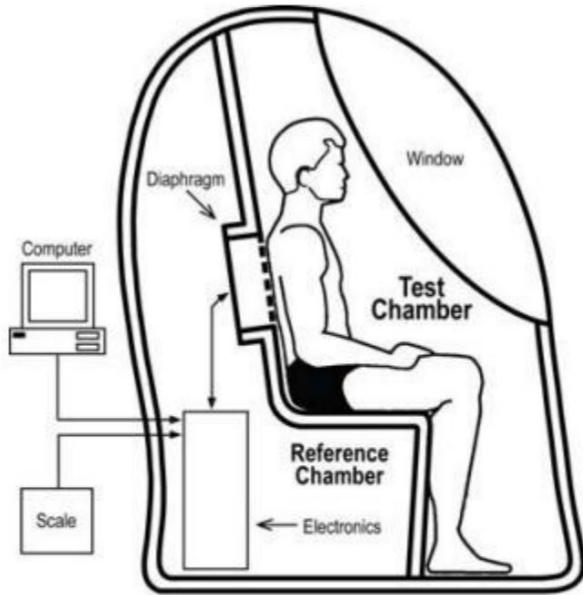
FITNESS TOWN
 Your Fitness Equipment Experts.

WWW.FITNESSTOWN.CA



<https://commons.wikimedia.org/>

The BOD POD



Moving diaphragm produces complementary pressure changes in the chambers.

- The BOD POD is an Air Displacement Plethysmograph (ADP)
- It uses whole body densitometry to determine body composition (fat vs. lean).
- Similar in principle to underwater weighing methods.



**What causes the
variation in body fat?**

Variability...



Which do you think is the single most important factor causing obesity?

- Lack of willpower?
- Lifestyle/environment?
- Biology/genes?



**Change
calories in
change
your body**

1st Law of
Thermodynamics:

$$\frac{\text{Energy} \leftarrow \text{input}}{\text{Energy} \rightarrow \text{used}} =$$

Δ in Energy Stored

Applies to
people too
—
consider...

Food ← intake
— Energy → burned

FAT STORED

1,000,000 cal/year



Weight changes less than 10 pounds per decade!

lifetime consumption



90

How long can you hold your breath?

seconds?

Basic Drive



- You can be highly motivated, but the basic drive will always win.

A collage of various fresh foods including avocados, blueberries, kiwi, and lentils. The background is a vibrant mix of colors from the different ingredients.

Eating food is a basic drive

- Breathing
- Sleeping
- Drinking
- Sex
- Eating



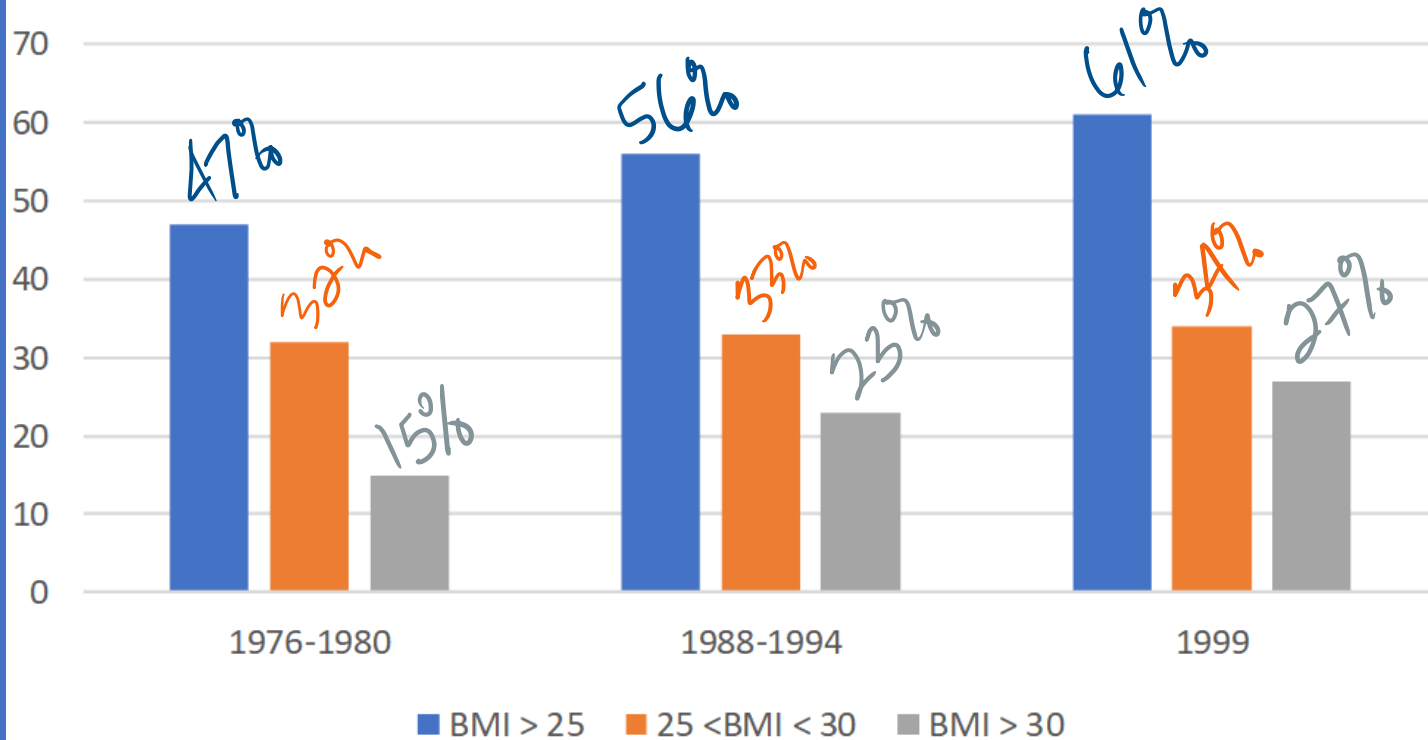
Basic drive to eat when you are hungry leads to diet failures.

LIFESTYLE AND ENVIRONMENT

Obesity rates are going up over time – so it must be the environment and lifestyle, right?



Obesity Levels are Rising



Obesity is not new...

Venus of Willendorf

From Wikipedia, the free encyclopedia

The **Venus of Willendorf** is an 11.1-centimetre-tall (4.4 in) **Venus figurine** estimated to have been made 30,000 **BCE**.^{[1] [2]} It was found on August 7, 1908 by a workman named Johann Veran^[3] or Josef Veram^[4] during excavations conducted by **archaeologists** **Josef Szombathy**, **Hugo Obermaier** and Josef Bayer at a **paleolithic** site near **Willendorf**, a village in **Lower Austria** near the town of **Krems**.^{[5][6]} It is carved from an **oolitic limestone** that is not local to the area, and tinted with **red ochre**. The figurine is now in the **Naturhistorisches Museum** in **Vienna**, Austria.^[7]





**Why is our perception
so skewed?**

Obesity categories (BMI)

Height = 5' 10"



Weight=167 lbs
BMI 24



Overweight

Weight=174 lbs
BMI 25

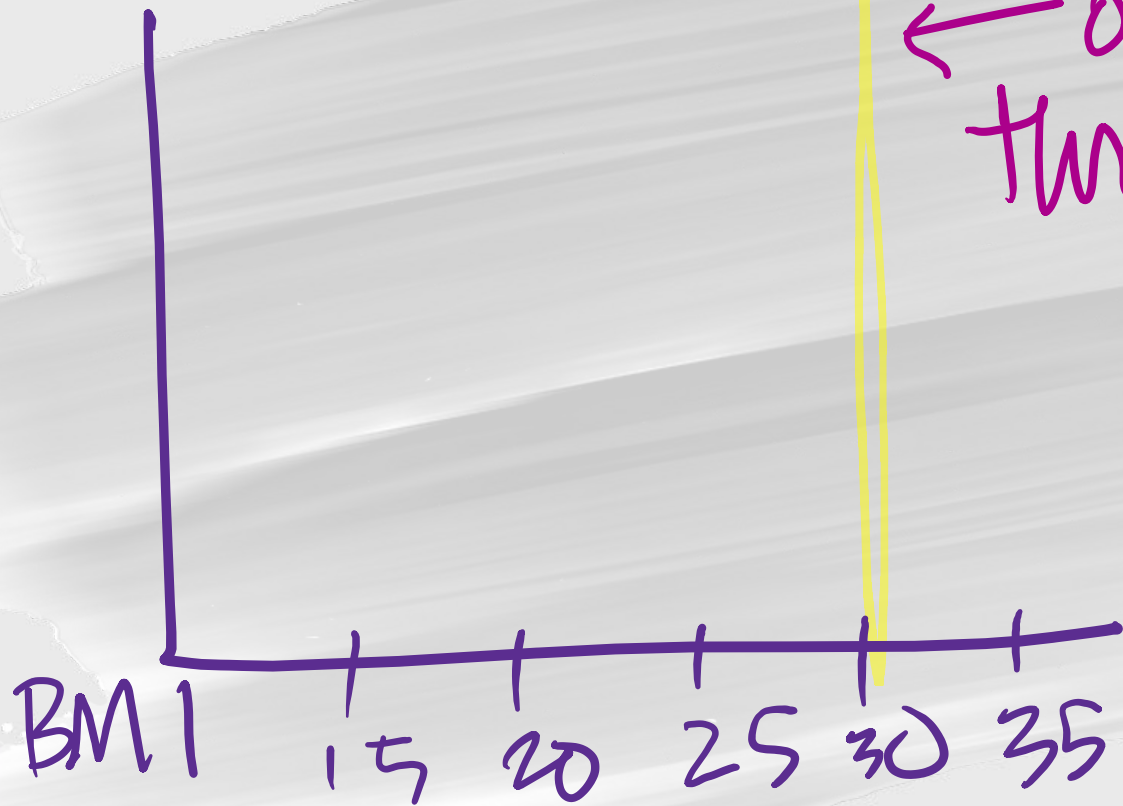


Obese

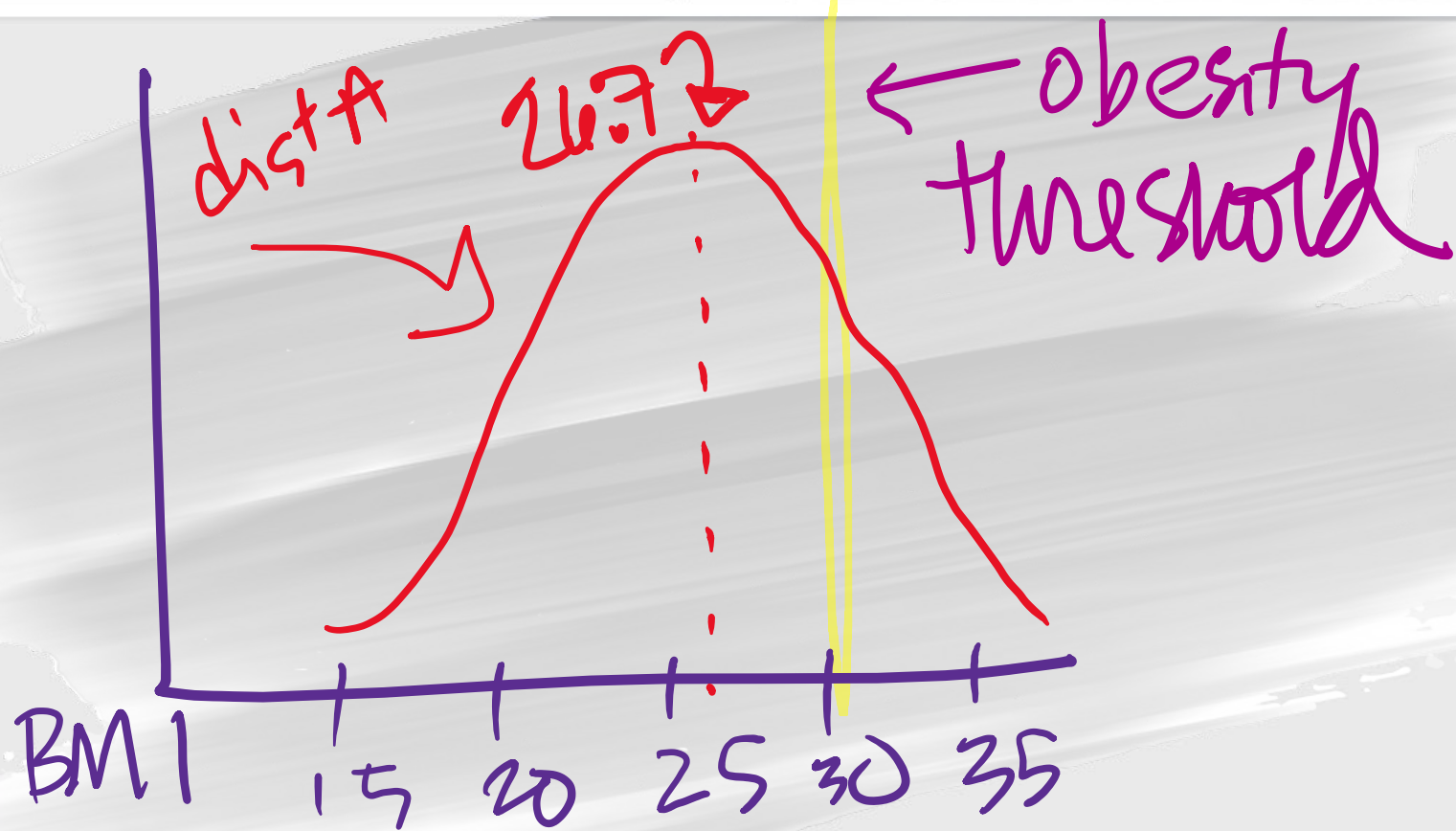
Weight=209 lbs
BMI 30

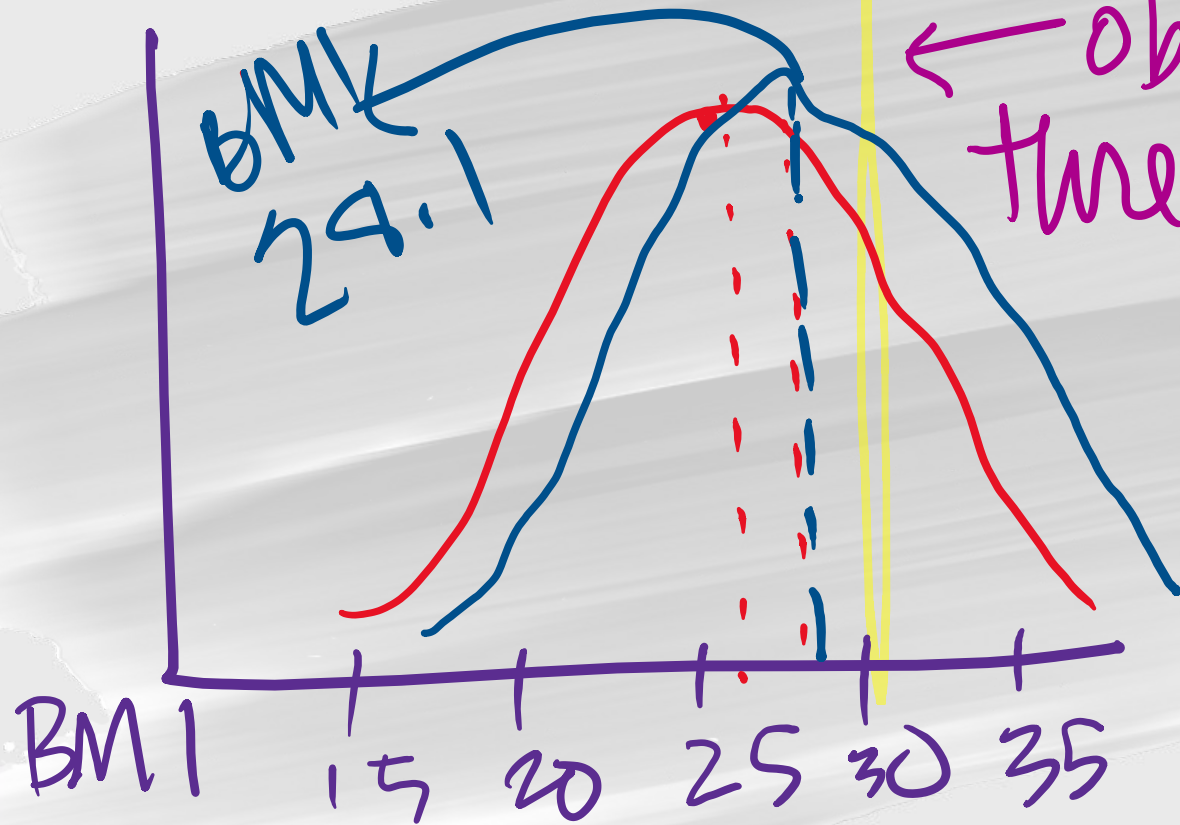


Weight=279 lbs
BMI 40



← obesity threshold

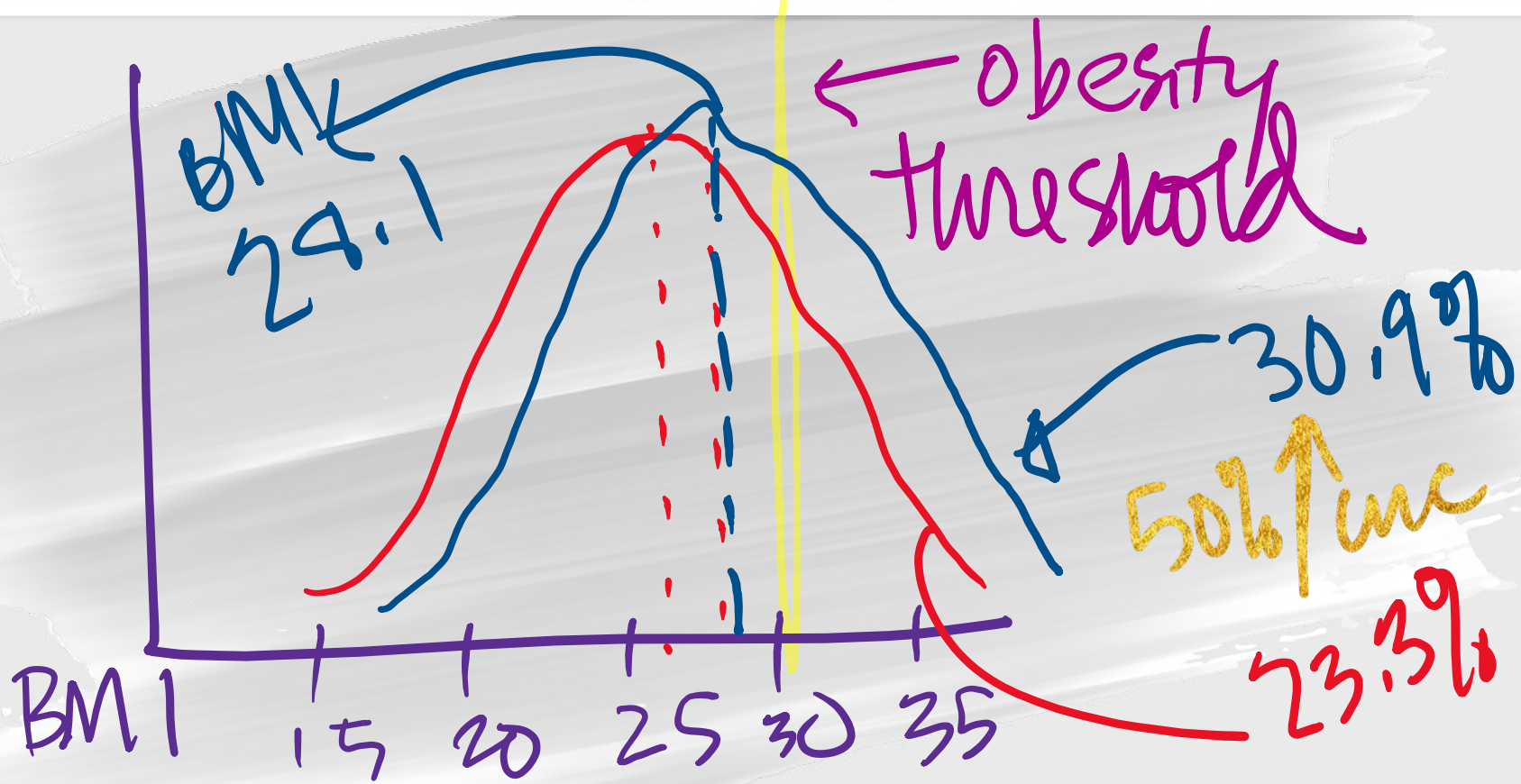


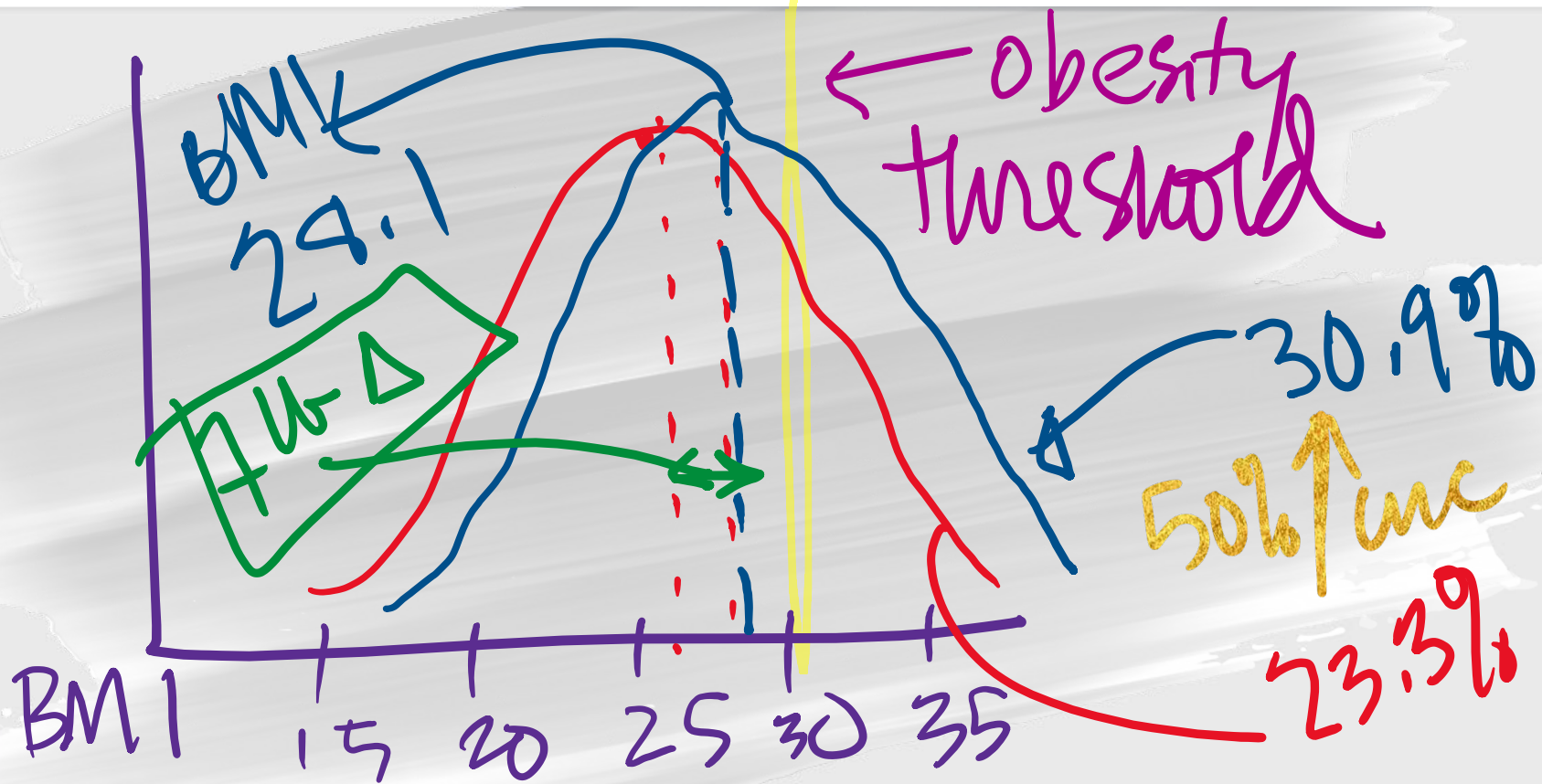


← obesity threshold

BMI
24.1

BMI 15 20 25 30 35







**Why is ^{*}weight so
variable within a
population?**



Genes!



Tish & Miley Cyrus



Reese Witherspoon & Ava Phillippe

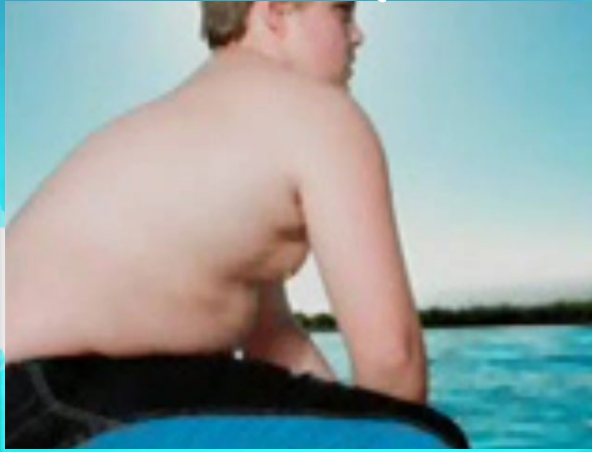


Kanye & North West



Kris & Kendall Jenner

adoptive
parents →



biological
parents →



TWIN STUDIES:



← monozygote

share genes



← dizygote

share environment

Height	.90
Schizophrenia	.68
Diabetes, Type 2	.60
Hypertension	.57
Alcoholism	.57
Heart disease	.49

% genetic contribution

How heritable is obesity?

Height	.90
Schizophrenia	.68
Diabetes, Type 2	.60
Hypertension	.57
Alcoholism	.57
Heart disease	.49

43

← obesity is .80-.90

- Normal birthweight
- Morbid obesity beginning infancy
- Marked overeating
- Very high insulin levels
- Pre-diabetic at 4yrs old
- 90 lbs with 50% body fat @ 4 years of age (normal is 20%)
- Highly inbred pedigree



20 YEARS OF LEPTIN

Human disorders of leptin action

I Sadaf Farooqi and Stephen O’Rahilly

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Abstract

The discovery of leptin has provided a robust framework upon which our current understanding of the mechanisms involved in energy homeostasis has been built. In this review, we describe how the identification of humans with mutations in the genes encoding leptin and the leptin receptor and the characterisation of the associated clinical phenotypes have provided insights into the role of leptin-responsive pathways in the regulation of eating behaviour, intermediary metabolism and the onset of puberty. Importantly, administration of recombinant human leptin in leptin deficiency represents the first mechanistically based targeted therapy for obesity and has provided immense clinical benefits for the patients concerned. In subsequent years, we and others have shown that human obesity can result from a multiplicity of defects in the pathways downstream of leptin signalling within the brain.

Key Words

- ▶ leptin
- ▶ receptors
- ▶ obesity
- ▶ signal transduction

Farooqi, S and O’Rahilly, S. (2014) *Journal of Endocrinology* 223, T63–T70

Journal of Endocrinology
(2014) **223**, T63–T70

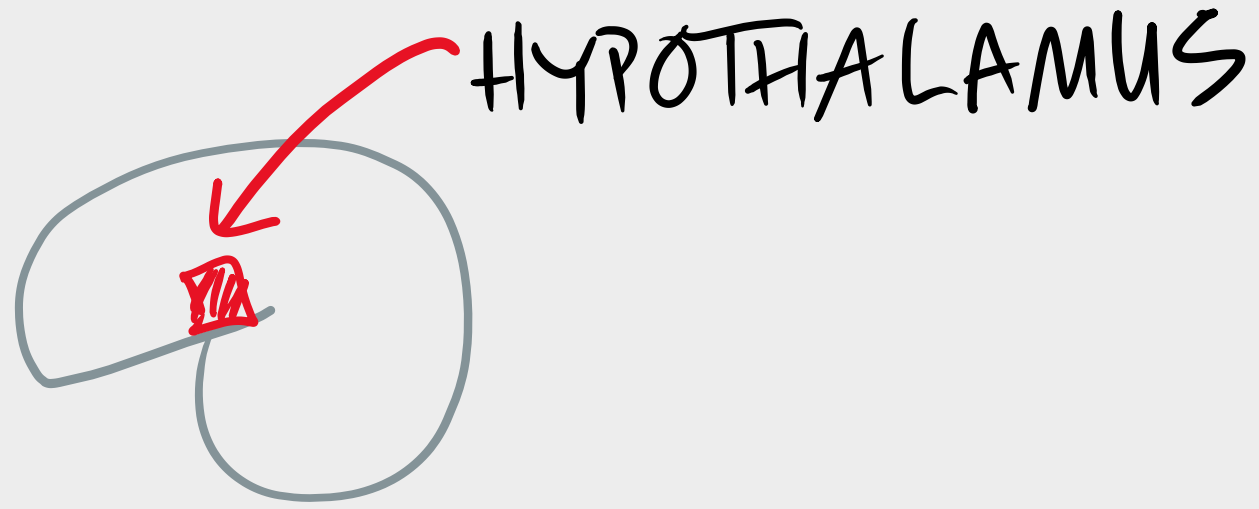
A large, white, cloud-like thought bubble with a thick black outline. Inside the bubble, the words "I THINK" and "THAT..." are written in a bold, black, sans-serif font, stacked vertically. Below the main bubble, there are two smaller, white, circular thought bubbles, also with thick black outlines, arranged in a descending line from left to right.

**I THINK
THAT...**

**What is
LEPTIN
??**



Leptin



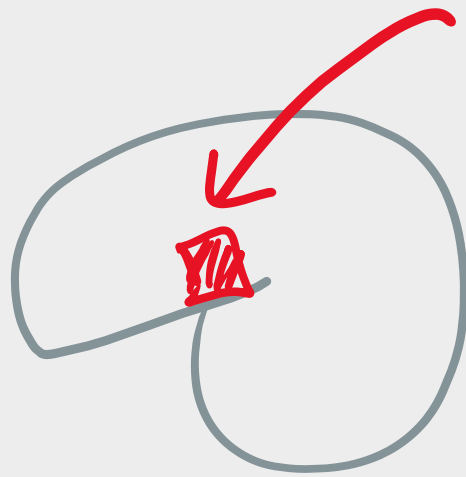
HYPOTHALAMUS



FAT TISSUE

Leptin

HYPOTHALAMUS



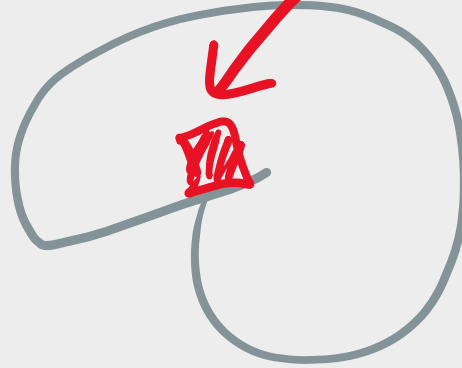
Leptin



FAT TISSUE

Leptin

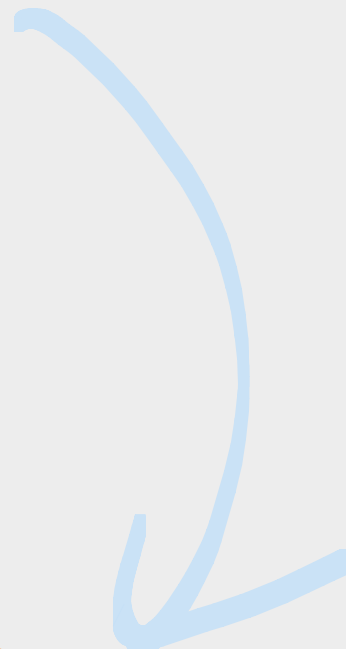
HYPOTHALAMUS



Leptin

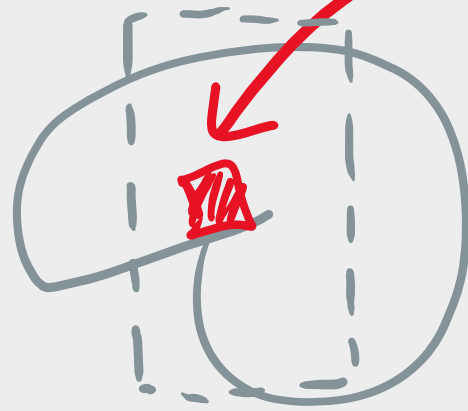


FAT TISSUE



Leptin
in obese

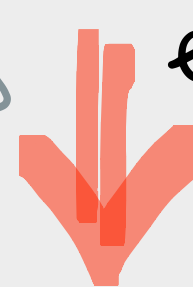
HYPOTHALAMUS



FOOD
intake

↓ less sensitive
to leptin ↓

Leptin



energy
expended



FAT TISSUE



inject leptin?

