



Mahidol University

Faculty of Medicine

Siriraj Hospital

MAP-C SIPS539 : Advanced Endocrine and Reproductive Physiology

Master of Science Program in Medical Physiology (International Program)

Thursday, 22nd January 2026



“Obesity”

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ในนามของมหาวิทยาลัย

Outline

- ✱ Obesity
- ✱ Energy balance
- ✱ Adipose tissue
- ✱ Weight-loss diet regimens
- ✱ Principle of Weight Management
- ✱ Weight regain
- ✱ Diet break or Cheat days
- ✱ Weight loss maintenance

Energy Balance

Energy Intake

Food intake

Appetite regulation

* Hypothalamus

- ✓ Orexigenic (NPY&AGRP) neurons

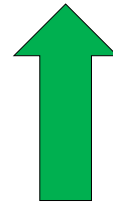
- ✓ Anorexigenic (POMC&CART) neurons

* Brainstem

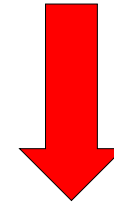
* Reward system

* Periphery

- ✓ Vagal signal
- ✓ Leptin, insulin
- ✓ Gut hormones



Positive
energy balance



Obesity

- ✓ Prevalence
- ✓ Related diseases
- ✓ Adipose tissue & adipokines

Energy Expenditure

- ✓ Basal metabolic rate (BMR)
- ✓ Thermic effect of food
- ✓ Non-exercise activity thermogenesis (NEAT)
- ✓ Exercise



Obesity



<http://cf067b.medialib.glogster.com/media/17/1766da671072324f3486b3785f97f2c5feed1e115e135f859505bac63a8b2def/really-fat-man-clip-art.jpg>

What is Obesity?

Obesity

WHO:

**“Abnormal or excessive
fat accumulation
that presents a risk to health”**

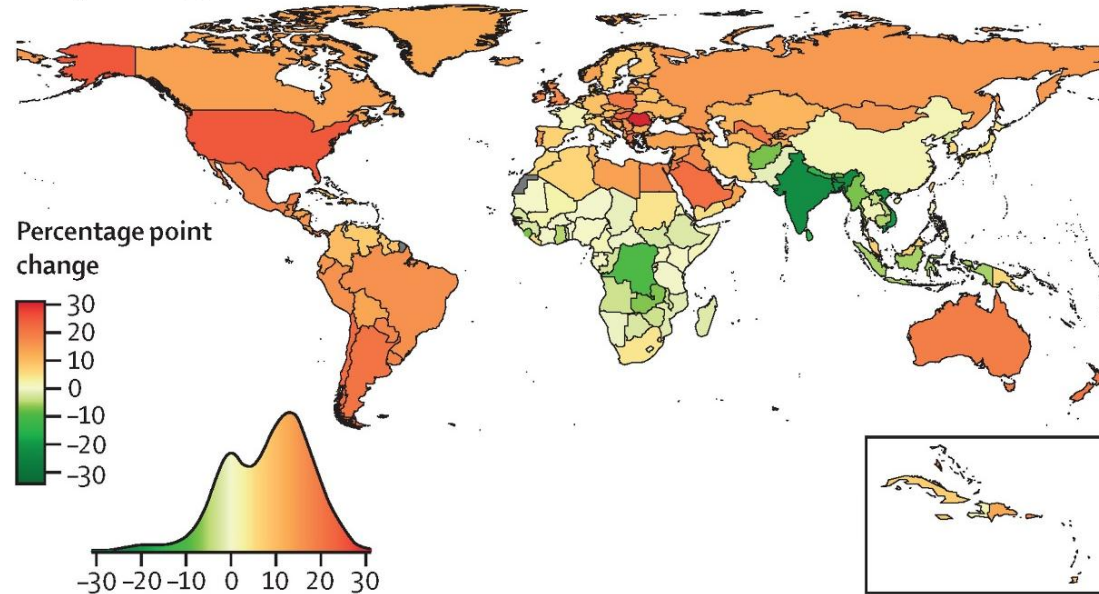
Obesity: World Health Organization (WHO) Available from: https://www.who.int/health-topics/obesity#tab=tab_1

Prevalence of Obesity

- ✱ Globally from 1975 to 2016
 - ✱ ↑ Prevalence of overweight or obese children and adolescents aged 5–19 years > four-fold from 4% to 18%
- ✱ In 2016,
 - ✱ Adults $\geq$ 18 years
 - ✱ >1.9 billion (39%) → **overweight**
 - ✱ >650 million (13%) → **obese**
 - ✱ Children $\leq$ 5 years
 - ✱ 39 million → **overweight** or **obese**
 - ✱ Children and adolescents, 5-19 years
 - ✱ >340 million → **overweight** or **obese**

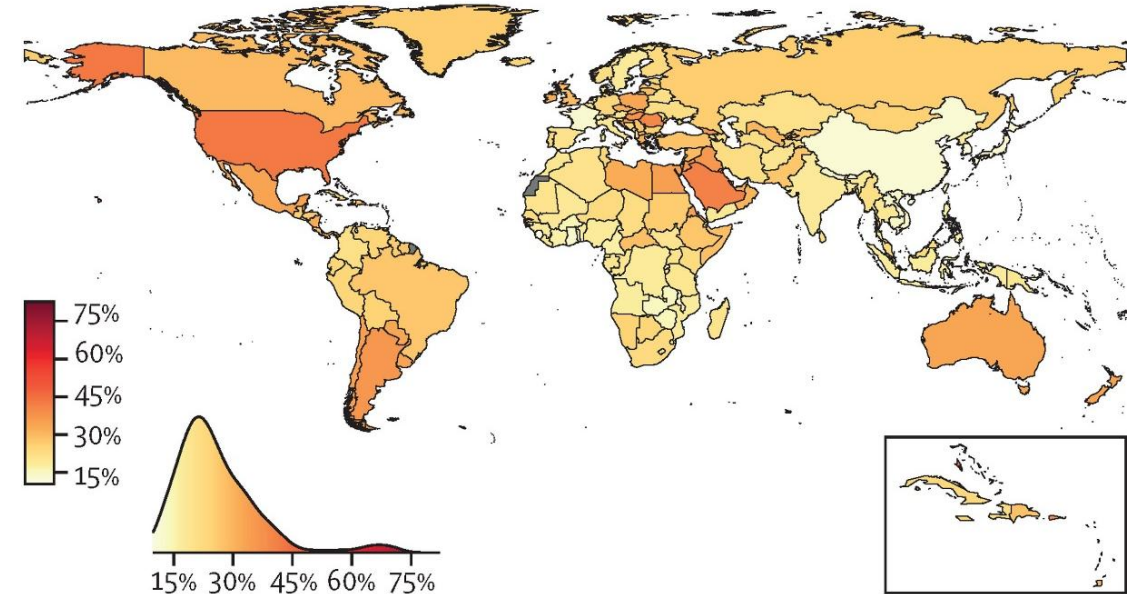
Men

Change from 1990 to 2022



American Samoa	Fiji	Montenegro	Solomon Islands
Bahrain	French Polynesia	Nauru	Tokelau
Bermuda	Kiribati	Niue	Tonga
Brunei	Maldives	Palau	Tuvalu
Cabo Verde	Marshall Islands	Samoa	Vanuatu
Comoros	Mauritius	São Tomé and Príncipe	
Cook Islands	Micronesia	Seychelles	

Prevalence in 2022



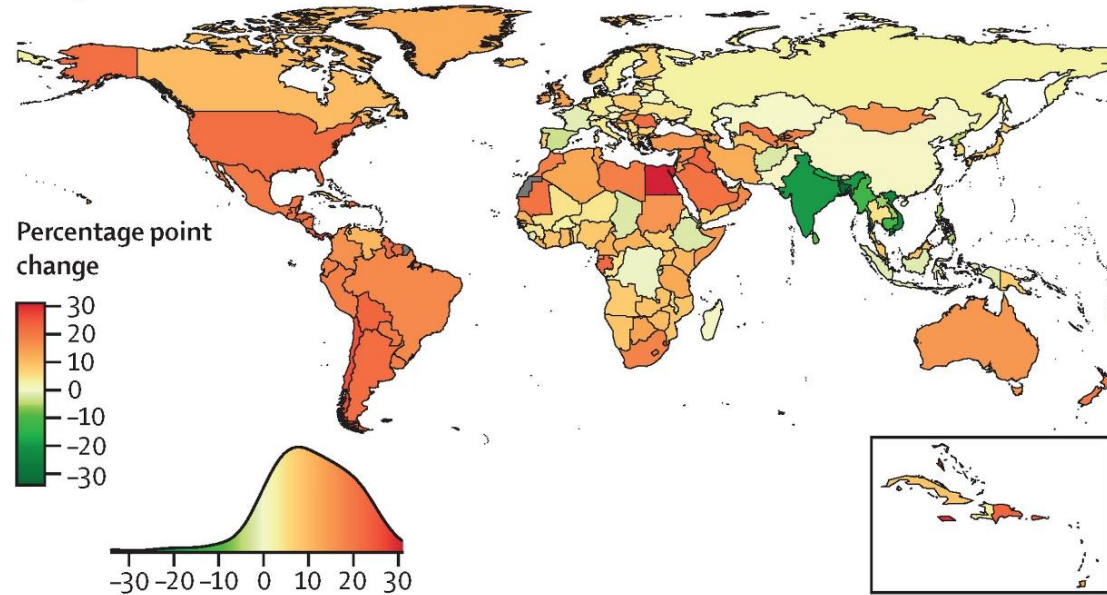
American Samoa	Fiji	Montenegro	Solomon Islands
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Brunei	Maldives	Palau	Tuvalu
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Cook Islands	Micronesia	Seychelles	

Age-standardized combined prevalence of underweight and obesity by country, for adults (age ≥ 20 years)

Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population representative studies with 222 million children, adolescents, and adults. Lancet (London, England). 2024;403(104301):1027-1050.

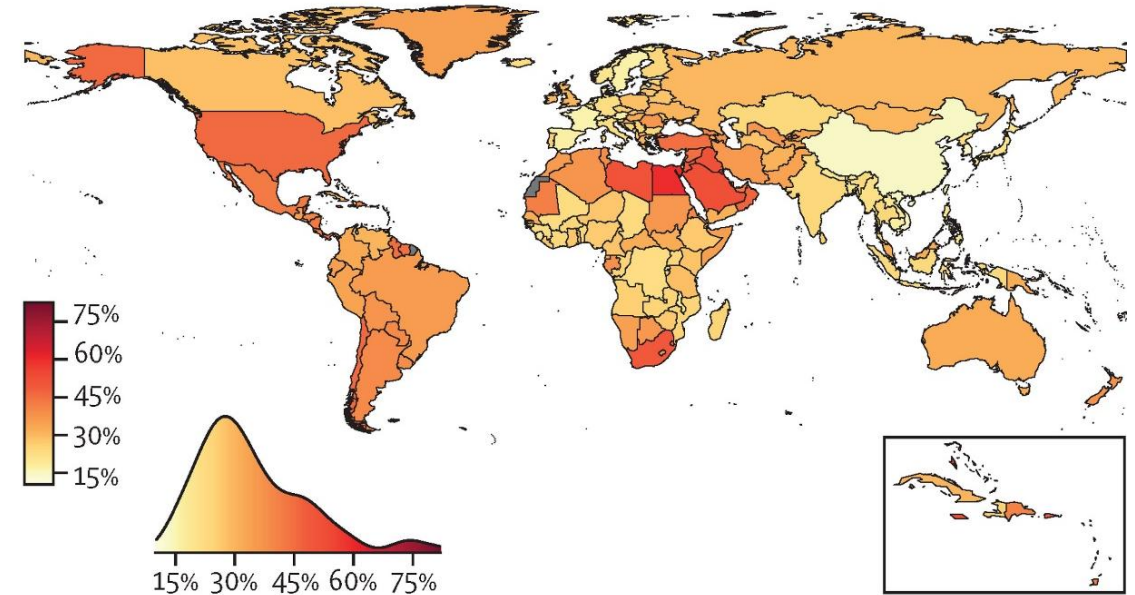
Women

Change from 1990 to 2022



American Samoa	Fiji	Montenegro	Solomon Islands
Bahrain	French Polynesia	Nauru	Tokelau
Bermuda	Kiribati	Niue	Tonga
Brunei	Maldives	Palau	Tuvalu
Cabo Verde	Marshall Islands	Samoa	Vanuatu
Comoros	Mauritius	São Tomé and Príncipe	
Cook Islands	Micronesia	Seychelles	

Prevalence in 2022

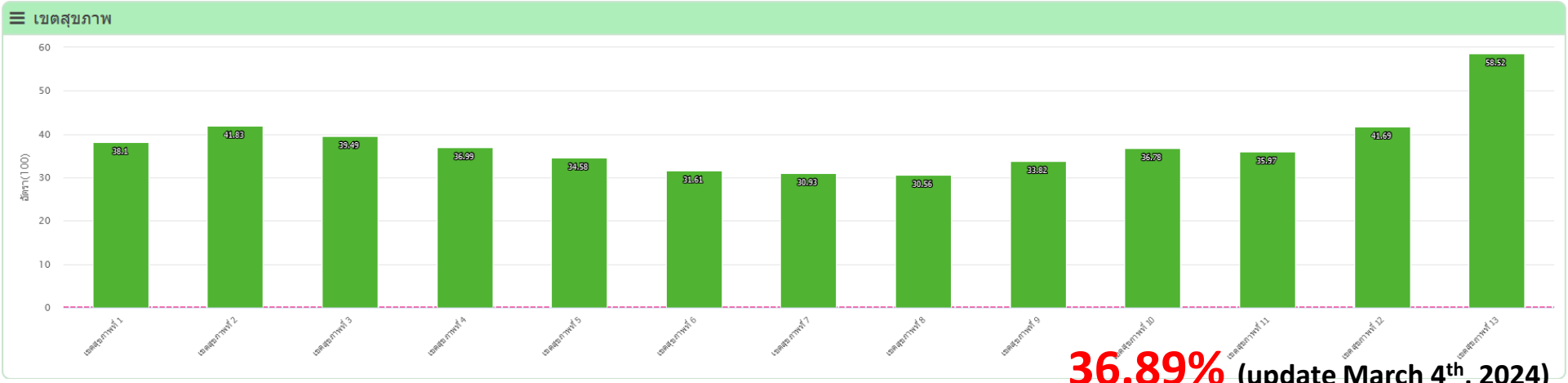


American Samoa	Fiji	Montenegro	Solomon Islands
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Age-standardized combined prevalence of underweight and obesity by country, for adults (age ≥ 20 years)

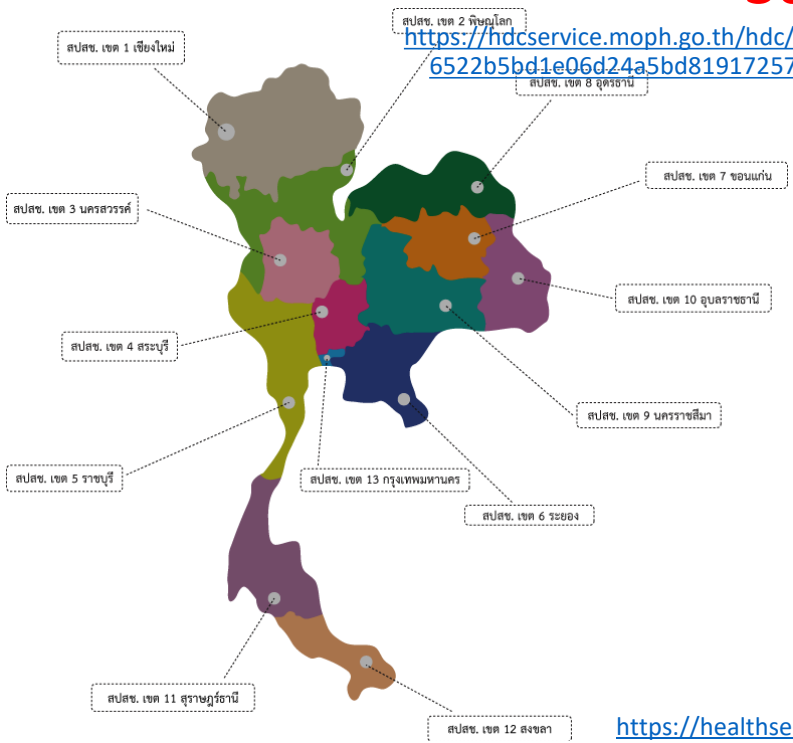
Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population representative studies with 222 million children, adolescents, and adults. Lancet (London, England). 2024;403(104301):1027-1050.

ความชุกของภาวะอ้วน (BMI ≥ 25 กก/ม² และหรือภาวะอ้วนลงพุง (รอบเอว ชาย ≥ 90 ซม. หญิง ≥ 80 ซม.)



36.89% (update March 4th, 2024)

https://hdcservice.moph.go.th/hdc/reports/report.php?source=kpi/kpi.php&cat_id=46522b5bd1e06d24a5bd81917257a93c&id=a75e43f7e044704ec9a993266d3f6704#



<https://healthserv.net/1330>

Available Metabolic Fuels in a Normal-Weight 70 kg Man and in an Obese 140 kg Man at the Beginning of a Fast

TABLE 23-5 Available Metabolic Fuels in a Normal-Weight 70 kg Man and in an Obese 140 kg Man at the Beginning of a Fast			
Type of fuel	Weight (kg)	Caloric equivalent (thousands of kcal (kJ))	Estimated survival (months)*
Normal-weight, 70 kg man			
Triacylglycerols (adipose tissue)	15	141 (589)	
Proteins (mainly muscle)	6	24 (100)	
Glycogen (muscle, liver)	0.225	0.90 (3.8)	
Circulating fuels (glucose, fatty acids, triacylglycerols, etc.)	0.023	0.10 (0.42)	
Total		166 (694)	3
Obese, 140 kg man			
Triacylglycerols (adipose tissue)	80	752 (3,140)	
Proteins (mainly muscle)	8	32 (134)	
Glycogen (muscle, liver)	0.23	0.92 (3.8)	
Circulating fuels	0.025	0.11 (0.46)	
Total		785 (3,280)	14

*Survival time is calculated on the assumption of a basal energy expenditure of 1,800 kcal/day.

Table 23-5

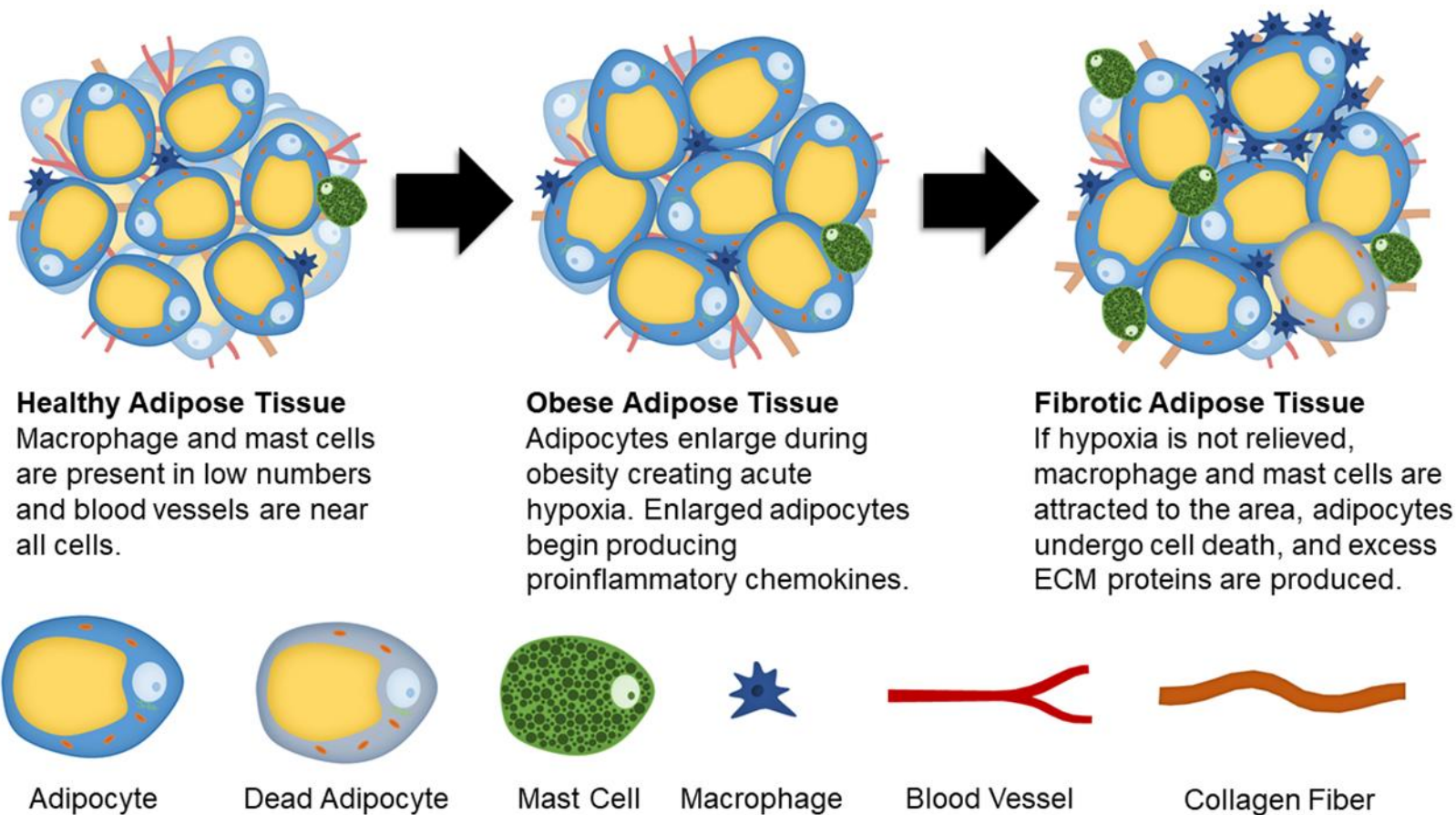
Lehninger Principles of Biochemistry, Fifth Edition

© 2008 W. H. Freeman and Company

Lehninger Principles of biochemistry

TAGs stored in the adipose tissue of a normal-weight adult could provide enough fuel to maintain a basal rate of metabolism for 3 months.
A very obese adult has enough stored fuel to endure a fast of more than a year.

Obesity: Chronic inflammatory state



Proinflammatory chemokines: tumor necrosis factor-alpha (TNF α), inducible nitric oxide synthase (iNOS), interleukin 6 (IL-6), interleukin 8 (IL-8), C-reactive protein, transforming growth factor beta 1 (TGF β 1), soluble intercellular adhesion molecule (ICAM), and monocyte chemoattractant protein 1 (MCP-1)

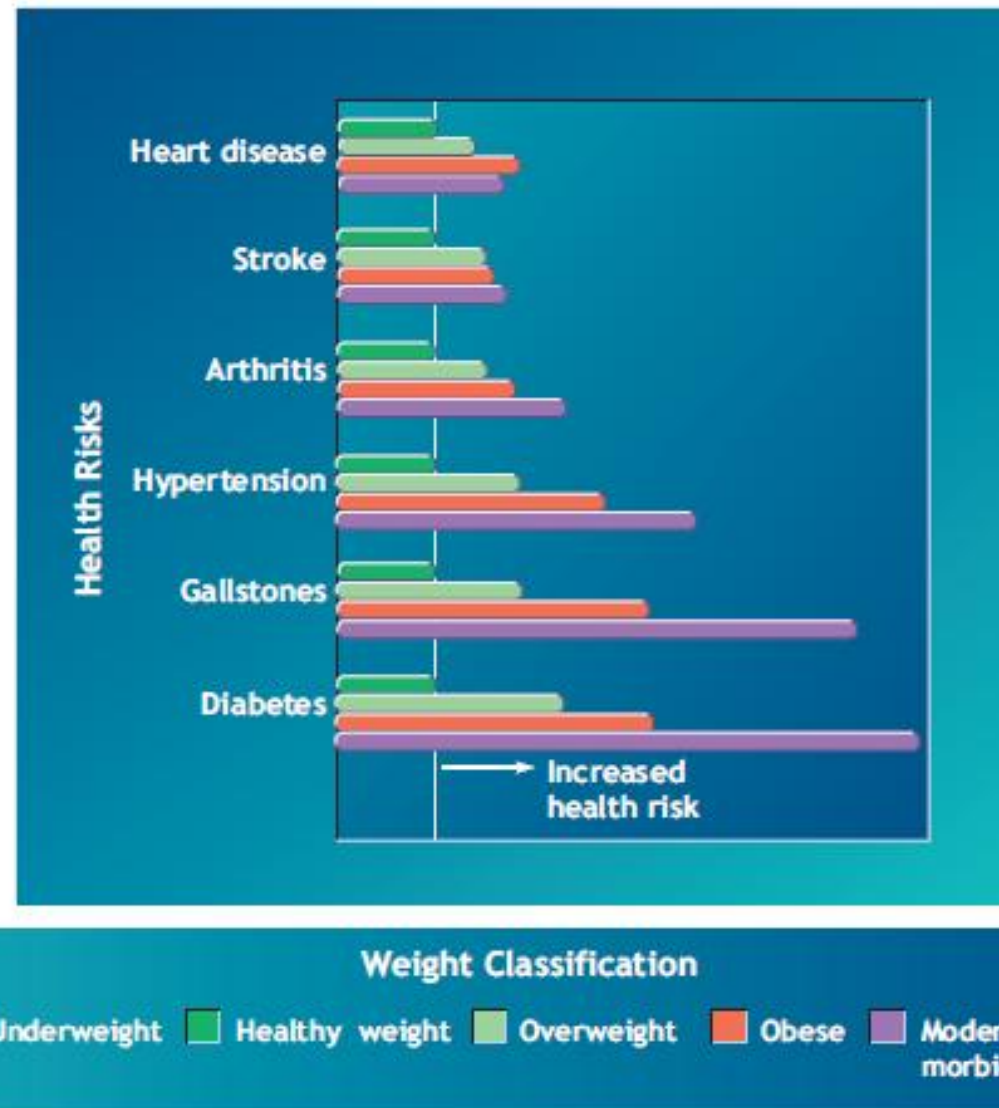


Figure 28.2 • Body mass index (BMI), weight classifications, and associated health risks.

How to **Classify** Obesity?

Classification of Obesity

Category	Caucasian BMI (Kg/m ²)	Asian BMI (Kg/m ²)
Underweight	<18.5	<18.5
Normal weight	18.5-24.9	18.5-22.9
Overweight	25-29.9	23-24.9
Obese	≥30.0	≥25
Obese class I	30.00 - 34.9	25.0-29.9
Obese class II	35.00 - 39.9	≥30.0
Obese class III	≥40.00	Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies, 2004, Jitnarin N et al 2011

Classification of Obesity

Asian compared to western people

✱ ↑ % Body fat for the same age and sex and BMI

✱ ↑ Risk factors for type 2 DM and cardiovascular diseases in the same BMI

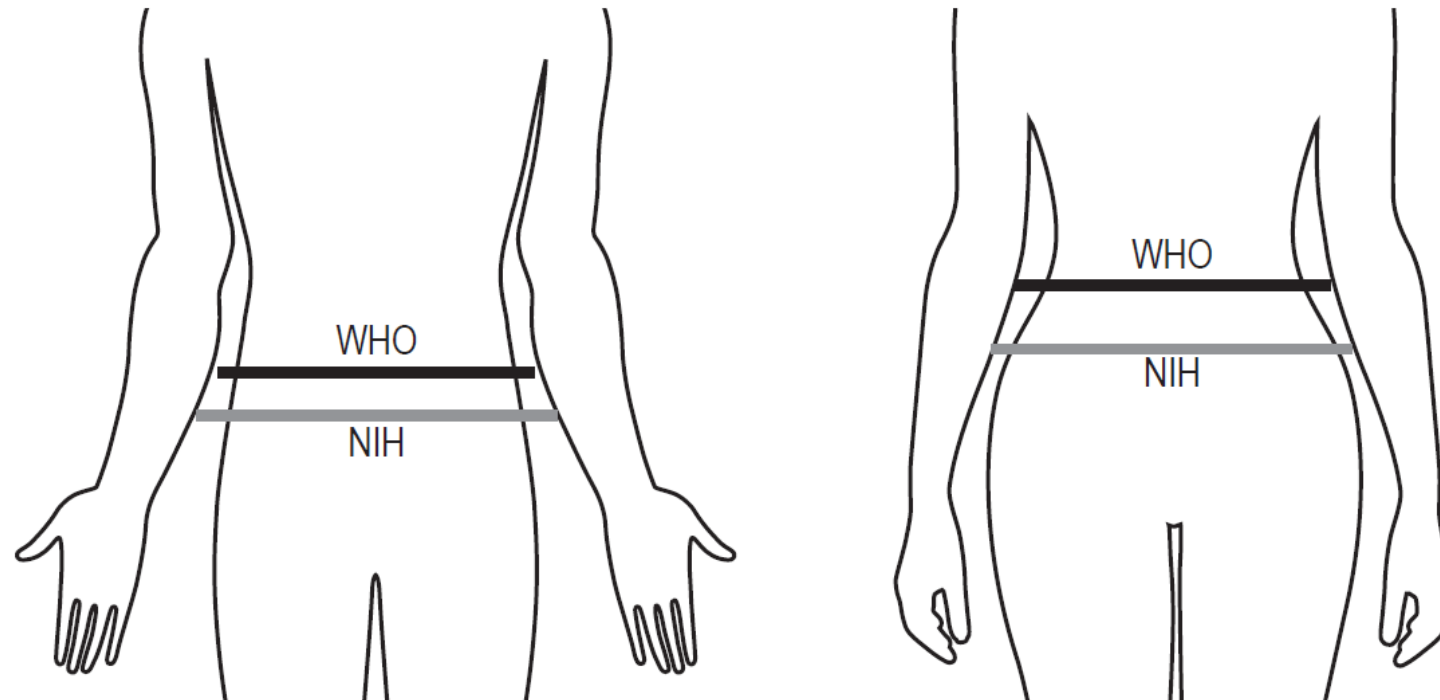
WHO 2016, The Asia-Pacific perspective: Redefining obesity and its treatment, 2000

Anthropometric data

- ✱ **Waist circumference and waist to hip ratio**
 - ✱ Highly associated with
 - ✱ Abdominal or central obesity
 - ✱ ↑ Risk of metabolic syndrome, cardiovascular diseases, chronic diseases
 - ✱ Better indicator of obesity related diseases > BMI

Waist circumference

Waist circumference measurement sites for men and women based on World Health Organization (WHO) and National Institutes of Health (NIH) protocols



Note: Following the WHO protocol, the measure is taken midway between the highest point of the iliac crest and the bottom of the ribcage. Following the NIH protocol, the measure is taken at the highest point of the iliac crest.

Adiposity measurements

* Skinfold thickness

* Relative “fatness” or

* To assess the size of specific subcutaneous fat depots

Biceps skinfold

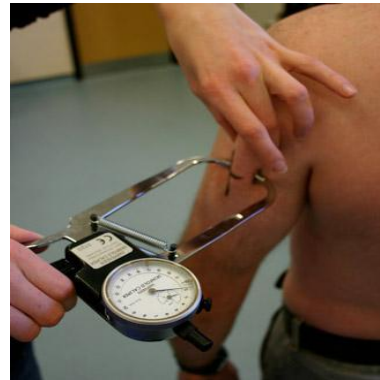
(front side middle upperarm)



<http://www.copdplatform.com/index.php?pg=home--ffmi-and-mamc-skinfold-measurement>

Triceps skinfold

(back side middle upperarm)



<https://nutritionalassessment.mumc.nl/en/skinfold-measurements>

Subscapular skinfold

(under the lowest point of the shoulder blade)



<http://www.copdplatform.com/index.php?pg=home--ffmi-and-mamc-skinfold-measurement>

Suprailiac skinfold

(above the upper bone of the hip)



<https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcSmJy6N4R8MG8WpbEyt0IMTESVhs3ZosHfe5x6osYpaes54bfvV>

Adiposity measurements

- ✱ **Bioelectrical Impedance Analysis (BIA)**

- ✱ Commonly used method for estimating body composition, in particular body fat and muscle mass
- ✱ A weak electric current flows through the body and the voltage is measured in order to calculate impedance (resistance) of the body.
- ✱ In recent years, BIA is more reliable and more acceptable way of measuring body composition.

- ✱ **Dual energy X-ray absorptiometry (DXA)**

- ✱ Measures bone mineral mass, FM, and FFM

- ✱ **Magnetic resonance imaging (MRI)**

- ✱ Estimates the volume rather than the mass of adipose tissue

- ✱ **DXA and MRI (not BIA) - reference method in body composition analysis**

Criteria for diagnosis of metabolic syndrome

3 out of 5

1. Waist circumference

✱ ≥ 102 cm in male or ≥ 88 cm in female

✱ Or ≥ 90 cm in male or ≥ 80 cm in female in Asians

2. Triglyceride ≥ 150 mg/dl

3. HDL-cholesterol

✱ < 40 mg/dl in male or < 50 mg/dl in female

4. BP $\geq 130/85$ mmHg

5. FBS ≥ 100 mg/dl or diabetes

Misra A et al. Waist circumference cutoff points and action levels for Asian Indians for identification of abdominal obesity. Int J Obes. [Multicenter Study Research Support, Non-U S Gov't Validation Studies]. 2006;30(1):106-11.

Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama. [Guideline Practice Guideline]. 2001;285(19):2486-97

Treatment for overweight and obesity in adult populations: a systematic review and meta-analysis, 2014

3 principal findings:

1. Every 1 kg of weight loss (people with impaired glucose tolerance)

- ✱ ↓16% Incidence of type 2 DM

2. Weight outcomes

- ✱ No significant difference between behavioral and pharmacologic
- ✱ Pharmacologic treatments >> potential adverse outcomes

3. Modest weight reduction

- ✱ Loss of ≥5% and ≥10% of baseline body weight
 - ✱ Clinically important effects
 - ✱ ↓38% Incidence of type 2 DM in prediabetic populations

Diseases caused from obesity...

TREAT OBESITY

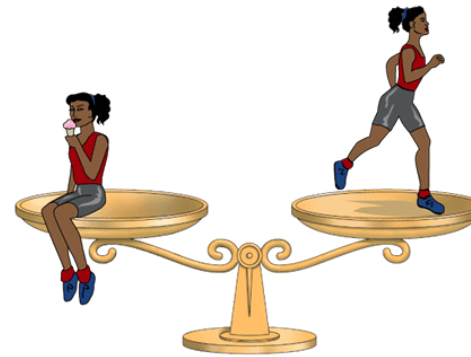
Case study



Case study



Energy balance

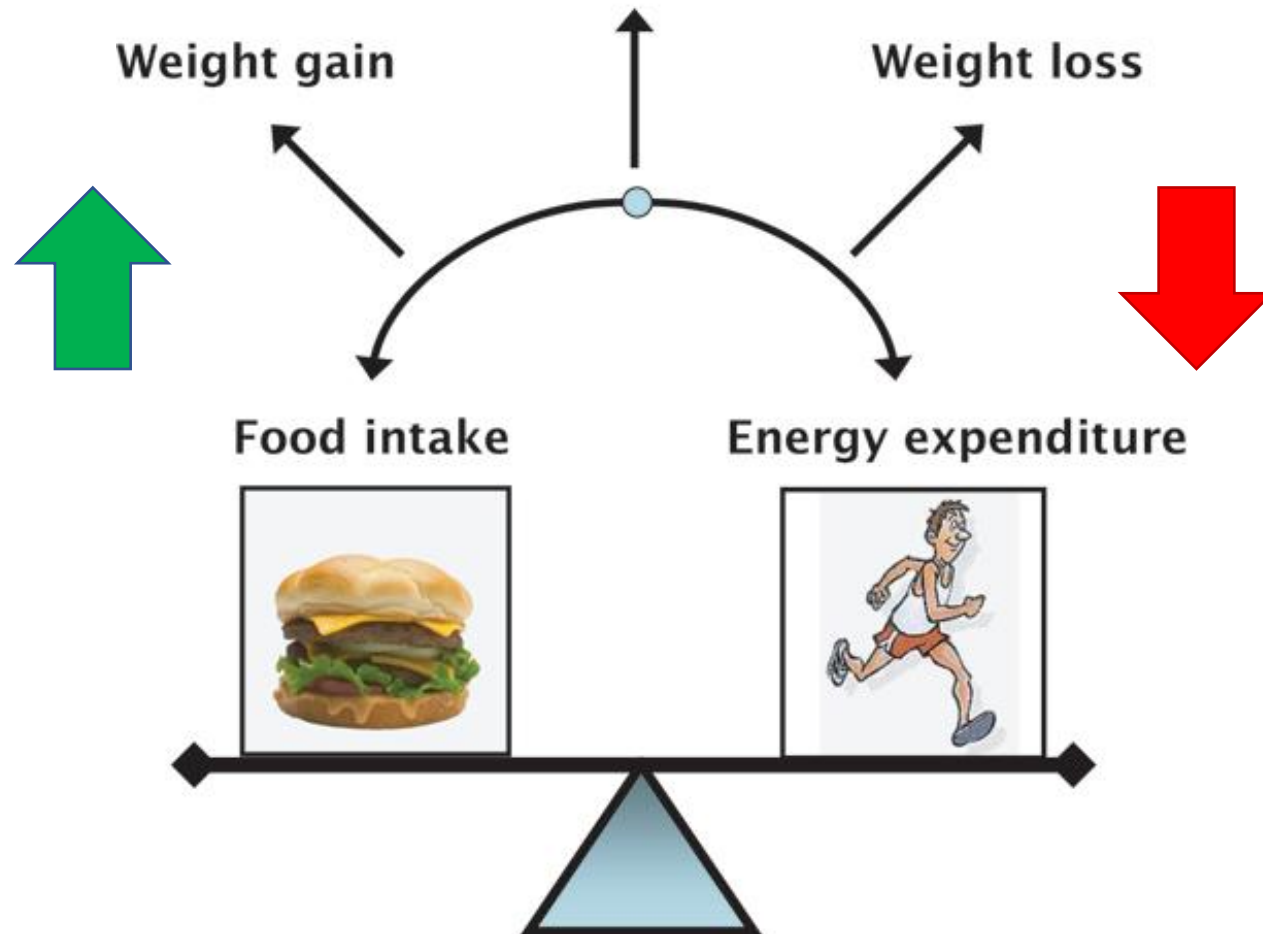


http://higheredbcs.wiley.com/legacy/college/smolin/047052474X/practice_quiz/smln2_ch07_pq_files/q35-1.png

Energy balance

Obesity

Weight maintenance



Quiz

Diet vs. *Exercise*

Which one has **more impact**
on **weight loss**?

1. Diet
2. Exercise

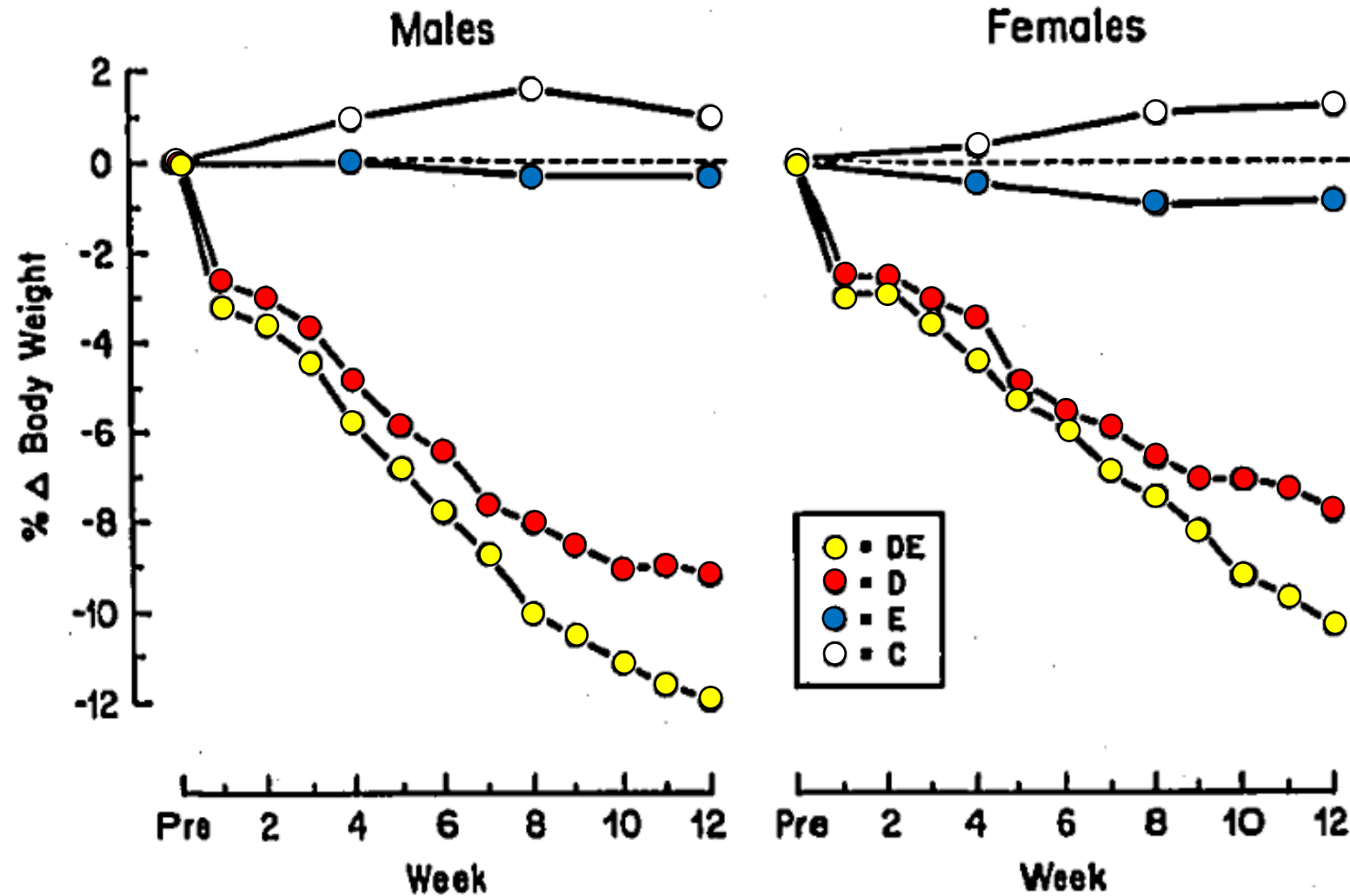


Figure 1—Percentage changes in body weight in males and females according to treatment effects of diet and exercise (DE), diet (D), exercise (E), and control (C).

Quiz

What is the **major factor**
determining **energy expenditure**?

1. BMR
2. Exercise
3. Thermic effects of food
4. Non-exercise activity thermogenesis (NEAT)

Energy output

Energy output

= Basal metabolic rate (BMR) **60-70%**

+ Spontaneous physical activities (PA) **20-30%**

+ Thermogenesis

(Harrison's Principles of Internal Medicine, 18th e)

= BMR **70%** + Active PA **5-10%**

+ The energy cost of metabolizing and storing food

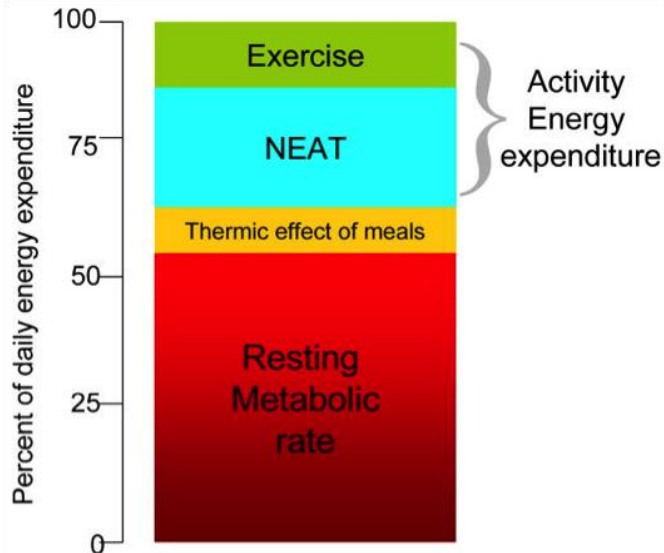
+ Adaptive thermogenesis

= External work (PA) + internal heat production (BMR + Diet induced thermogenesis - DIT)

± stored energy

(Human physiology, 7th e, 2010)

Energy output



http://4.bp.blogspot.com/-obEju6EGjzo/T6FmPh8cgol/AAAAAExA/euaH3NKQBss/s1600/NEAT_graph.png

✳ **Exercise** (การออกกำลังกาย) ~ **5-15%**

✱ Continuous activity at an intensity which **↑ oxygen consumption or heart rate to an appropriate training level**

C J Caspersen et al. , Public Health Rep., 1985,
Petrella RJ et al. Diabetes Care., 2005

✳ **Non-exercise activity thermogenesis, NEAT** (กิจกรรมทางกาย) ~ **15-25%**

✱ Energy expenditure due to **physical activities** other than active sports-like exercise and resistance training

✱ The main determinant of variability in total daily energy expenditure

✳ **Thermic effect of meals** ~ **10-15%**

✱ The consumption, digestion, metabolism, and storage of food

✳ **Resting metabolic rate** ~ **60%**

✱ Energy expenditure at rest

Basal metabolic rate (BMR)

- ✱ Amount of energy expended while at rest
- ✱ Vital activities (respiration, pumping of blood around the body, maintenance of body temperature, brain function, etc.)
- ✱ In a neutrally temperate environment
- ✱ Post-absorptive state (inactive digestive system ~ 12 hours fasting)
- ✱ BMR/body surface area ($\text{Cal}/\text{m}^2/\text{hr}$)
- ✱ Closely related to resting metabolic rate (RMR)

Factors determining BMR

1. **Genetics**
2. **Gender:** Male (↑muscle mass, ↓fat) > Female
3. **Age:** ↓ ~ 2 %/decade after 20 years
4. **Weight:** the heavier weight, the higher BMR
5. **Height:** the taller, the higher BMR
6. **Body Surface Area:** the greater BSA, the higher BMR
7. **%Body Fat:** the lower % body fat, the higher BMR
8. **Fasting:** starvation, serious abrupt calorie-reduction, restrictive low-calorie weight loss diets
→ dramatically ↓ BMR by up to 30 %

Fasting in humans

- * The first 36-60 hours

- * ↑ BMR

- * ↑ NE and GH production

- * Afterwards (72 or more)

- * ↓ BMR

- * ↓ NE and GH production

Factors determining BMR

9. **Body Temperature:** $\uparrow 0.5^{\circ}\text{C}$ body T $\rightarrow \uparrow \text{BMR} \sim 7\%$

10. **External temperature:**

Cold T $\rightarrow \uparrow \text{BMR}$

Short exposure to hot T $\rightarrow$ Little effect on BMR (compensated by $\uparrow$ heat loss)

Prolonged exposure to heat $\rightarrow \uparrow \text{BMR}$

11. **Hormones:** Thyroxine $\rightarrow \uparrow \text{BMR}$

12. **Exercise:** $\uparrow \text{BMR}$ ($\uparrow$ muscle mass)

13. **Diets**

Quiz

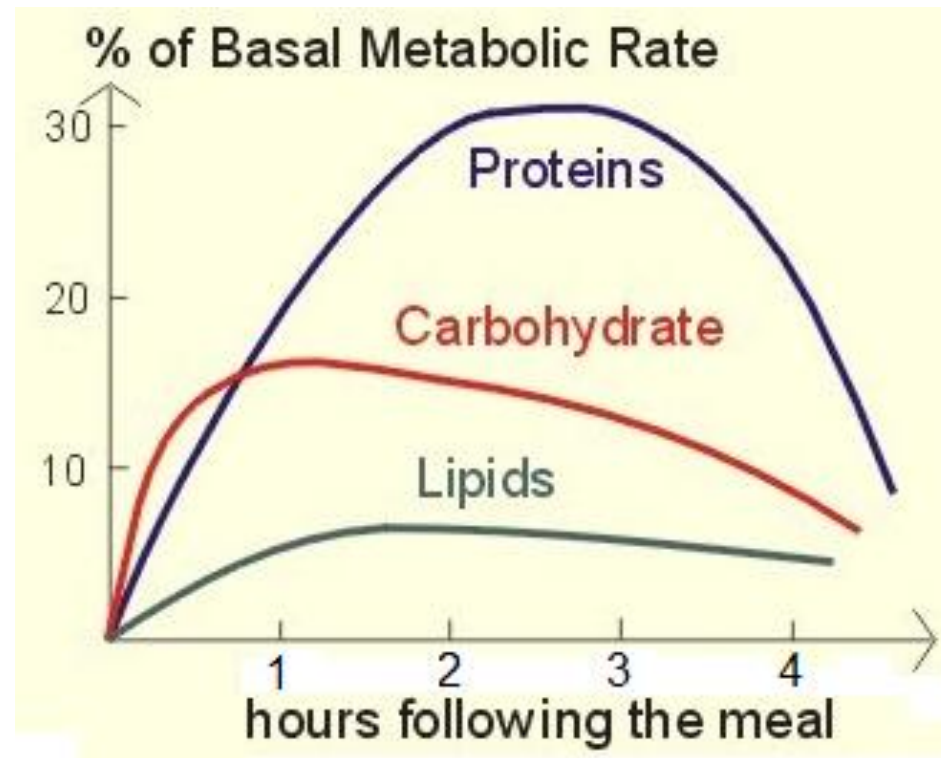
Which nutrient generates
the **highest thermic effect of food (TEF)**?

1. CHO
2. Lipid
3. Protein
4. Vitamins
5. Minerals

Basal metabolic rate

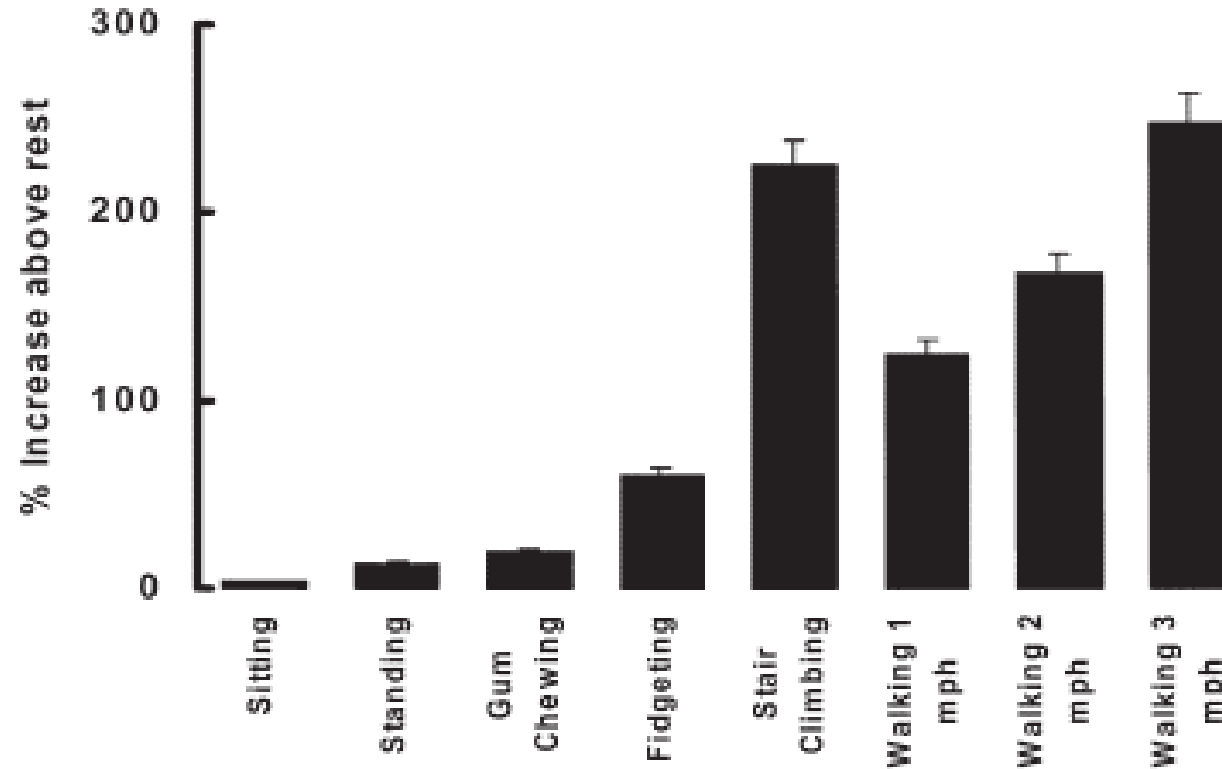
Thermic effects of nutrient are **0-3% for fat**,
5-10% for carbohydrates and **20-30% for proteins**.

Tappy L. Thermic effect of food and sympathetic nervous system activity in humans. *Reproduction Nutrition Development*. 1996;36(4):391–397.



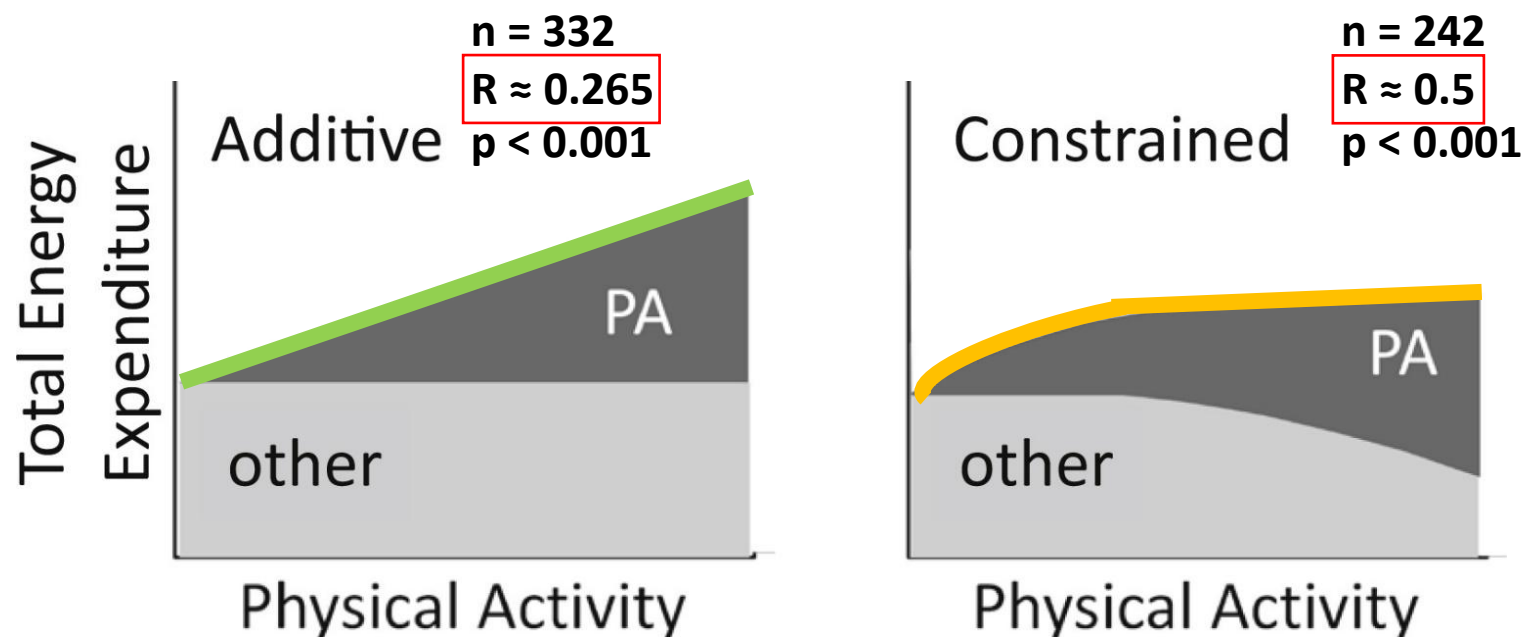
http://upload.wikimedia.org/wikipedia/commons/8/81/Postprandial_thermogenesis.png

Non-exercise activity thermogenesis (NEAT)



1 mph (miles per hour) = 0.44704 m/s

Long term effect of exercise on total energy expenditure

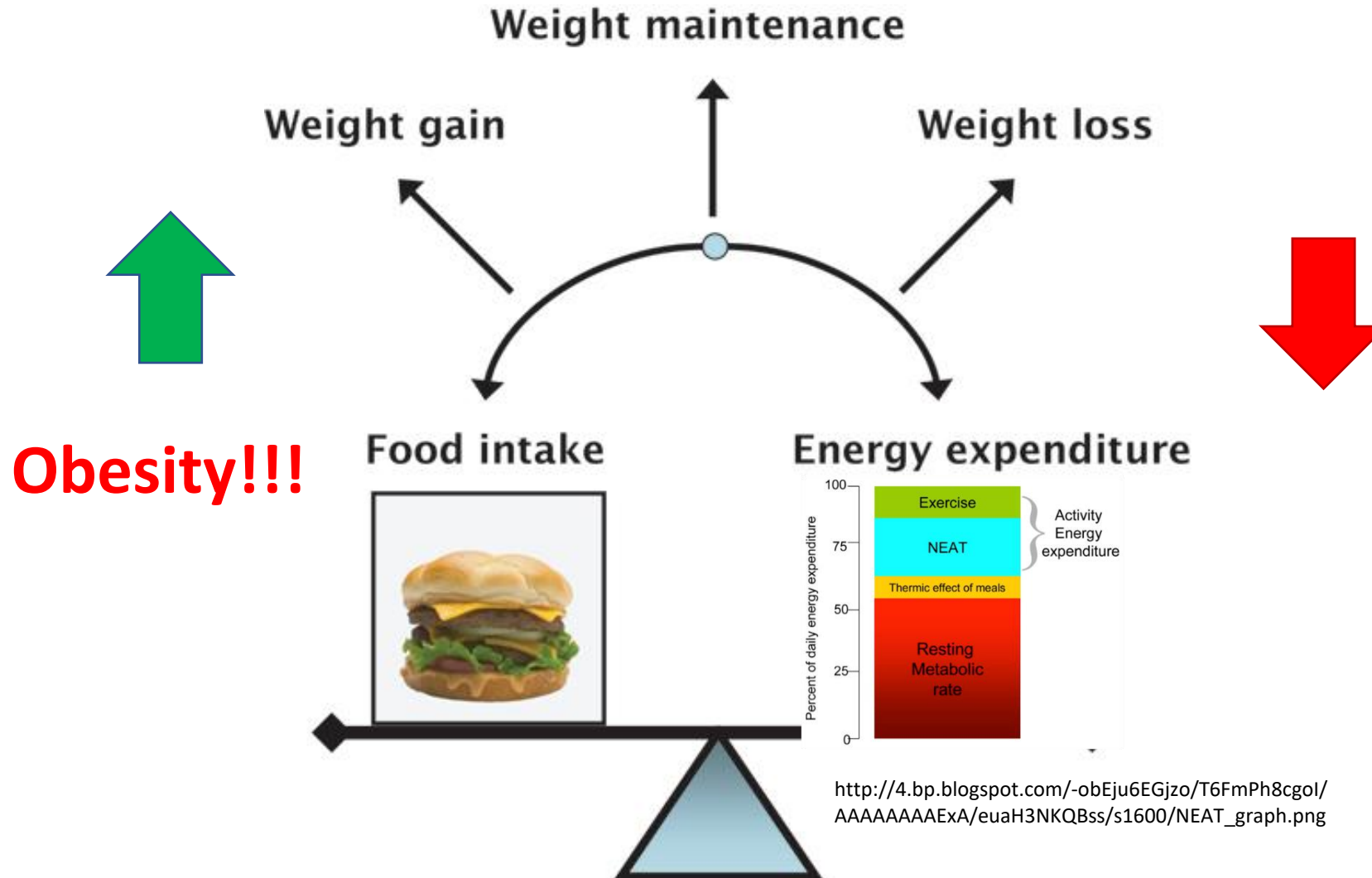


Pontzer H et al., Curr Biol., 2016

PA = physical activity energy expenditure,
 TEE = total energy expenditure

- ✱ ↓ BMR at week 40
- ✱ Behavior change
 - ✱ Sitting instead of standing
 - ✱ Less fidgeting

Energy balance



EXERCISE PHYSIOLOGY

Seventh Edition

NUTRITION, ENERGY, AND HUMAN PERFORMANCE

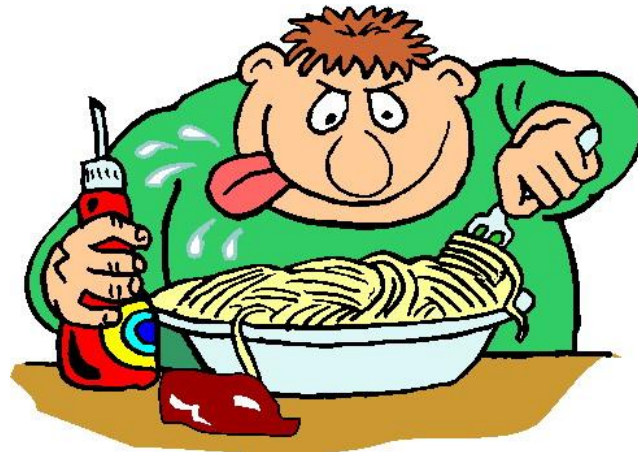
Calories In Versus Calories Out:
The Amount of Exercise Required for a 150-Pound Person
to Burn Off the Calories in Some Popular Foods



Calories in versus calories out: the amount of exercise required for a 150-pound person to burn off the calories in some popular foods.

- * Exercise alone cannot effectively reduce body weight
 - * A relatively slow elimination of energy due to its relatively low rate of energy expenditure
 - * Take a long time to exercise or engage in physical activity to produce the same amount of energy as the food ingested
- * Many people do not assess or are unable to assess the energy of the food eaten and/or the energy used in exercise correctly.

Appetite regulation



<http://www.picgifs.com/clip-art/activities/eating/clip-art-eating-577214.jpg>



http://www.bestfoodfacts.org/images/thought/4313895320_e68c831828.jpg

Appetite, Food intake, and Feeding Behavior

- ✱ Appetite

- ✱ Sensations of hunger and fullness or the desire to eat food or the state of willingness to accept food primarily for its pleasurable or rewarding properties

- ✱ Food intake

- ✱ The amount of food consumed

- ✱ Appetite $\neq$ Food intake

[Kissileff et al., 1982]

Appetite, Food intake, and Feeding Behavior

- ✱ Appetite

- ✱ Also regulated by short-term and long-term control systems

- ✱ Short-term control

- ✱ The initiation and termination of meals

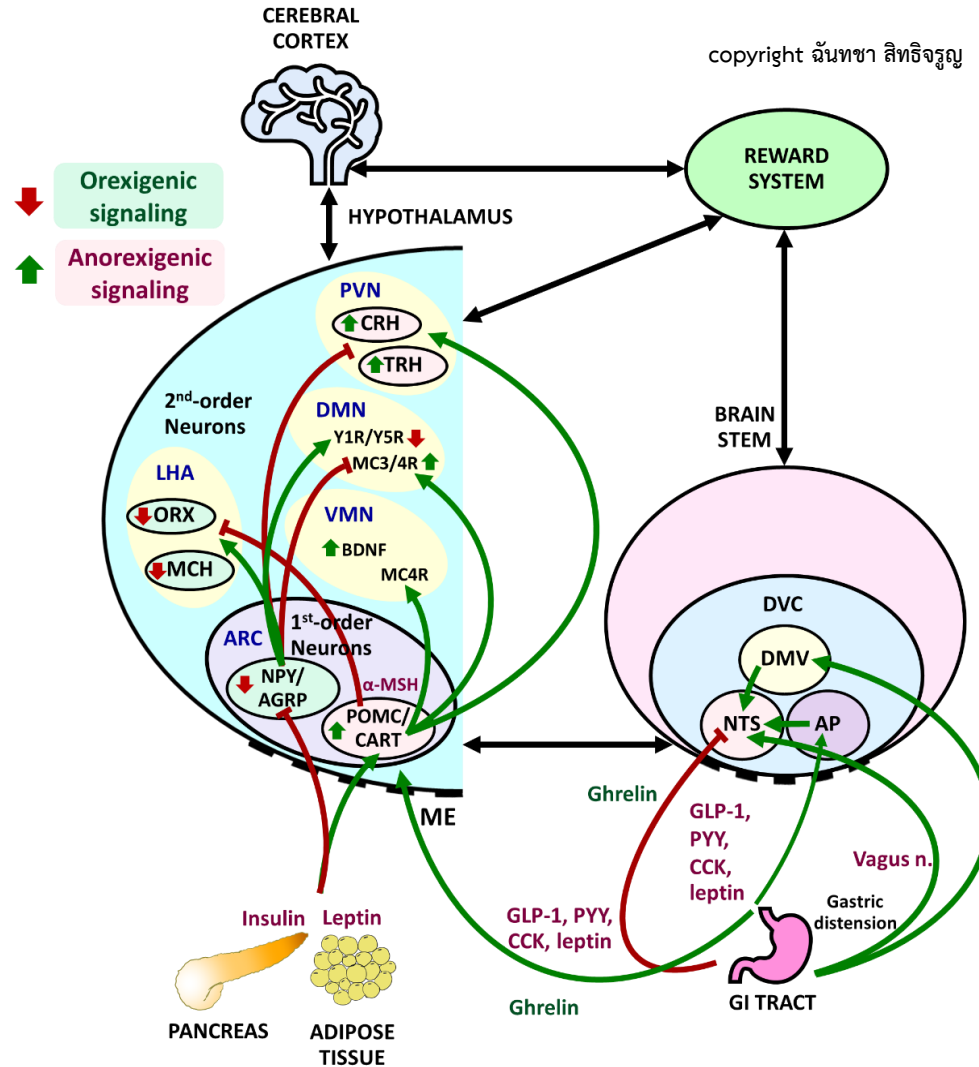
- ✱ Long-term control

- ✱ Signals that reflect the status of energy stores, such as the fat-derived hormone, leptin, provide information to the central nervous system (CNS) for further regulation of feeding behaviour to promote energy homeostasis

[Spiegelman et al., 2001].

[Ahima et al., 2000b]

Homeostatic system & Hedonic system



Homeostatic system

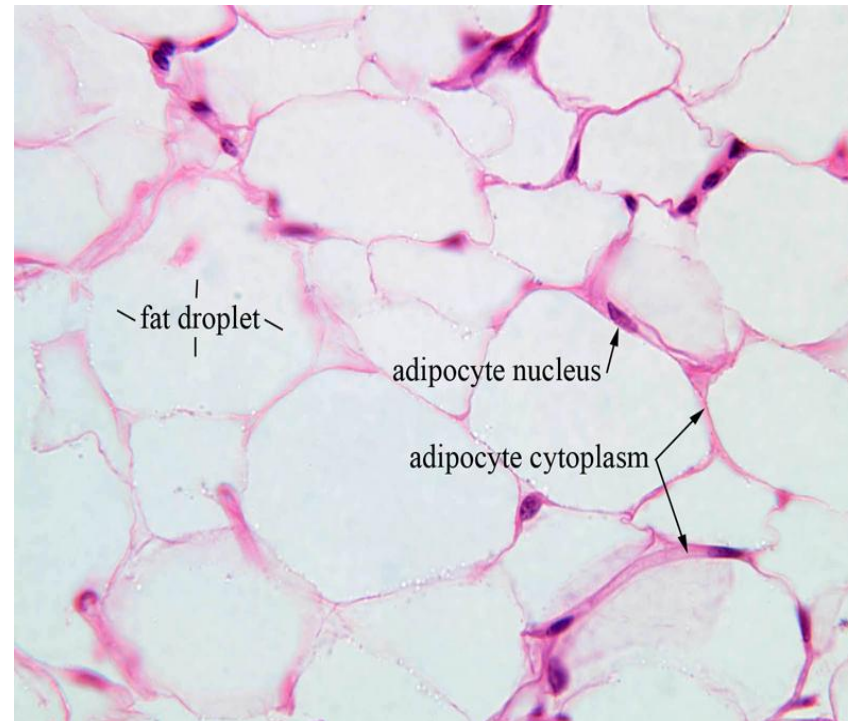
- ✿ The physiological system that maintains energy balance by regulating hunger and satiety based on signals from the body, such as hormones and nutrients.

Hedonic system

- ✿ The brain's reward system that influences appetite and food intake based on the pleasurable sensations associated with eating, responding to sensory cues and promoting the desire for certain foods.

Appetite Control

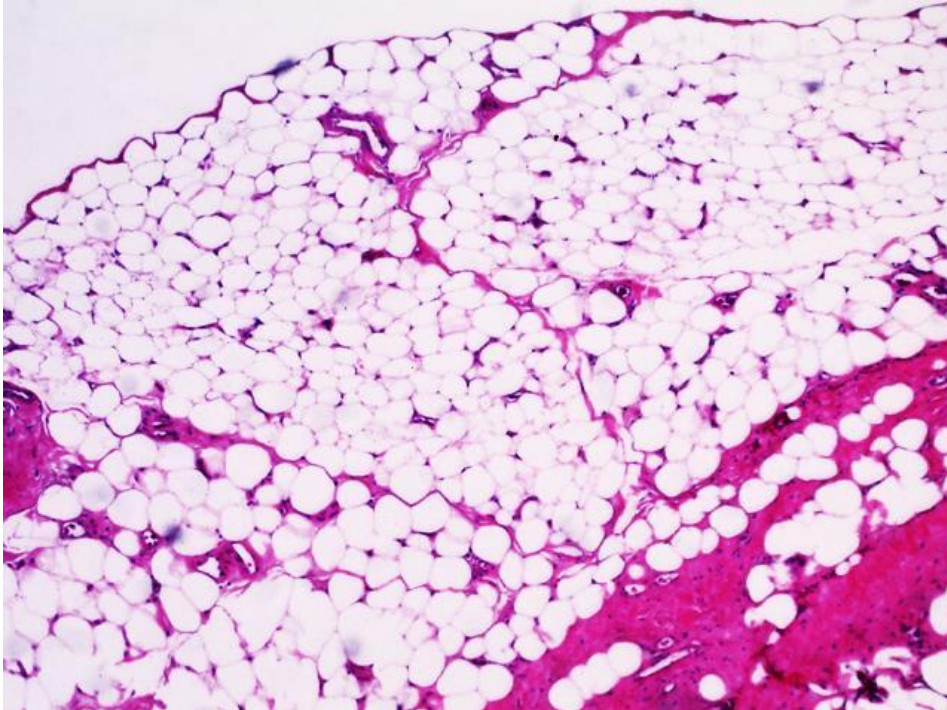
Adipose tissue



http://www.medicalhistology.us/twiki/pub/Main/ChapterT woSlides/a73b_adipose_tissue_neck_40x_labeled.jpg

**What are components
of adipose tissue?**

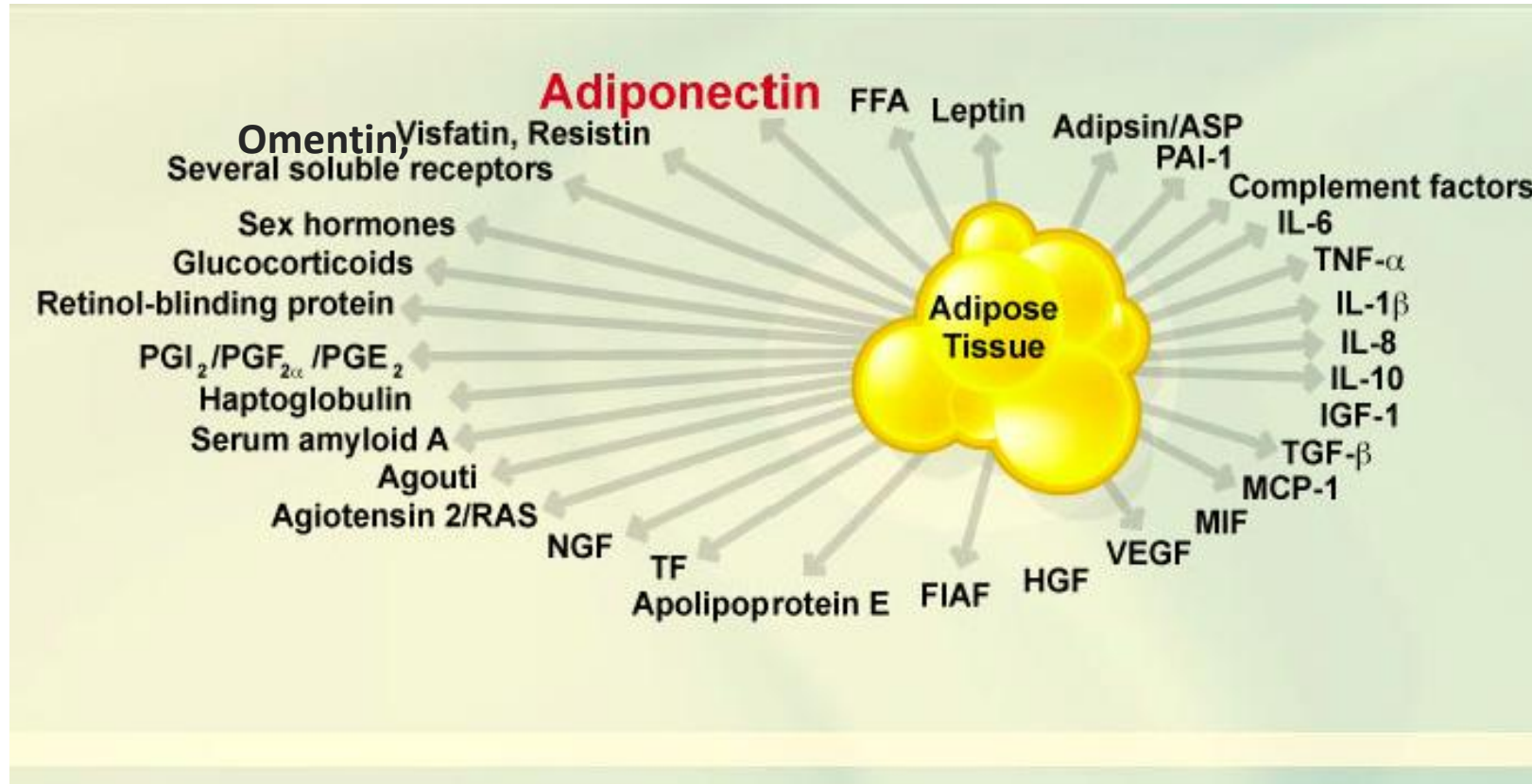
Adipose tissue



http://medpics.ucsd.edu/images/hist_640/CNT/hist_cnt_014_00.jpg

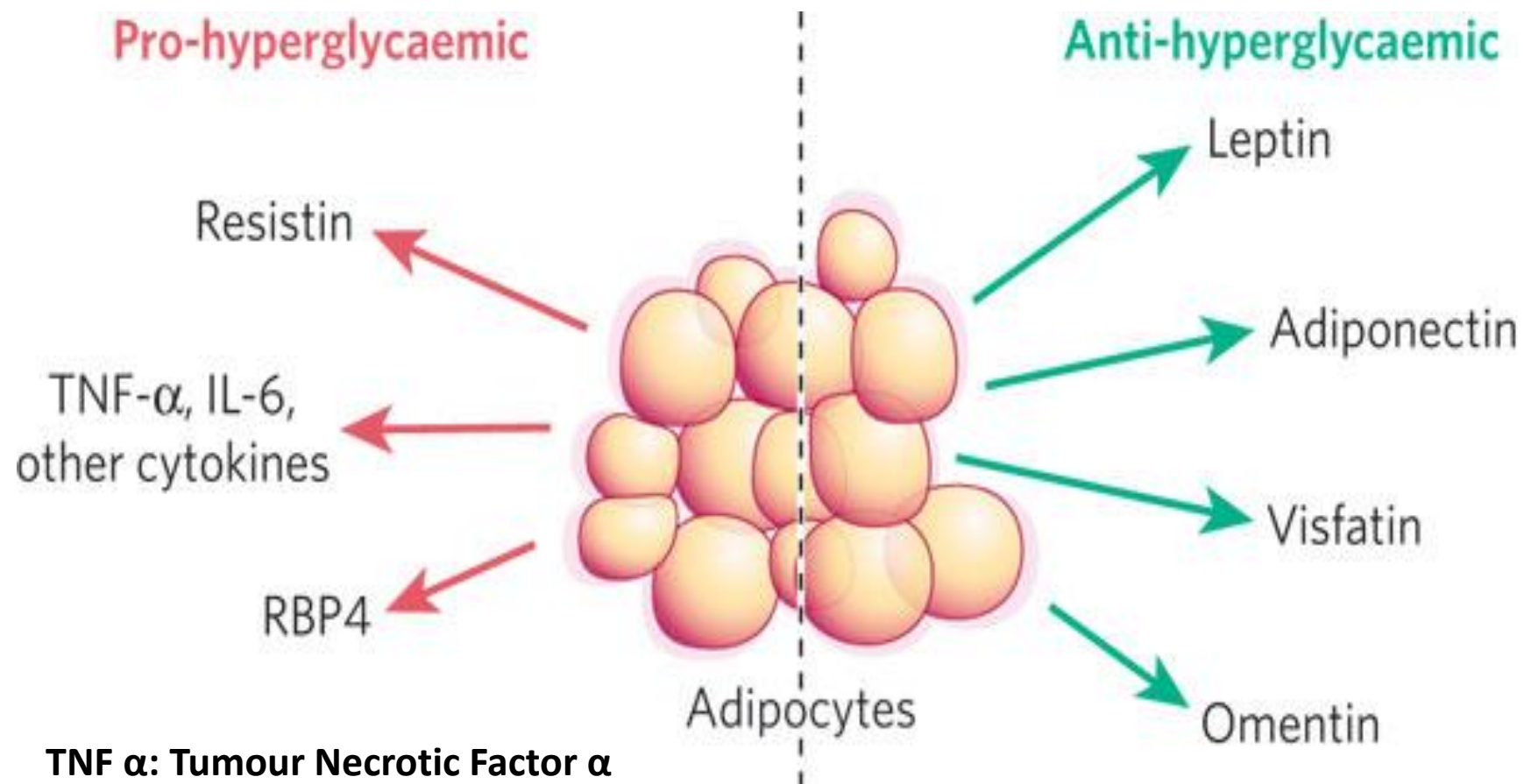
- ✱ Stores the excess consumed energy
- ✱ **Active endocrine gland**
composed of the mature adipocytes, vascular endothelium cells, fibroblasts, and immune cells including M1 and M2 macrophages, T helper 2 cells, and T regulatory cells

Adipokines



Guerre-Millo M et al., 2003

Adipokines

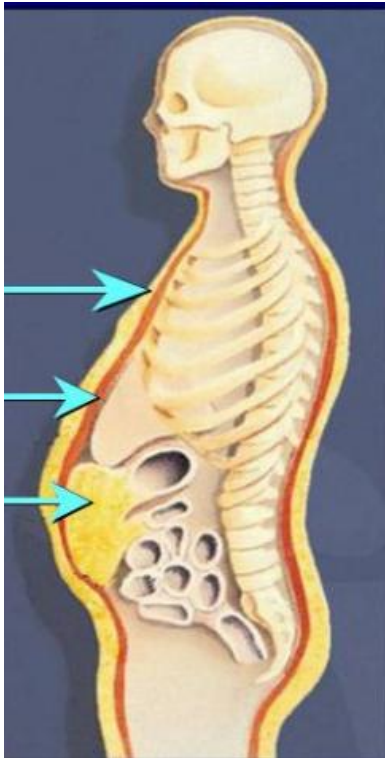


TNF α : Tumour Necrotic Factor α
IL 6: Interleukin 6
RBP4: Retinol Binding Protein 4

Evan D. Rosen et al., 2006

Adipose tissue

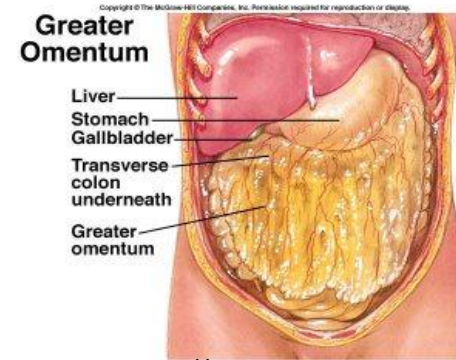
Subcutaneous adipose tissue



- * The hypodermis fat depot all over the body

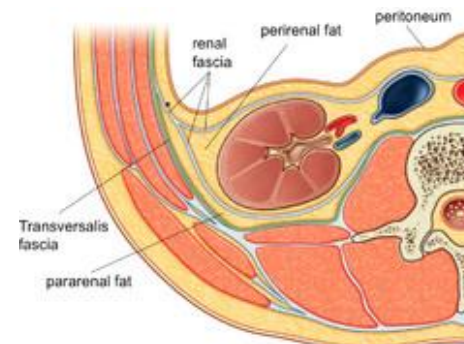
<http://www.cadiresearch.org/topic/obesity/abdominal-obesity/abdominal-obesity-causes>

Visceral adipose tissue



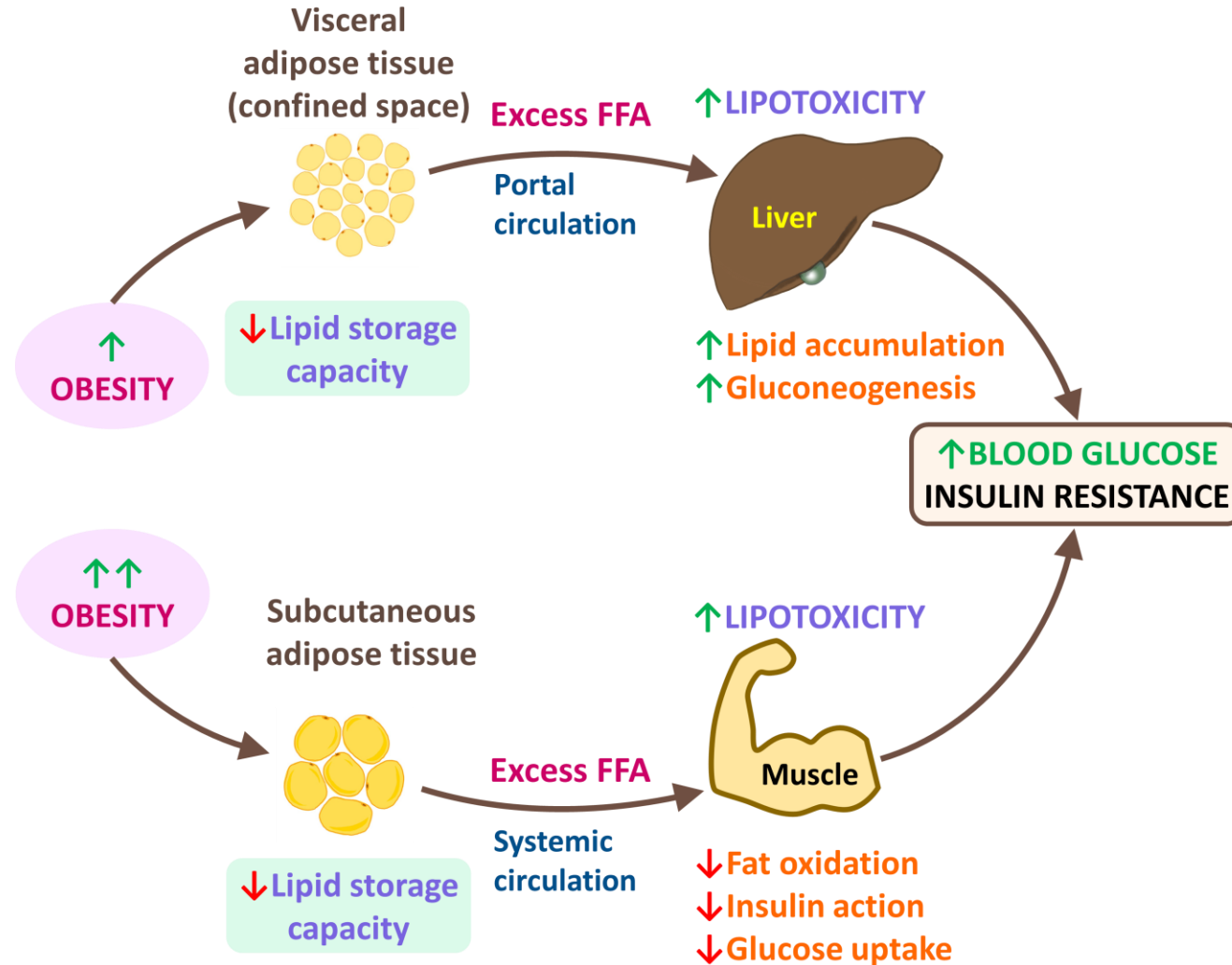
<http://www.drsharma.ca>

- * Fat tissue of
 - ✓ Mesenteric
 - ✓ Omental
 - ✓ Retroperitoneal
 - ✓ Perirenal
 - ✓ Pericardial
 - ✓ Perigonadal



<http://quizlet.com>

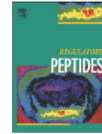
Adipose tissue





Contents lists available at SciVerse ScienceDirect

Regulatory Peptides

journal homepage: www.elsevier.com/locate/regpep

Expressions of neuropeptide Y and Y1 receptor in subcutaneous and visceral fat tissues in normal weight and obese humans and their correlations with clinical parameters and peripheral metabolic factors

Chantacha Sitticharoon*, Saimai Chatree, Malika Churintaraphan

Department of Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand



Peptides 62 (2014) 164–175



Contents lists available at ScienceDirect

Peptides

journal homepage: www.elsevier.com/locate/peptides

Interactions between adiponectin, visfatin, and omentin in subcutaneous and visceral adipose tissues and serum, and correlations with clinical and peripheral metabolic factors

Chantacha Sitticharoon*, Nay Chi Nway, Saimai Chatree, Malika Churintaraphan, Peerada Boonpuan, Pailin Maikaew

Department of Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand



Original Research

Adipose Y5R mRNA is higher in obese than non-obese humans and is correlated with obesity parameters

Saimai Chatree, Chantacha Sitticharoon, Pailin Maikaew, Panapat Uawithya and Supornpim Chearskul

Department of Physiology, Department of Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand
Corresponding author: Chantacha Sitticharoon. Email: chantacha.sit@mahidol.ac.th

Experimental Biology and Medicine 2018; 243: 786–795. DOI: [10.1177/1535370218774889](https://doi.org/10.1177/1535370218774889)



ORIGINAL ARTICLE

Correlations between the expression of the insulin sensitizing hormones, *adiponectin*, *visfatin*, and *omentin*, and the appetite regulatory hormone, *neuropeptide Y* and its receptors in subcutaneous and visceral adipose tissues



Nay Chi Nway, Chantacha Sitticharoon*, Saimai Chatree, Pailin Maikaew

Department of Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

Original Article

Expression of Y2R mRNA Expression in Subcutaneous and Visceral Adipose Tissues Compared between Normal Weight and Obese Female Subjects

Saimai Chatree, Malika Churintaraphan, Nay Chi Nway, Chantacha Sitticharoon, M.D.*

Department of Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

scientific reports

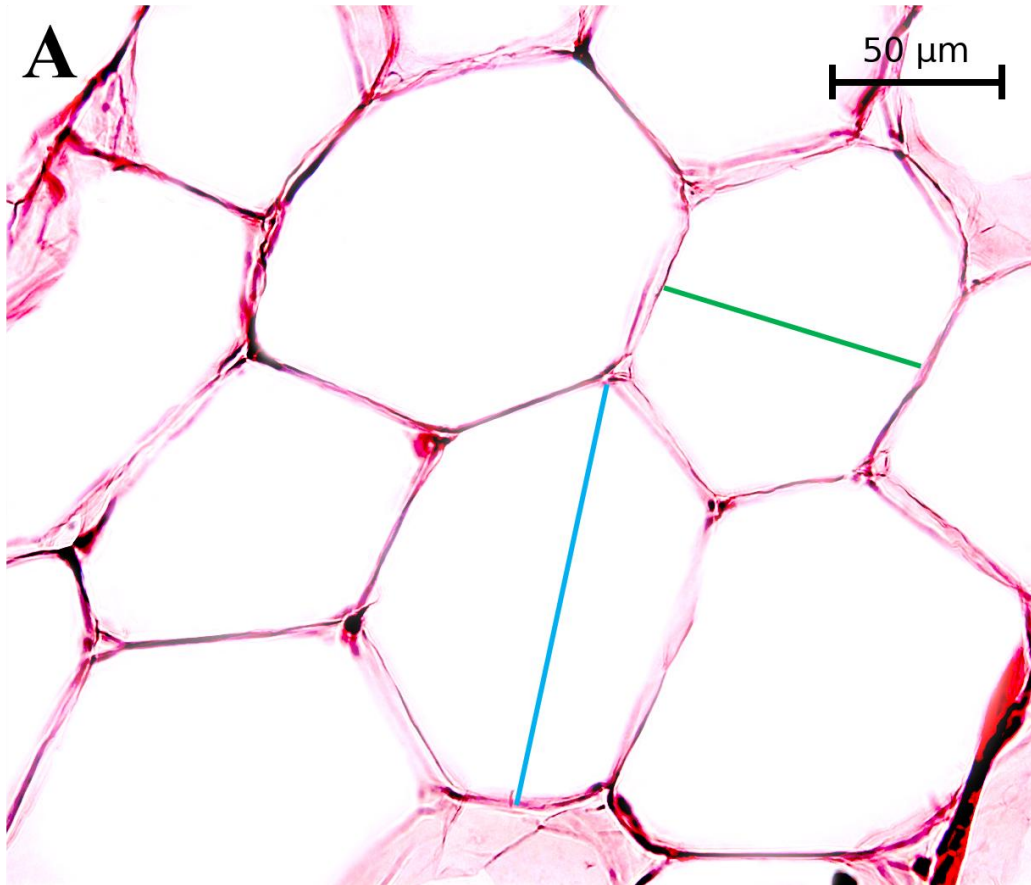


OPEN

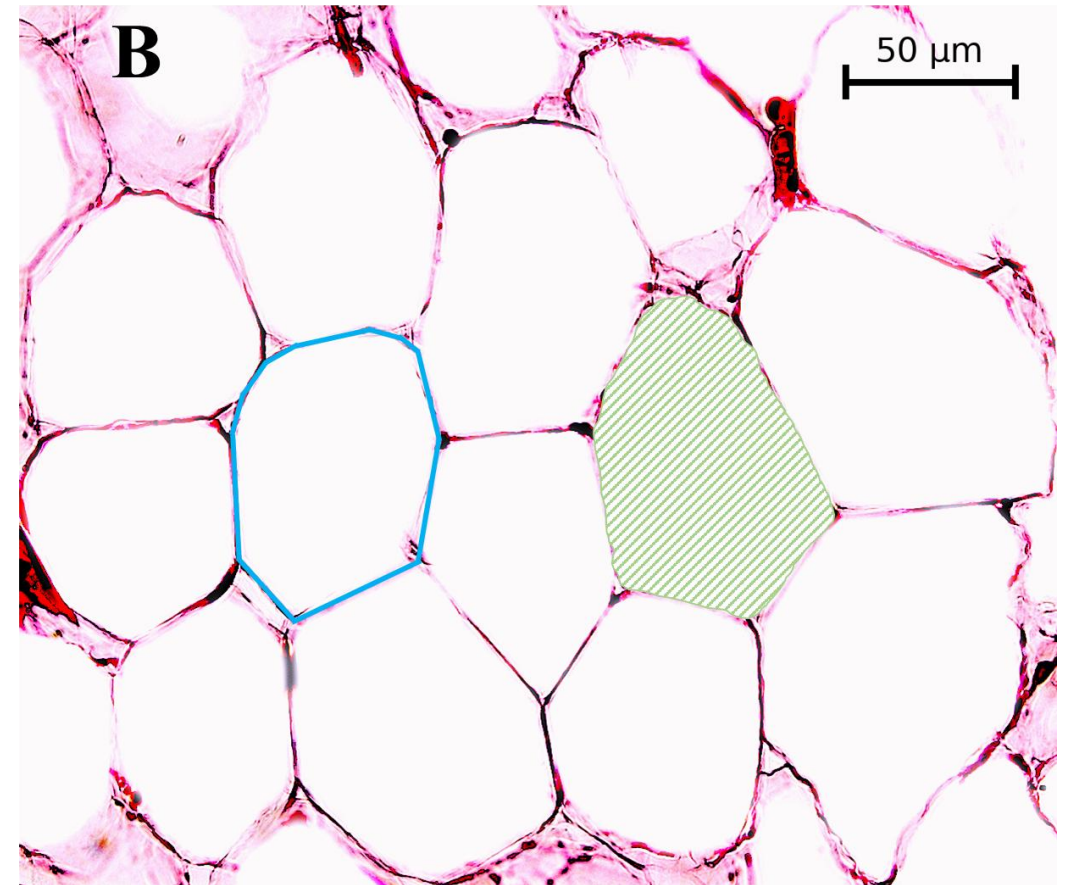
Distinct metabolic associations of subcutaneous and visceral adipocyte morphology in women with or without obesity

Pailin Maikaew, Trittamon Phattanakiatsakul, Chantacha Sitticharoon & Issarawan Keadkraichaiwat

Subcutaneous vs. Visceral adipose tissue

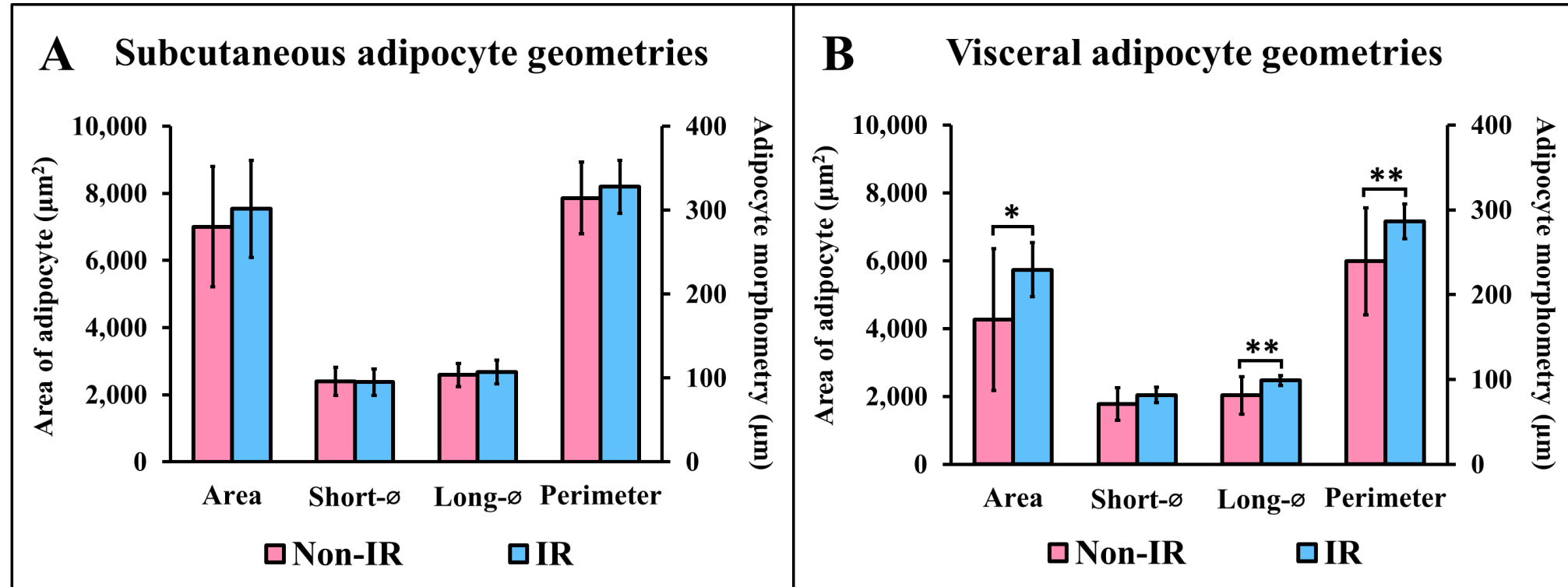


Subcutaneous



Visceral

Subcutaneous vs. Visceral adipose tissue



Non-IR=participants without insulin resistance; IR=participants with insulin resistance;
 Short-ø=shortest diameter; Long-ø=longest diameter;
 Subcut.=subcutaneous adipose tissue; Vis.=visceral adipose tissue.
 *P <0.05, **P <0.01 compared between participants with and without IR.

Subcutaneous vs. Visceral adipose tissue

Maikaew P, [Sitticharoon C](#), et al., Scientific Reports. 2025 Nov 21;15(1):41287

	Participants without obesity (N=13)								Participants with obesity (N=14)										
Age															†	†			
BW	*		*	*	***	**	***	***		†				†	*	†			
BMI	†		*	*	**	**	**	**							†				
WC	†		*	*	*	†	*	*							*				
HC	†		†	†	†	†	†	†							*				
WHR																			
SBP																			
DBP			†		*	*		†											
Glucose							†	†											
Insulin																			
HOMA-IR							†												
QUICKI					†		*	†							†				
LEP mRNA					*	*		†											
Adipo mRNA									*		*	*	**	**	**	**			
Omentin mRNA									†	*		†	†						
Visfatin mRNA									*		†	*							
Se. Lep					*	*	*	*							†				
Se. Adipo	†	*	*	*	†	*	†	*											
Adipo/Lep ratio	*	*		*	*	*	*	*					**	*	**	**			
Se. Omentin					†				†			†			†				
Se. Visfatin									†		*	†			†	†			
	Area	Short-ø	Long-ø	Peri	Area	Short-ø	Long-ø	Peri	Area	Short-ø	Long-ø	Peri	Area	Short-ø	Long-ø	Peri			
	Subcut. adipocyte				Visceral adipocyte				Subcut. adipocyte				Visceral adipocyte						
R	0.900	0.800	0.700	0.600	0.500	0.400	0.300	0.200	0.100	0.000	-0.100	-0.200	-0.300	-0.400	-0.500	-0.600	-0.700	-0.800	-0.900

The fasting state

↑ ↓ Blood glucose → ↓ Insulin

↑ ↑ Counter regulatory hormones (oppose the action of insulin) → ↑ Blood sugar

- ✱ Glucagon
- ✱ Epinephrine
- ✱ Norepinephrine
- ✱ Cortisol
- ✱ GH

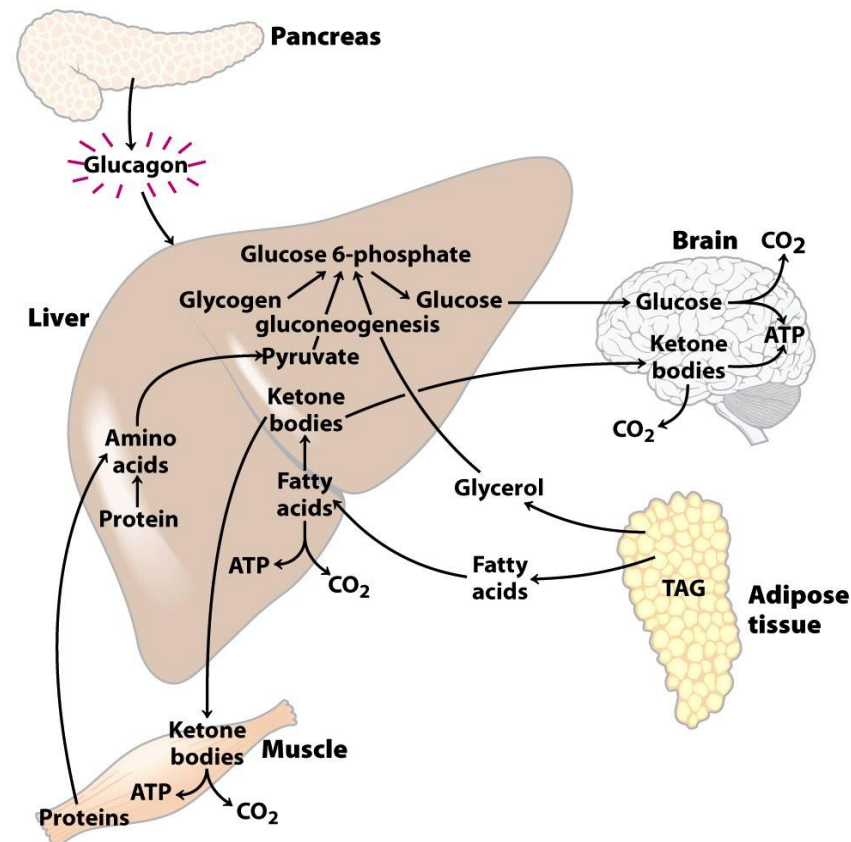


Figure 23-30
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

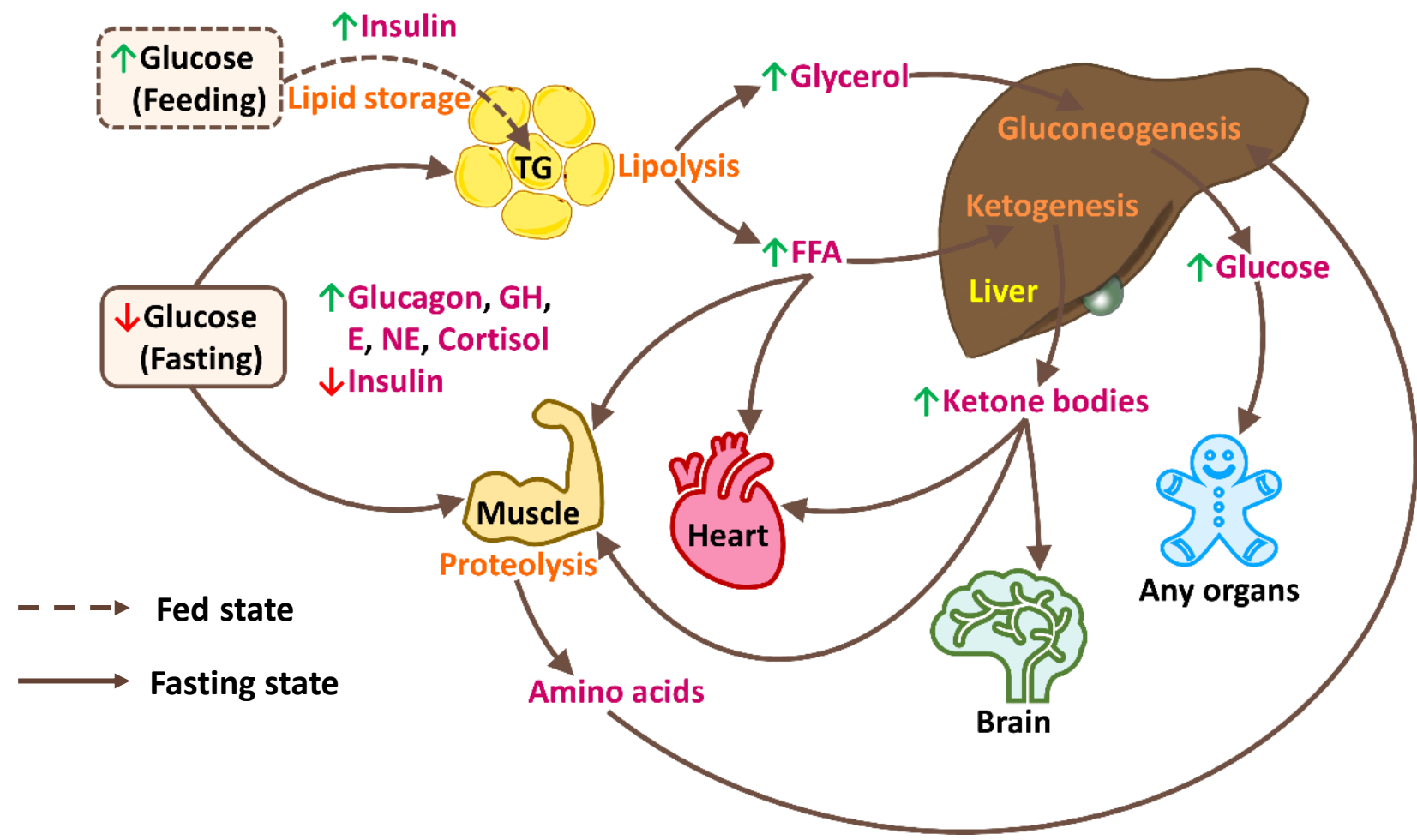
Lipolysis

- ✱ A breakdown of triglyceride accumulated in adipocytes into FFA and glycerol by hormone-sensitive lipase (HSL), a rate-limiting enzyme of fat catabolism

Zechner R et al. Lipolysis: pathway under construction.
Curr Opin Lipidol. [Research Support, Non-U S Gov't Review]. 2005

- ✱ The rate of lipolysis
 - ✱ Low in the subcutaneous femoral/gluteal region
 - ✱ Intermediate in the subcutaneous abdominal region
 - ✱ High in the visceral (i.e. omental) region
- ✱ The lipolytic beta 1 and beta 2 adrenoceptors, as well as the newly discovered beta 3, are most active in the visceral fat cells.
- ✱ The antilipolytic insulin receptors, alpha 2 adrenoceptors and adenosine receptors are most active in the subcutaneous fat cells.

The fasting state



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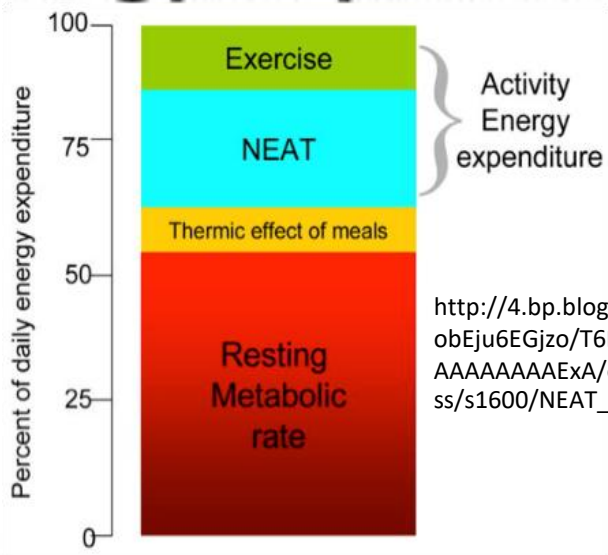
TG: triglyceride; FA: free fatty acid; GH: growth hormone; E: epinephrine; NE: norepinephrine

Energy balance

Food intake



Energy expenditure



http://4.bp.blogspot.com/-obEju6EGjzo/T6FmPh8cgol/AAAAAAAAExA/euaH3NKQBss/s1600/NEAT_graph.png

NEAT = Non-exercise activity thermogenesis

BMR calculator

Weight-loss diet regimens

Weight loss diet regimens

1. **General Recommendation** (↓ Carbohydrate, ↓ Sugar, ↑ Protein, ↓ Fat, ↑ Vegetable/Fiber, ↑ Drinking water)
 - **Metabolism boosting meals** (High protein, Low fat, No carb with 1 day cheating/week)
 - **Plate method**
2. **Calories reduction**
3. **Paleolithic diet**
4. **Mediterranean diet**
5. **“Eating breakfast like a king, lunch like a prince, and dinner like a pauper”**
6. **Intermittent fasting** (including Time-restricted eating, TRF)
7. **Ketogenic Diet**

1. General Recommendation

✱ ↓ Carbohydrate

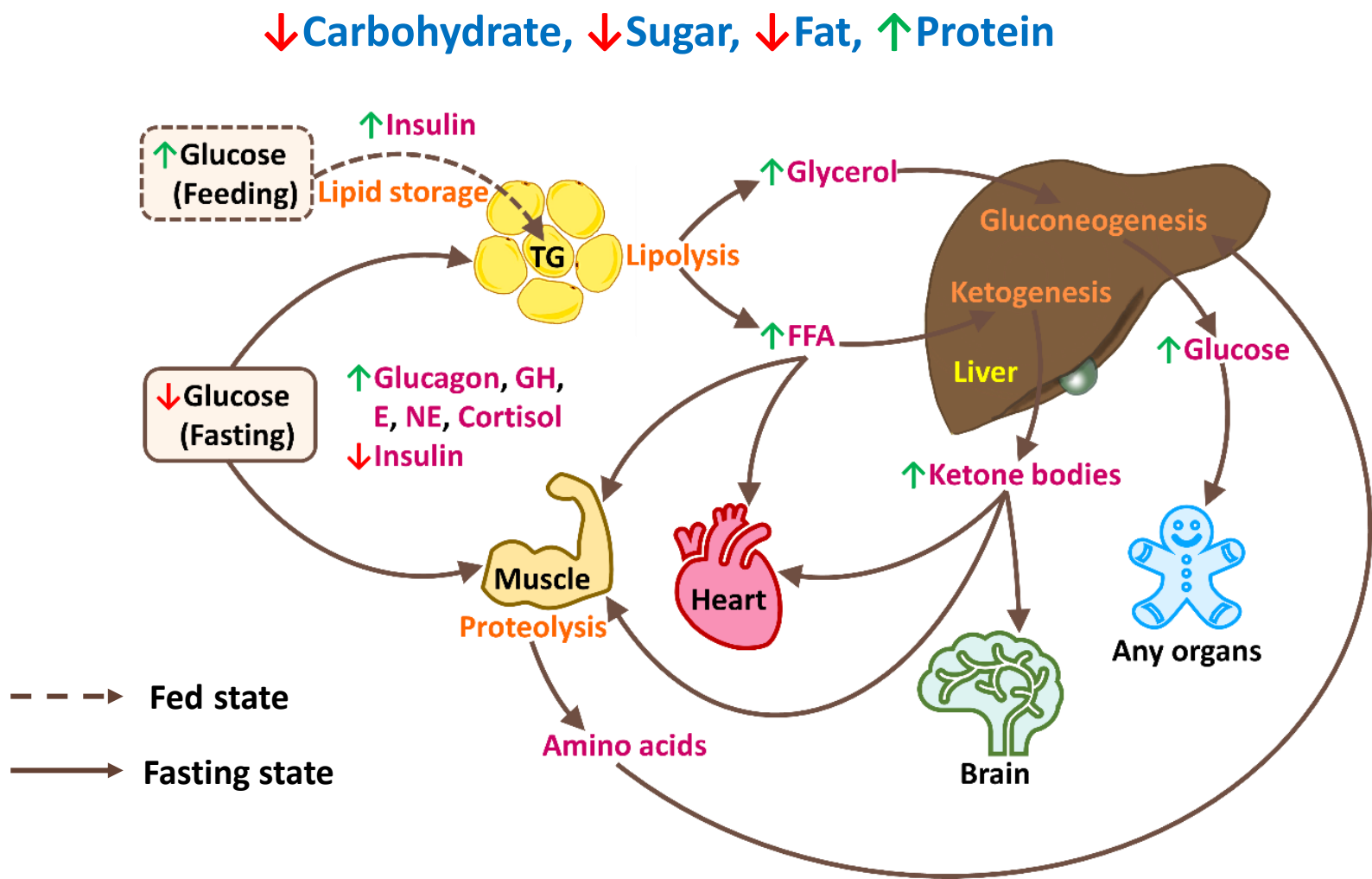
✱ ↓ Sugar

✱ ↓ Fat

✱ ↑ Protein

✱ ↑ Vegetable/Fiber

✱ ↑ Drinking water



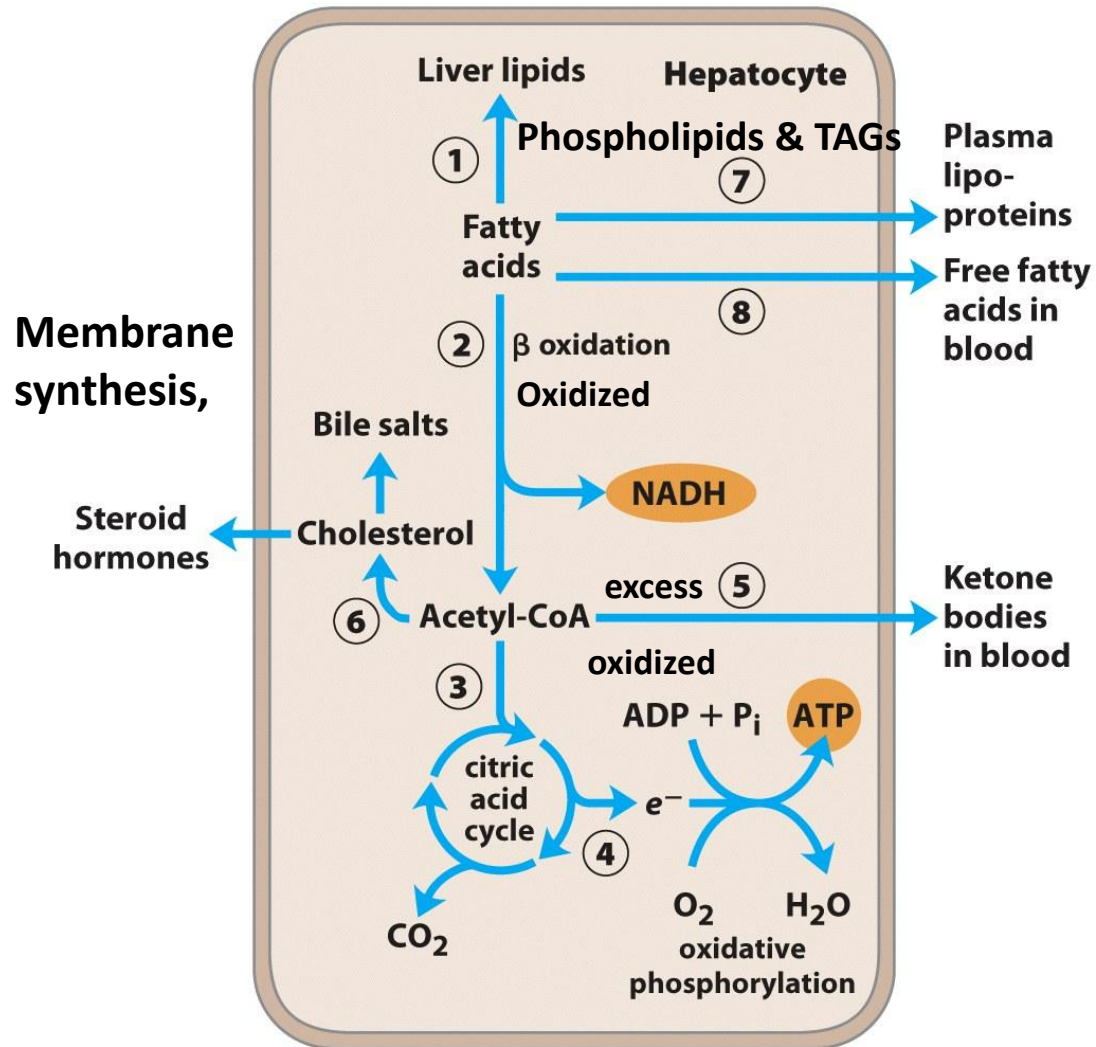
copyright ฉันทพา สิทธิจรรยา

✱ Carbohydrates & Protein 1 g → 4 calories

✱ Fat 1 g → 9 calories

TG: triglyceride; FA: free fatty acid; GH: growth hormone; E: epinephrine; NE: norepinephrine

Metabolism of fatty acids in the liver



* Carry lipids to adipose tissue for storage of TAG.

* Bound to serum albumin and carried to the **heart** and **skeletal m.** which take up and oxidize FFA as a major fuel.

Acetoacetate,
 β -hydroxybutyrate

* Fuel for the citric acid cycle for other tissues

* Supply energy for up to 1/3 $\rightarrow$ **heart**, 60-70% $\rightarrow$ **brain, muscle**

Figure 23-15
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

Hyperglycemic conditions

✿ Advanced glycation end products (AGEs)

- Non-enzymatic modifications of proteins or lipids after exposure to sugars
- Loss of protein function and impaired elasticity of tissues such as blood vessels, skin, and tendons
- Acceleration of the aging process (the accumulation of glycated macromolecules, including proteins, is a hallmark of aging both in humans and experimental animals.
- Triggering organ dysfunction and tissue aging

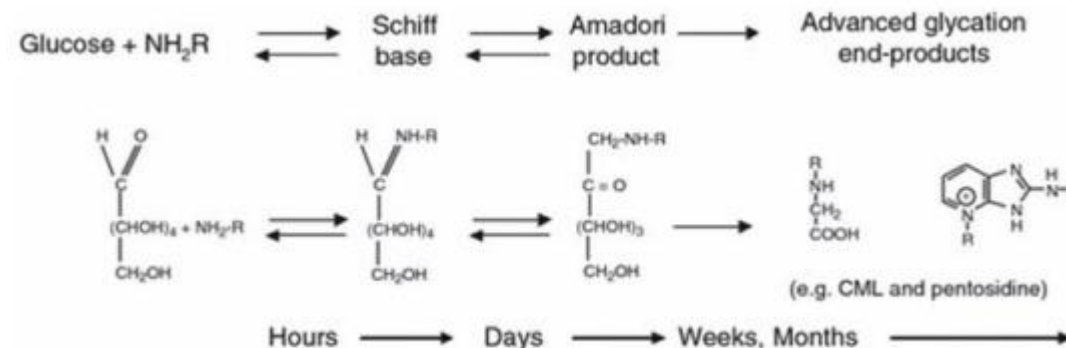


Illustration from
Bohlender et al., 2005

✿ Glycation process $\rightarrow$ the formation of advanced glycation end-products (AGEs).

Dietary Protein

- ✱ Recommended Dietary Allowance of protein for a healthy adult with minimal physical activity → **0.8 g protein/kg** body weight/day.
- ✱ To meet the functional needs such as promoting skeletal-muscle protein accretion and physical strength
 - 🌿 Dietary intake of **1.0, 1.3, and 1.6 g** protein per kg BW per day → minimal, moderate, and intense physical activity, respectively.
- ✱ Long-term consumption → **2 g protein/kg** body weight/day is safe for healthy adults (**1-2 g protein per kg BW per day**)
- ✱ The tolerable upper limit → **3.5 g protein/kg** body weight/day for well-adapted subjects.

Wu G. Dietary protein intake and human health. Food Funct. 2016 Mar;7(3):1251-65. doi: 10.1039/c5fo01530h. PMID: 26797090.

✱ Protein in food (g/100 g)

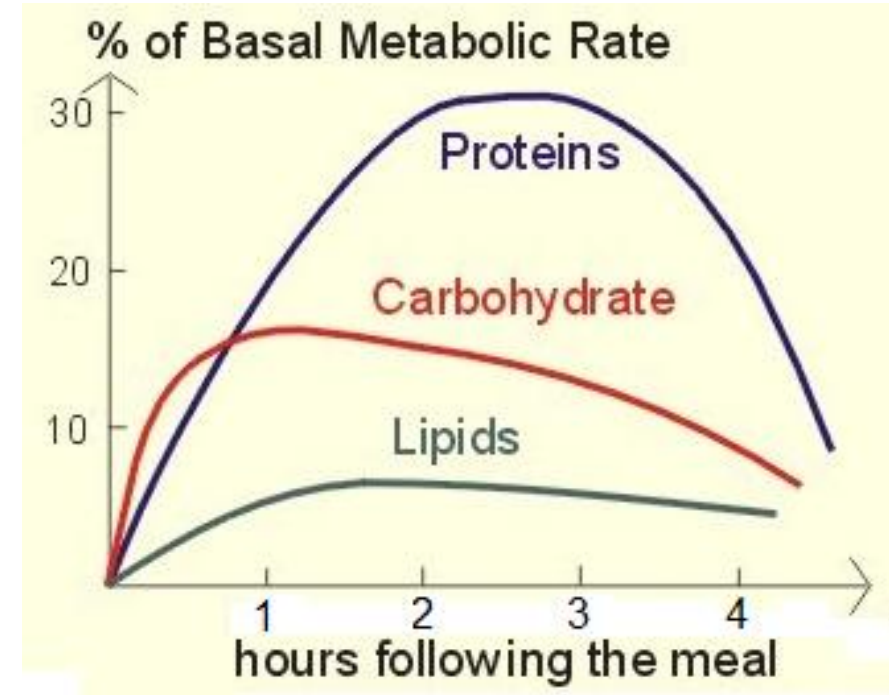
- | | |
|----------------------|--|
| 🌿 Chicken 32 g (1/3) | 🌿 Egg 12 g |
| 🌿 Beef 26 g (1/4) | 🌿 Soy bean 34 g |
| 🌿 Pork 24 g (1/4) | 🌿 Peanut 26 g (Protein 26.3%, Fat 49%) |
| 🌿 Fish 20 g (1/5) | 🌿 green beans 20 g |

Basal metabolic rate

Thermic effects of nutrient		Energy expenditure	
Protein	20-30%	Amino acids	20-30%
Carbohydrate	5-10%	Glucose	5-10%
Fat	0-3%	fat	0-3%

Tappy L. Thermic effect of food and sympathetic nervous system activity in humans. *Reproduction Nutrition Development*. 1996;36(4):391–397.

Jequier E. The influence of nutrient administration on energy expenditure in man. *Clinical nutrition* (Edinburgh, Scotland). 1986;5(4):181-6.



http://upload.wikimedia.org/wikipedia/commons/8/81/Postprandial_thermogenesis.png

Effects of macronutrient on appetite regulating hormones

Agatha A. et al. High protein intake stimulates postprandial GLP1 and PYY release, Obesity, 2013

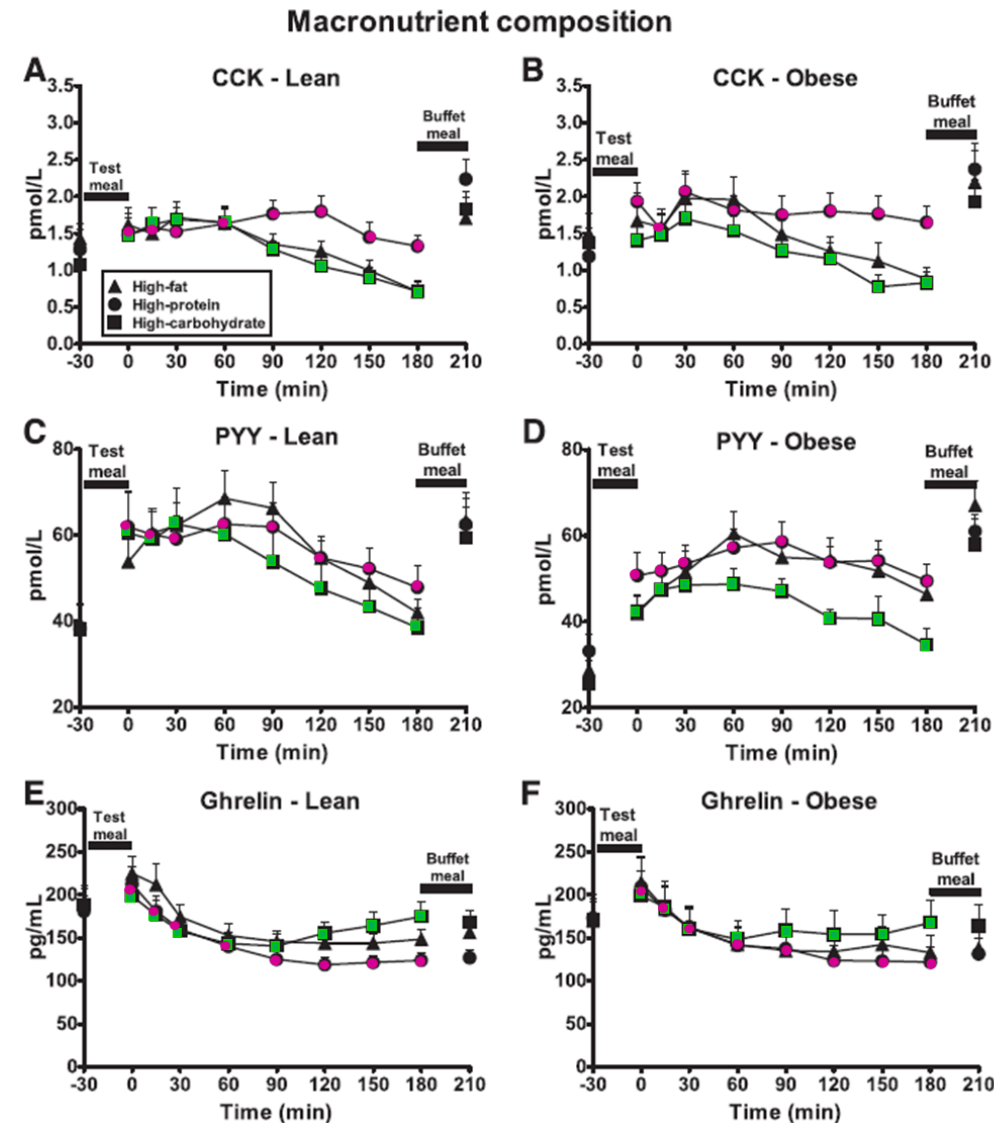


Fig. 2. Plasma concentrations (means $\pm$ SE) for cholecystikinin (CCK), peptide YY (PYY), and ghrelin in lean and obese subjects following ingestion of test meals varying in their macronutrient composition (i.e., high-fat, high-protein, high-carbohydrate). Repeated-measures ANOVAs, with treatment and time as factors, were used to determine statistical differences. Treatment-by-time interaction: $P < 0.05$ (A); treatment-by-time interaction: $P < 0.05$ (B); treatment-by-time interaction: $P < 0.01$ (C); treatment-by-time interaction: $P < 0.05$ (D); treatment-by-time interaction: $P < 0.01$ (E); treatment-by-time interaction: $P < 0.05$ (F). Data are absolute values, $n = 16$ lean and $n = 16$ obese subjects.

Effects of Low-CHO vs Low-Fat Diets on Weight Loss and Cardiovascular Risk Factors

- ✱ Systematic Reviews and Meta- and Pooled Analyses
- ✱ Randomized controlled trials for 6-24 months, mean energy intake ~ 2,000 Cal
- ✱ **Low-CHO diet** (4-45 %, mean 23% CHO) **Vs. Low-fat diet** (10-30 %, mean 26% fat)
 - 🍃 ~ **↓Weight** (−6.1 Vs. −5.0 kg)
 - 🍃 **↓Waist circumference** (−6.2 Vs. −6.0 cm)
 - 🍃 **Improved metabolic risk factors**
 - ✱ **>↓TG** (−30.4 Vs. −17.1 mg/dL)
 - 🍃 **↑HDL** (4.5 Vs. 1.6 mg/dL)
 - ✱ **<↓Total cholesterol** (−4.6 Vs. −10.1 mg/dL),
 - 🍃 **↓LDL** (−2.1 vs. −6.0 mg/dL)
 - ✱ ~ **SBP** (−3.5 Vs. −3.0 mmHg), **FBS** (−10.4 Vs. −10.1 mg/dL)

A High Protein, Low Carbohydrate Diet

✱ A high protein, low carbohydrate (20 g/day) or low fat (30%) diet for 13 weeks

🍃 >↓ BMI-Z-score than low fat group

🍃 No serious adverse effects related to metabolic profiles, cardiac function, or subjective complaints

J Pediatr. 2010 Aug; 157(2): 252–258.

✱ A high protein, low carbohydrate diet

🍃 Improve satiety through their actions on measures of adiposity and gut peptides that influence appetite and caloric intake

🍃 Specific macronutrients such as low glycemic index carbohydrates and dietary protein → appetite, calorie intake, and metabolic parameters independent of weight loss

🍃 The long-term safety of low-carbohydrate, high-protein diets on cardiovascular disease risk remains undetermined.

Increased vegetable/High Fiber

✱ ↑ Gastric volume → gastric distension → satiety

✱ Vitamin and minerals

High-fiber vegetable diet compared with the **starch-based** and **low-fat diets** for 2 weeks

✱ ↓ LDL (33%)

✱ ↑ Fecal bile acid (1.13 ± 0.30 g/d)

✱ ↑ Fecal bulk (906 ± 130 g/d)

✱ ↑ Fecal short-chain fatty acid outputs (78 ± 13 mmol/d)

✱ ↑ Urinary mevalonic acid excretion **reflecting large fecal steroid losses**

Drinking water

✱ Drinking 1.5 L of water, over and above the usual intake for 8 weeks

✱ ↓ Body weight (-1.44 kg)

✱ ↓ BMI (-0.5778 kg/m²)

✱ ↓ Sum of skinfold thickness (-3.048 mm)

✱ ↓ The appetite score (- 2.207)

J Nat Sci Biol Med. 2014 Jul-Dec; 5(2): 340–344.

✱ Appetite suppressant

✱ ↑ Gastric volume → Gastric distension → ↑ Satiety signal

✱ ↓ Core body temperature

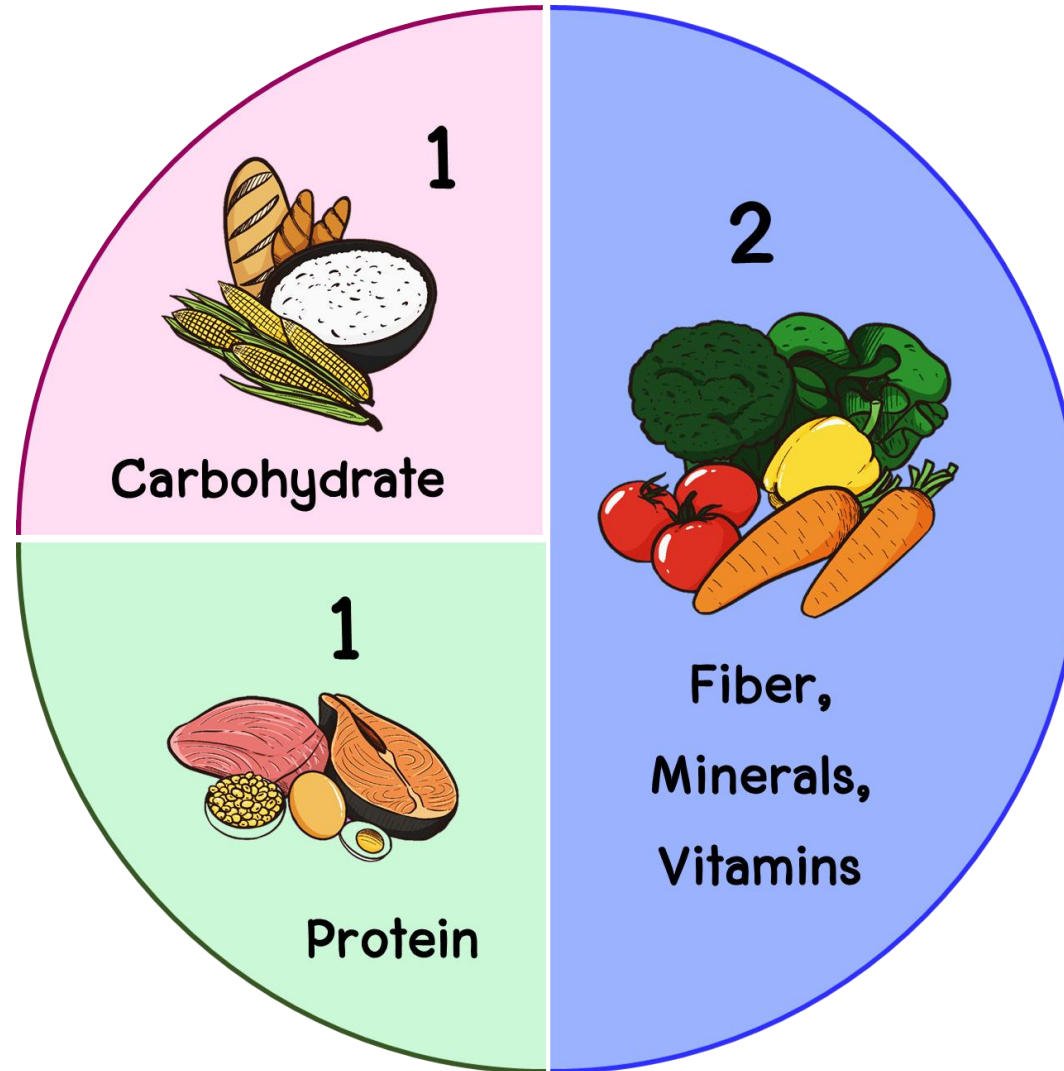
✱ ↑ Activity of the SNS (↑ NE levels and ↑ Muscle SNS activity)

✱ ↑ Thermogenesis

✱ ↑ Resting energy expenditure by 30% within 10 min of drinking (peaked at 30-40 min) and sustained for over an hour

✱ Proper hydration (remove waste, metabolizing fat or CHO)

Plate method



Reduce sweet, oily, and salty with the formula 6: 6: 1

Sugar



≤

6

Teaspoon/day

Oil



≤

6

Teaspoon/day

Salt



≤

1

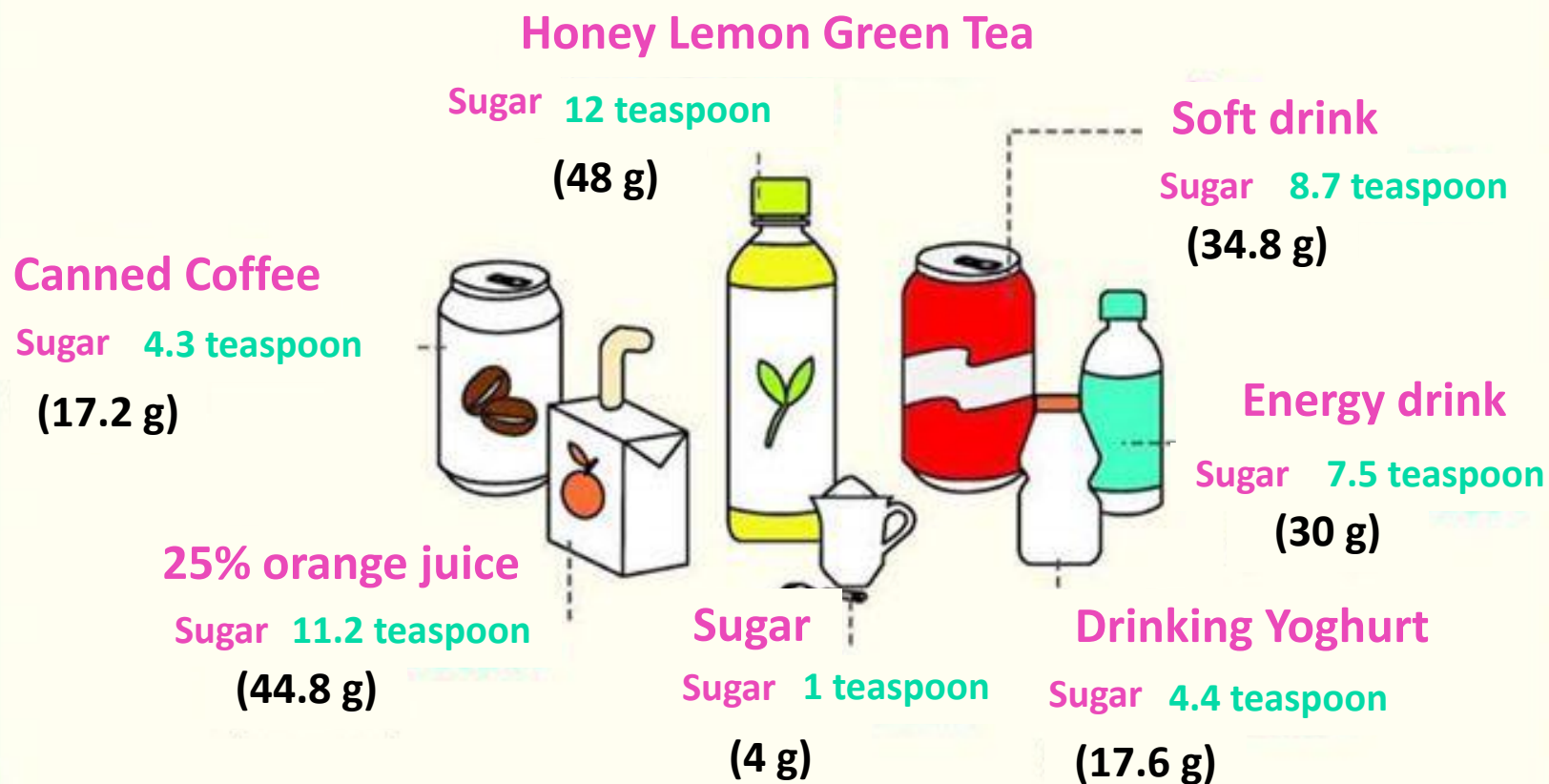
Teaspoon/day

1 Teaspoon = 5 g 1 Tablespoon = 15 g



Sugar

Be aware of the hidden sugar content





Fat

Be aware of the hidden fat content



**Thai stir-fried
noodles 1 dish**
Oil 6 teaspoon



**Fried mussel
pancakes 1 dish**
Oil 6 teaspoon



**Chicken rice
1 dish**
Oil 5 teaspoon



**Fried chicken
1 piece**
Oil 2.6 teaspoon



**Fried egg
1 egg**
Oil 4.2 teaspoon



**Stewed pork leg
with rice 1 dish**
Oil 6 teaspoon



**Barbecued red
pork in sauce
with rice 1 dish**
Oil 5 teaspoon



**Shrimp-paste
fried rice 1 dish**
Oil 5 teaspoon

Metabolism boosting meals

- ✱ No CHO, No sugar
- ✱ Low fat
- ✱ High protein - metabolism boosting
- ✱ 1 day cheating in a week - metabolism boosting
- ✱ Limitation
 - 🌿 Susceptible to hypoglycemia

2. Calories reduction

$$E \text{ intake} < E \text{ expenditure}$$

Energy Expenditure

= BMR + physical activity

= BMR x activity factor (1.25)

BMR Estimation by Harris-Benedict Equation

M: $66.5 + (13.75 \times \text{kg}) + (5.003 \times \text{cm}) - (6.775 \times \text{age})$

F: $655.1 + (9.563 \times \text{kg}) + (1.850 \times \text{cm}) - (4.676 \times \text{age})$

BMR calculator

<https://www.calculator.net/bmr-calculator.html>

The basal metabolic rate (BMR) is the amount of energy needed while resting in a temperate environment when the digestive system is inactive. It is the equivalent of figuring out how much gas an idle car consumes while parked. In such a state, energy will be used only to maintain vital organs, which include the heart, lungs, kidneys, nervous system, intestines, liver, lungs, sex organs, muscles, and skin. For most people, upwards of ~70% of total energy (calories) burned each day is due to upkeep. Physical activity makes up ~20% of expenditure and ~10% is used for the digestion of food, also known as thermogenesis.

The BMR is measured under very restrictive circumstances while awake. An accurate BMR measurement requires that a person's sympathetic nervous system is inactive, which means the person must be completely rested. Basal metabolism is usually the largest component of a person's total caloric needs. The daily caloric need is the BMR value multiplied by a factor with a value between

Calories reduction

“3,500 kcal per pound rule”

1 pound
of fat



= 3,500 kcal

Negative

✱ 3,500 kcal/wk

✱ 500 kcal/day

✱ Weight loss 1 pound/wk

✱ ~(0.5 kg/wk)

Minimum weight loss to achieve health benefits

✱ 5 - 10% of initial body weight

Calorie counter Application



The screenshot shows the 'อาหารเข้า' (Food Intake) screen. It has a search bar at the top with the text 'ค้นหาจากชื่อ..'. Below the search bar are four tabs: 'ค้นหา' (Search), 'ล่าสุด' (Latest), 'รายการโปรด' (Favorites), and 'อาหารของฉัน' (My Food). There are four icons representing different food categories: 'ค้นหาจากหมวด' (Search by category), 'ดูไดอารี' (View diary), 'สแกนบาร์โค้ด' (Scan barcode), and 'เปลี่ยนเนื้อ' (Change meat). Below these icons is a section titled 'เมนูที่ค้นหาบ่อย' (Frequently searched menu). It lists several food items with their calorie counts and a percentage of daily intake.

Food Item	Calories (kcal)	Percentage of Daily Intake
ข้าวสวย 100 กรัม	130	15 % ของแคลอรี่ที่ควรบริโภคต่อวัน
ข้าวกล้อง	111	13 % ของแคลอรี่ที่ควรบริโภคต่อวัน
ข้าวเหนียว	97	12 % ของแคลอรี่ที่ควรบริโภคต่อวัน
ไข่ต้ม	81	10 % ของแคลอรี่ที่ควรบริโภคต่อวัน
หมูบึ่ง	94	11 % ของแคลอรี่ที่ควรบริโภคต่อวัน
โยเกิร์ต	90	11 % ของแคลอรี่ที่ควรบริโภคต่อวัน

The screenshot shows the 'อาหารเข้า' (Food Intake) screen. It has a search bar at the top with the text 'ค้นหาจากชื่อ..'. Below the search bar are four tabs: 'ค้นหา' (Search), 'ล่าสุด' (Latest), 'รายการโปรด' (Favorites), and 'อาหารของฉัน' (My Food). There are four icons representing different food categories: 'ค้นหาจากหมวด' (Search by category), 'ดูไดอารี' (View diary), 'สแกนบาร์โค้ด' (Scan barcode), and 'เปลี่ยนเนื้อ' (Change meat). Below these icons is a list of food items with their calorie counts and a percentage of daily intake.

Food Item	Calories (kcal)	Percentage of Daily Intake
เวย์โปรตีน, Whey Protein	120	14 % ของแคลอรี่ที่ควรบริโภคต่อวัน
สลัดผัก	88	10 % ของแคลอรี่ที่ควรบริโภคต่อวัน
แอปเปิ้ล	52	6 % ของแคลอรี่ที่ควรบริโภคต่อวัน
กาแฟดำ	1	0 % ของแคลอรี่ที่ควรบริโภคต่อวัน
อกไก่	98	12 % ของแคลอรี่ที่ควรบริโภคต่อวัน
กล้วย	72	9 % ของแคลอรี่ที่ควรบริโภคต่อวัน

Caloric restriction

✱ ↓ Energy intake 20-40 %

Longo VD, et. al. Nature Aging. 2021;1(1):47-59.

✱ ↓ Body weight, BMI, body fat, fat mass, waist circumference

✱ ↓ Blood sugar and lipid levels

✱ ↓ Blood pressure

✱ ↓ Fat-free mass

✱ ↓ 5-7 % resting energy expenditure

✱ ↓ Total daily energy expenditure

✱ ↓ T3

✱ ↓ Fat mass 75-80% and fat-free mass 20-25 %

3. Paleolithic diet

- ✱ Hunter-gatherer diet or stone-age diet
- ✱ The paleolithic era, ~2.5 million to 10,000 years ago
- ✱ Consumption of meat, fish, eggs, vegetables, fruits, roots, and nuts,
- ✱ No consumption of many cultivated products, such as dairy products, oils, cereals, and legumes (as well as salt and refined sugars)
- ✱ A traditional paleolithic diet ~35% fat, 35% CHO, and 30% proteins
- ✱ A low-carbohydrate diet, high fiber
- ✱ Weight loss
- ✱ Improvement of lipid profile, carbohydrate metabolism, and insulin sensitivity
- ✱ ↓ Blood pressure
- ✱ ↓ Oxidative stress
- ✱ Anti-inflammatory benefits

3. Paleolithic diet

- ✱ A systematic review and meta-analysis
- ✱ In overweight and obese individuals with or without calorie restriction
- ✱ ↓Weight (-3.52 kg)
- ✱ ↓BMI
- ✱ ↓Blood glucose HbA1c and insulin levels
- ✱ ↓HOMA-IR
- ✱ No different from other diets, including the Mediterranean diet, the diabetes diet, and the diet recommended by the Dutch health council

4. Mediterranean diet

- ✱ Food traditionally eaten by countries bordering the Mediterranean Sea (Greece, Italy, France, Spain, etc.)



<https://images.everydayhealth.com/images/diet-nutrition/mediterranean-diet/mediterranean-diet-recipes-01-722x406.jpg?w=768>



<https://images.everydayhealth.com/images/diet-nutrition/mediterranean-diet/mediterranean-diet-recipes-mediterranean-sheet-pan-baked-shrimp-and-vegetables-406x406.jpg?w=768>

✱ High consumption

- 🍃 Fruits and vegetables
- 🍃 Monounsaturated fats (primarily from olive oil)
- 🍃 Legumes and grains

✱ Moderate consumption

- 🍃 Poultry
- 🍃 Fish
- 🍃 Dairy products

- ✱ Little to no consumption of red meat

Am J Med. 2016 Apr;129(4):407-415.e4.

4. Mediterranean diet

✱ Grains, Vegetables, Fruits should be eaten at most meals.

🍃 Important sources of vitamins, minerals, energy, antioxidants, and fiber

✱ Grains

🍃 The majority → whole grains (wheat, oats, rice, rye, barley, and corn)

🍃 Best consumed in whole, minimally-processed forms (refining and processing can remove many valuable nutrients, including vitamins, minerals, and fiber)

🍃 Common → barley, buckwheat, bulgur, farro, millet, oats, polenta, rice, wheatberries, breads, couscous, and pastas

✱ Vegetables

🍃 Important (valuable nutrients and satiety)

🍃 Common → artichokes, arugula, beets, broccoli, brussels sprouts, cabbage, carrots, celery, celeriac, chicory, collard greens, cucumbers, dandelion greens, eggplant, fennel, kale, leeks, lemons, lettuce, mache, mushrooms, mustard greens, nettles, okra, onions (red, sweet, white), peas, peppers, potatoes, pumpkin, purslane, radishes, rutabaga, scallions, shallots, spinach, sweet potatoes, turnips, zucchini

✱ Fruits

🍃 Whole fresh or No-sugar-added fruit juices (portion and total calories control)

🍃 Common → apples, apricots, avocados, cherries, clementines, dates, figs, grapefruits, grapes, melons, nectarines, olives, oranges, peaches, pears, pomegranates, strawberries, tangerines, tomatoes



4. Mediterranean diet

✿ Olives & Olive Oil

- ✿ Olives → eaten whole and widely used for cooking and flavoring
- ✿ Olive oil → principal source of dietary fat used for cooking, baking, and for dressing salads and vegetables (extra virgin olive oil → highest in health-promoting fats, phytonutrients and other important micronutrients)



✿ Nuts, Beans, Legumes & Seeds

- ✿ Good sources of healthy fats, protein, and fiber (add flavor and texture)
- ✿ Common → almonds, cannellini beans, chickpeas, cashews, fava beans, green beans, hazelnuts, kidney beans, lentils, pine nuts, pistachios, sesame seeds, split peas, tahini sauce, walnuts



✿ Herbs & Spices

- ✿ adding flavors and aromas to foods, ↓ need to add salt or fat when cooking
- ✿ rich in a broad range of health-promoting antioxidants
- ✿ Common → anise, basil, bay leaf, chiles, cloves, cumin, fennel, garlic, lavender, marjoram, mint, oregano, parsley, pepper, pulbiber, rosemary, sage, savory, sumac, tarragon, thyme, za'atar



✿ Cheese & Yogurt

- ✿ Eaten regularly, but low to moderate amounts
- ✿ The calcium in cheese and yogurt → important for bone and heart health
- ✿ Common → brie, chevre, corvo, feta, haloumi, manchego, Parmigiano-Reggiano, pecorino, ricotta, yogurt (including Greek yogurt)



4. Mediterranean diet

* Fish and shellfish



- Important sources of healthy protein
- Tuna, herring, sardines, salmon and bream → rich in essential heart-healthy omega-3 fatty acids (also shellfish and crustaceans including mussels, clams and shrimp)
- Common seafood → abalone, clams, cockles, crab, eel, flounder, lobster mackerel, mussels, octopus, oysters, salmon, sardines, sea bass, shrimp, squid, tilapia, tuna, whelk, yellowtail

* Eggs

- Good source of high-quality protein
- Common → chicken, duck, and quail eggs



* Meats

- Eaten in small portions
- Poultry → good source of lean protein without the high levels of saturated fat
- With ground meats (90% lean/10% fat)
- Common poultry and red meat → beef, chicken, duck, goat, guinea fowl, lamb, mutton, pork



* Wine

- Consumed regularly but moderately
(Women, up to 1/5, Men, up to 2/5-ounce glass of wine/day)



4. Mediterranean diet

- ✱ A systematic review of randomized controlled trials (RCTs)
- ✱ Long-term effects (at ≥ 12 months)
- ✱ In overweight and obese individuals with or without calorie restriction

- ✱ $\downarrow$ **Weight** (-4.1 to -10.1 kg)
 - 🌿 **>Low-fat diet** (-2.9 to -5.0 kg)
 - 🌿 **~Low-CHO diet** (-4.7 to -7.7 kg)

- ✱ $\downarrow$ **BMI** (-1.0 to -3.3 kg/m²)
 - 🌿 **>Low-fat diet** (1.4 to -1.8 kg/m²)
 - 🌿 **~Low-CHO diet** (-1.5 to -2.8 kg/m²)
 - 🌿 Similar trend with **waist circumference**

4. Mediterranean diet

✱ Compared to **low-fat diet**, **low-CHO** diets

🍃 ~ **↓ Glycemic control**

🍃 > Significant improvement in DM type 2 patients

⬆ **↓ Fasting glucose, HbA1c, serum insulin, and the homeostatic model assessment of insulin resistance**

⬆ **↓ Fasting glucose levels** (-0.89 to -4.30 mmol/L vs 0.67 to -3.10 mmol/L)

🍃 ~ **↓ LDL, ↑ HDL**

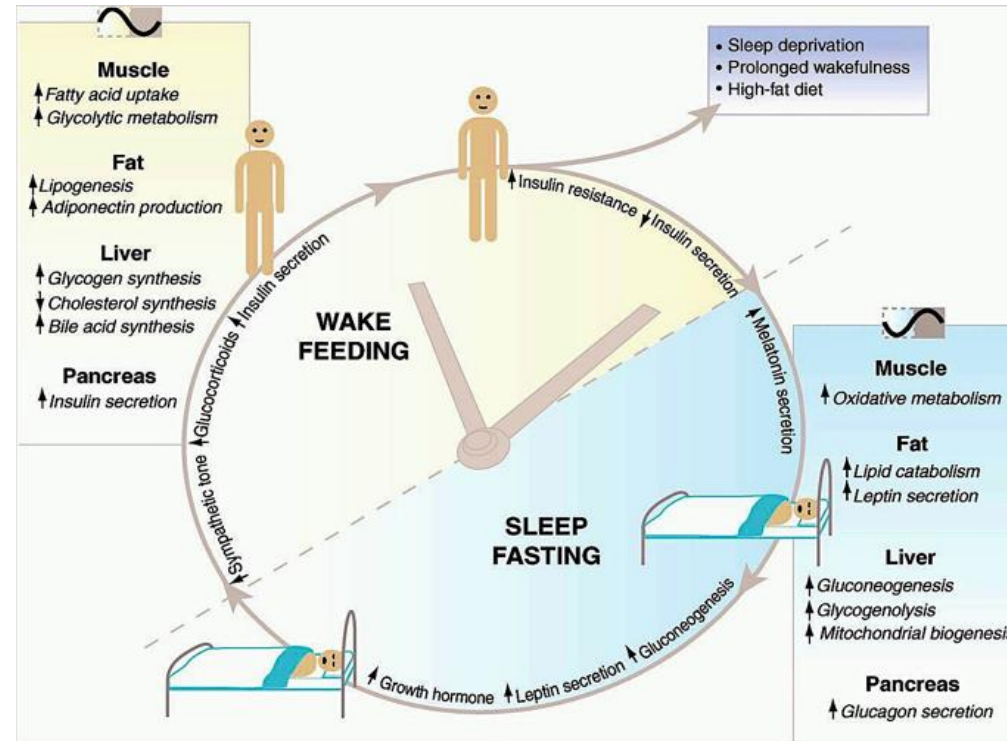
🍃 > **↓ TG** (-0.25 to -1.50 vs -0.03 to -0.70 mmol/L)

🍃 ~ **↓ Blood pressure (some)**

5. “Eating breakfast like a king, lunch like a prince, and dinner like a pauper”

- ✱ A seminal randomized controlled trial (Silver Spring) 2013;21: 2504–2512
- ✱ Overweight and obese women randomized to eat isocaloric diet ~1400 kcal for 12 weeks
 - 🍃 A large breakfast compared to A large dinner
 - 🍃 700/200 kcal breakfast vs. dinner, 500 kcal lunch
 - 🍃 > ↓ Weight 5.1 kg (8.7 ± 1.4 kg vs. 3.6 ± 1.5 kg)
 - 🍃 > ↓ Waist circumference
 - 🍃 > Fasting glucose, insulin, and HOMA-IR
 - 🍃 ↓ TG 33.6% vs. ↑ 14.6%
 - 🍃 ↓ Ghrelin and Hunger scores
 - 🍃 ↑ Satiety scores
- ✱ Several other interventional and cohort studies
 - 🍃 Shifting food intake to earlier during the daytime increases weight loss.

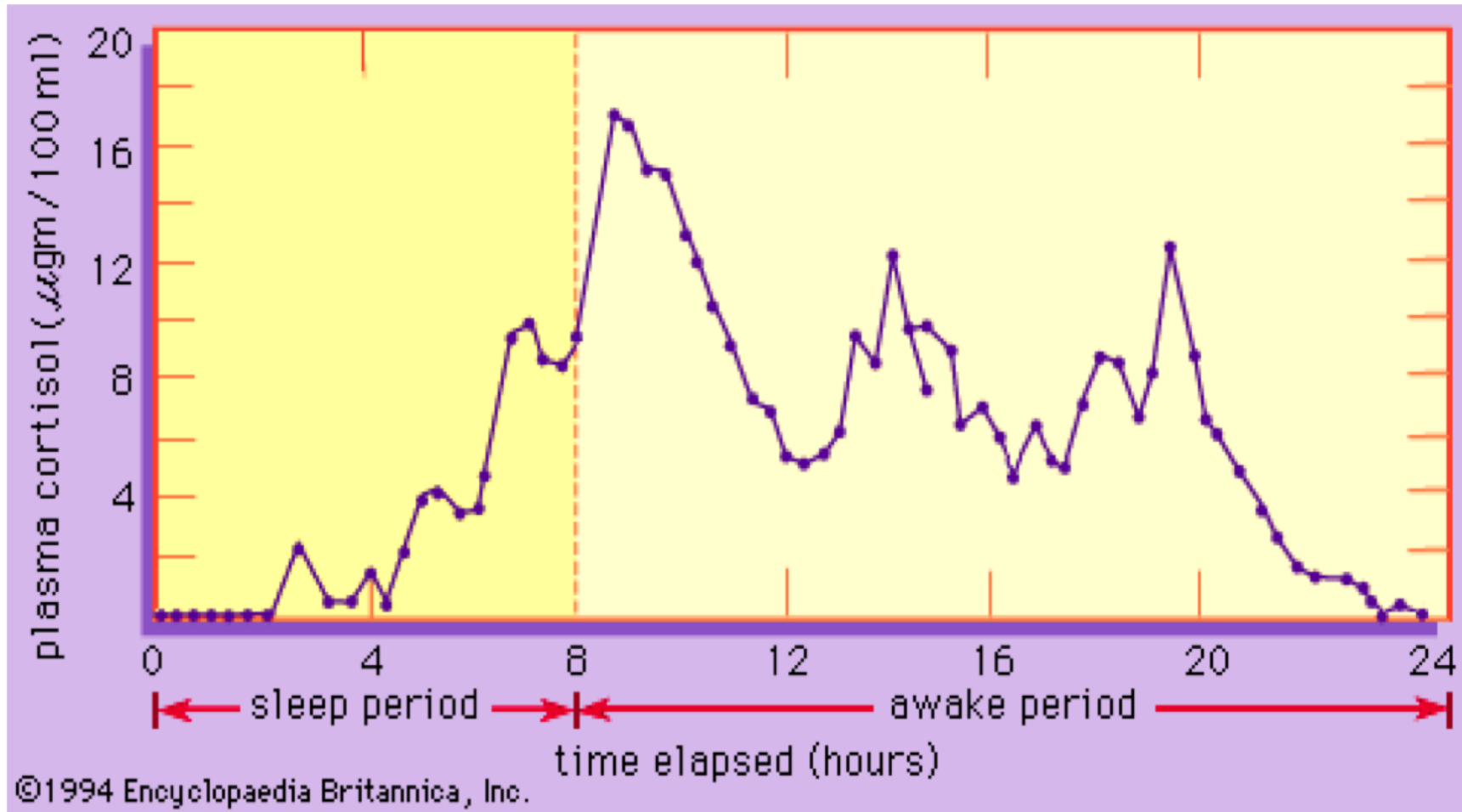
The circadian system



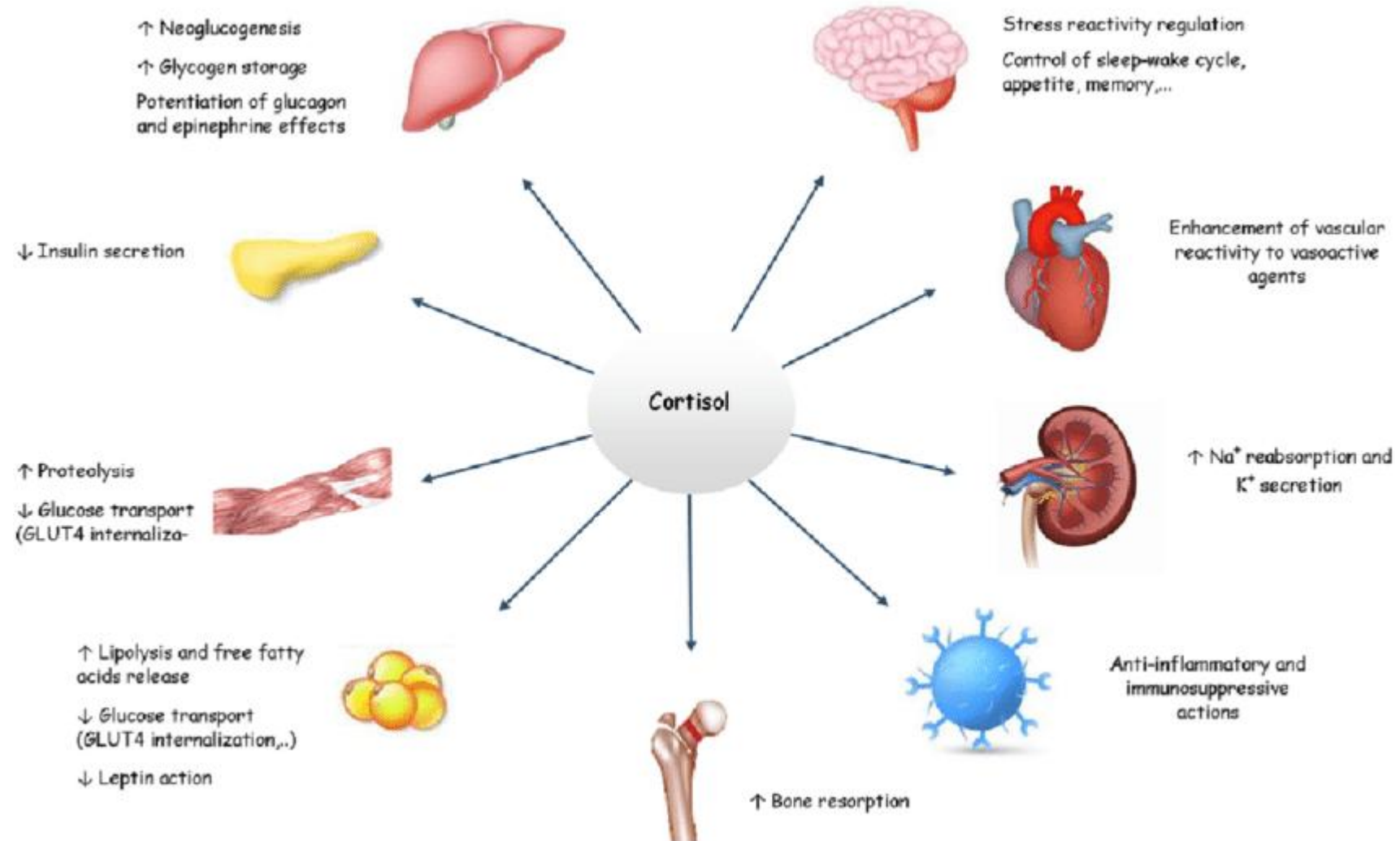
Joseph Bass, 2010

- ✿ In humans, ↑insulin sensitivity, beta cell responsiveness, and the thermic effect in the morning than in the afternoon or evening
- ✿ Human metabolism is optimized for food intake in the morning.

Plasma Cortisol Levels

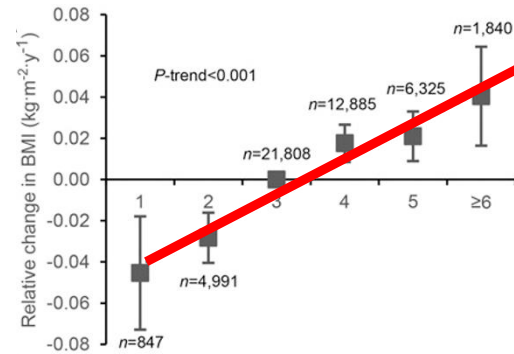


Cortisol

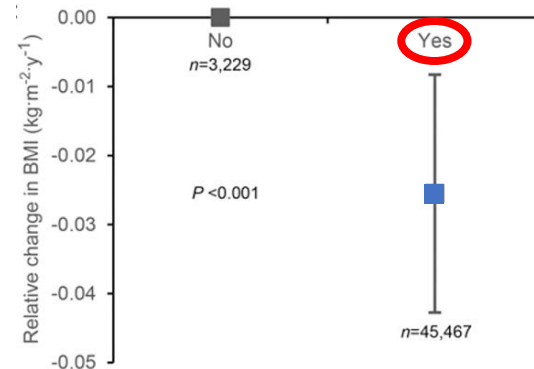


A Longitudinal Study Over 7 Years

Number of meals



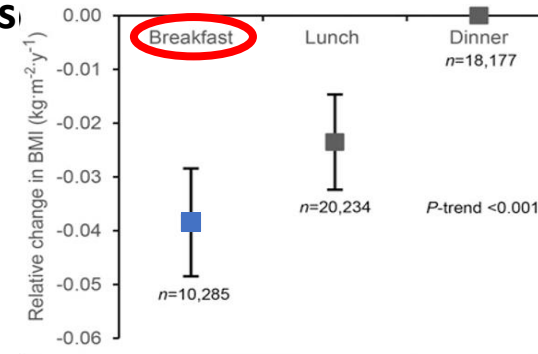
Meals and snacks (n/d)	1	2	3	4	5	≥6
Cohort %	1.74	10.3	44.8	26.5	13.0	3.78



Breakfast Consumption

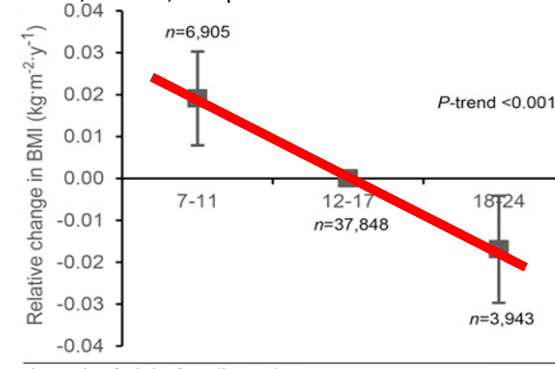
48,696
subjects

Largest meal



Time of largest meal	0500 – 1100 h	1200 – 1600	1700 – 2300 h
Cohort %	21.1	41.6	37.3

The Journal of Nutrition, Volume 147, Issue 9, 1 September 2017



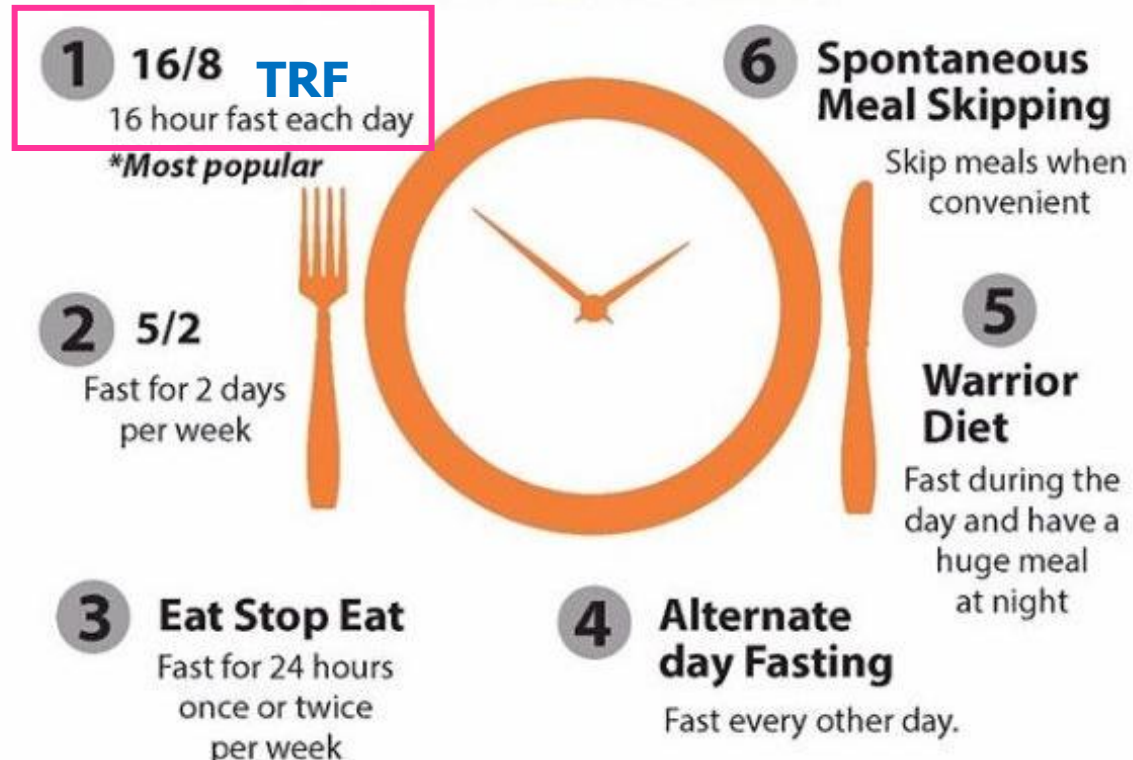
Length of night fast (hours)	7-11	12-17	18-24
Cohort %	14.2	77.7	8.10

Overnight Fast

6. Intermittent fasting (IF)

Any diet that alternates between periods of restricting calories and eating normally

Intermittent fasting (IF)



- * Complete alternate day fasting
- * Modified alternate day fasting
- * 5:2 intermittent fasting
- * TRF

TRF = Time-restricted feeding

Intermittent fasting (IF)

Eating patterns that alternate between periods of restricting calories and eating normally

“**Fasting**” no consumption of energy-containing foods or beverages

“**Feeding**” consumption of foods and beverages ad libitum

Protocols of IF

- ↑ **Complete alternate-day fasting (ADF)**: eating ad libitum days alternating with no-energy food days
- ↑ **Modified alternate-day fasting (MADF)**: eating ad libitum days alternating with <25% of baseline energy need days
- ↑ **5:2 IF**: 5 days/week of ad libitum feeding alternating with 2 days/week of absolute fasting which can be consecutive or not consecutive
- ↑ **Time-restricted feeding (TRF)**: ad libitum intake during specific times (few hours) followed by fasting for a prolonged time during each day

6. Intermittent fasting (IF)

Benefits of IF (Data from rodents and humans trials)

- * ↓ Body weight/BMI/body fat
- * ↑ Oxygen consumption/energy expenditure
- * ↓ Blood Glucose/insulin levels
- * Improved insulin sensitivity
- * Improved lipid profiles
- * ↓ Blood pressure
- * ↓ Markers of inflammation and oxidative stress
- * Reverse type 2 Diabetes
- * Slows and reverses aging and disease processes
- * Increases longevity and survival in many species (animal models)

The fasting state

↑ ↓ Blood glucose → ↓ Insulin

↑ ↑ Counter regulatory hormones (oppose the action of insulin) → ↑ Blood sugar

- ✱ Glucagon
- ✱ Epinephrine
- ✱ Norepinephrine
- ✱ Cortisol
- ✱ GH

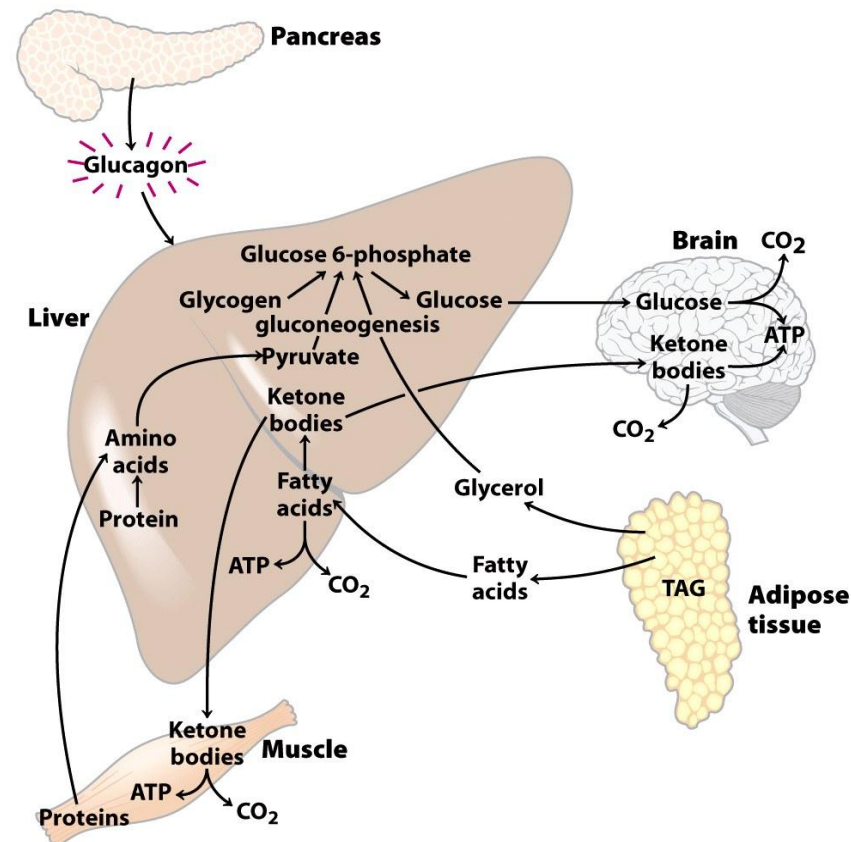
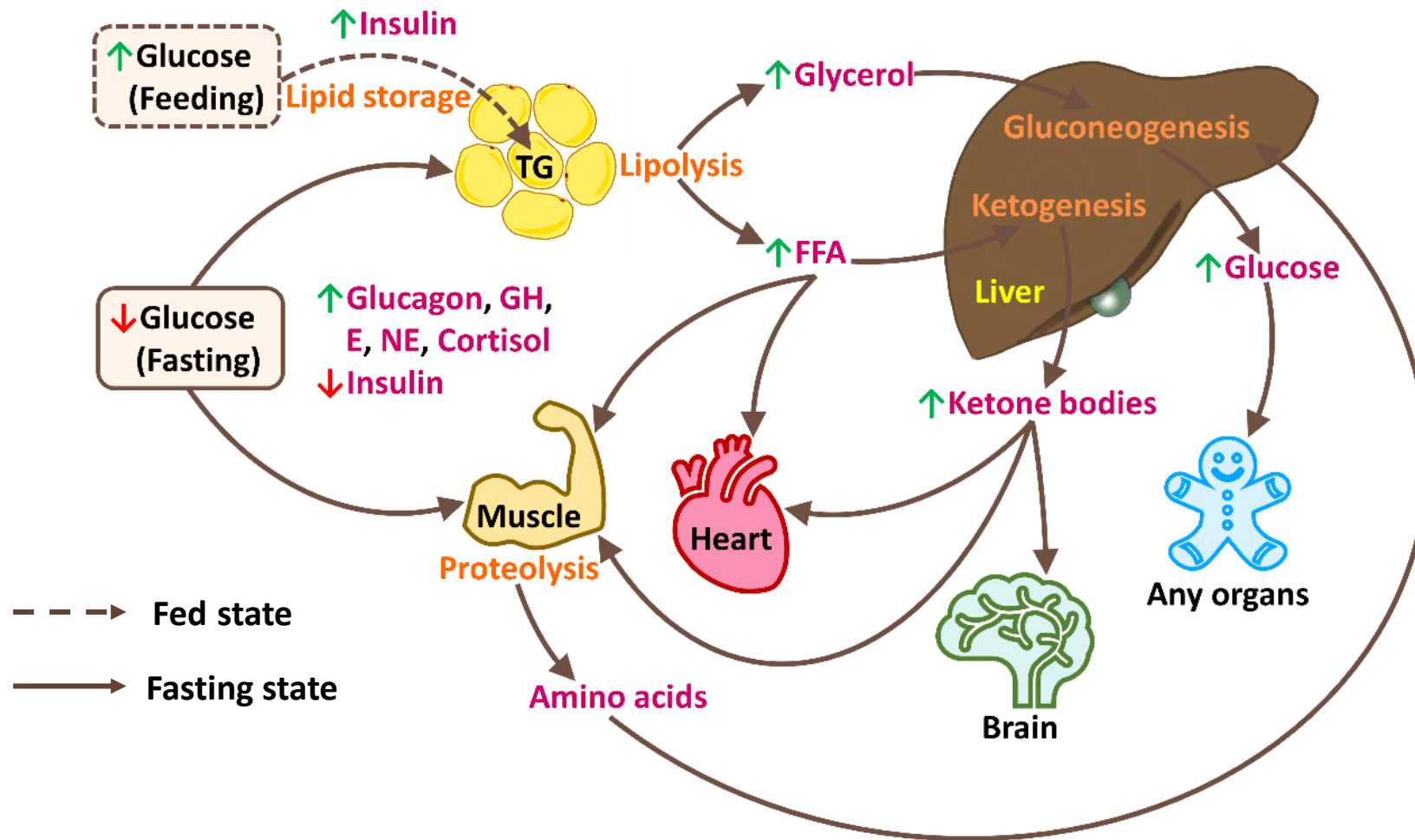


Figure 23-30
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

The fasting state



Copyright: ฉันทชา สิทธิจรรยา ภาวะอ้วนและการลดน้ำหนัก 2565

TG: triglyceride; FA: free fatty acid; GH: growth hormone; E: epinephrine; NE: norepinephrine

Fasting in humans

↑ The first 36-60 hours

✱ ↑ BMR

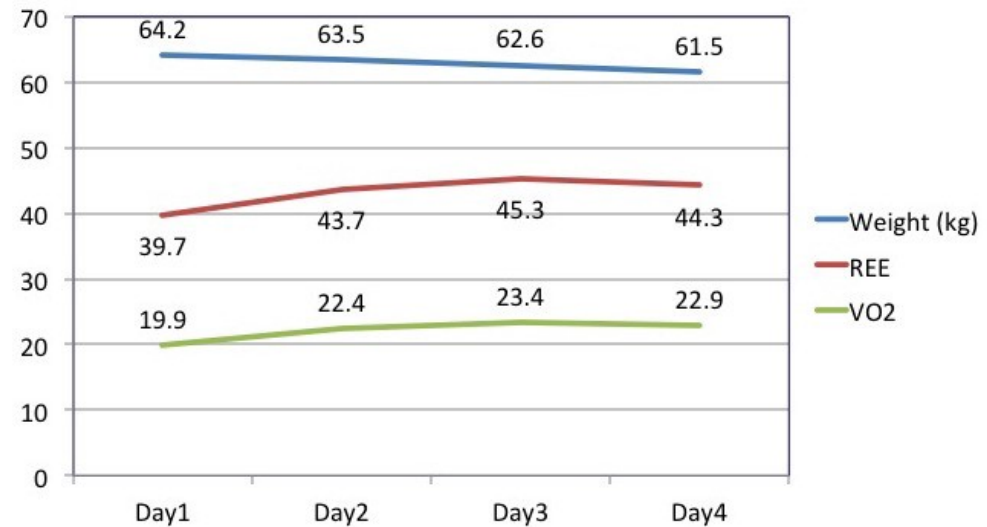
✱ ↑ NE and GH production

↑ Afterwards (72 or more)

✱ ↓ BMR

✱ ↓ NE and GH production

Metabolic Changes over 4 days of fasting



Zaunders C Am J Clin Nutr 2000;71:1511-5.

BMR = basal metabolic rate

NE = noradrenaline

GH = growth hormone

Plasma concentrations of fatty acids, glucose, and ketone bodies during the first week of starvation

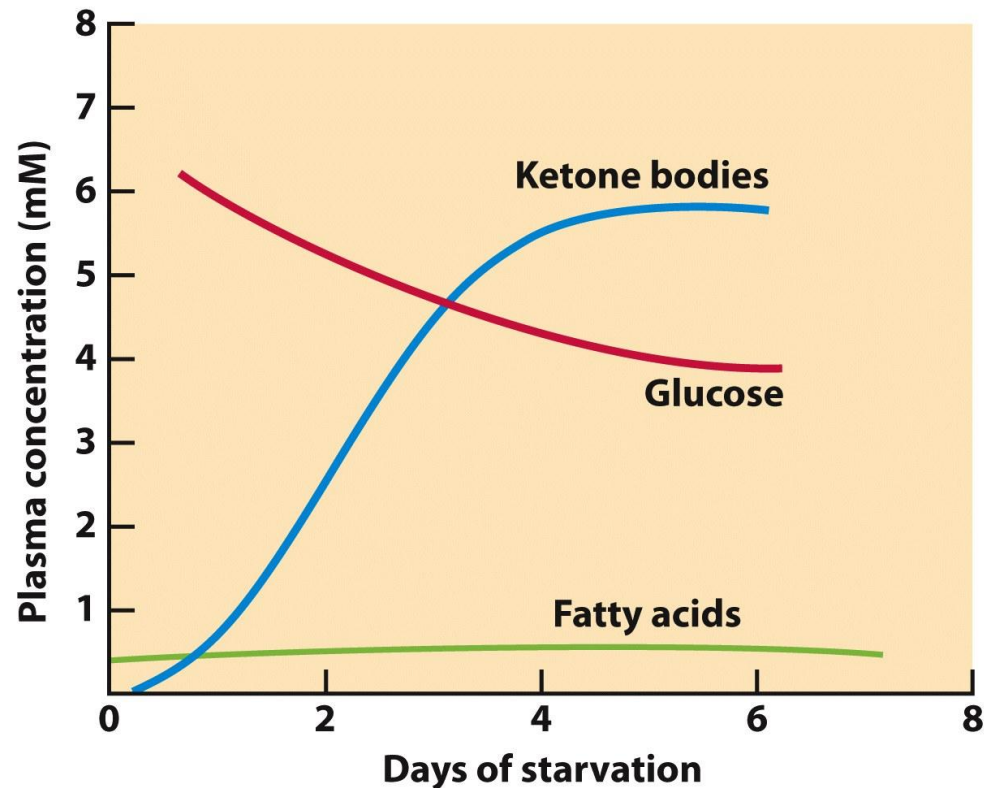


Figure 23-32
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

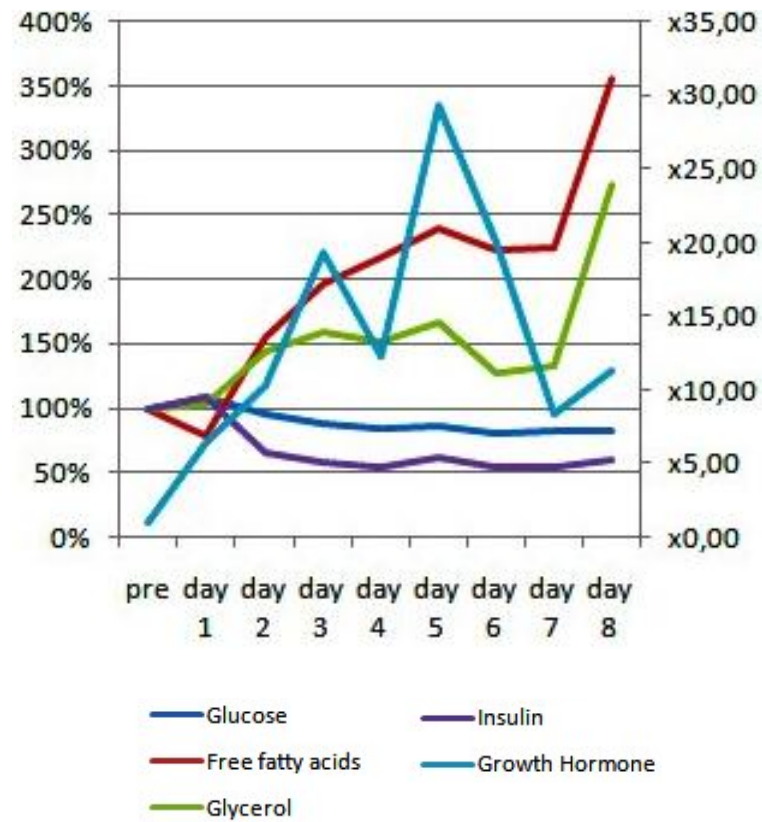
↓ **Glucose** after 2 days of fasting

Fatty acids cannot serve as a fuel for the brain; they do not cross the blood-brain barrier.

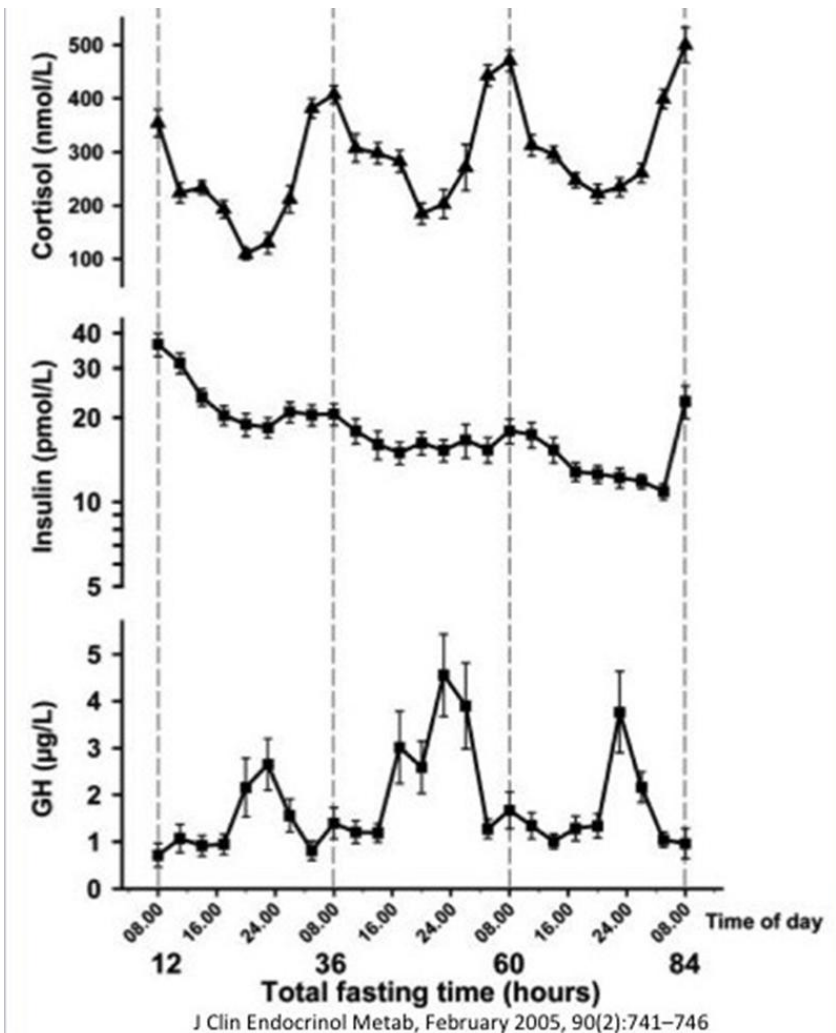
Ketone bodies, almost unmeasurable before the fast, rises dramatically after 2 to 4 days of fasting. These water-soluble **ketones**, **acetoacetate** and **β -hydroxybutyrate**, supplement glucose as an energy source during a long fast.

Fasting in humans

Effects of 8 days of fasting in 6 perfectly healthy subjects

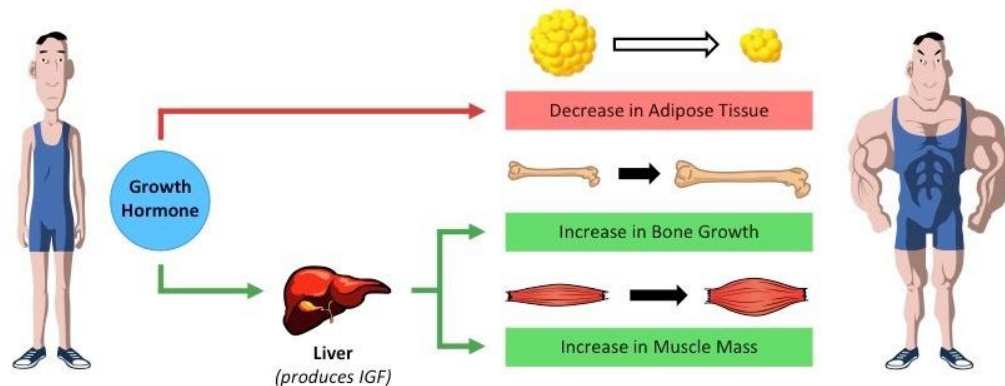
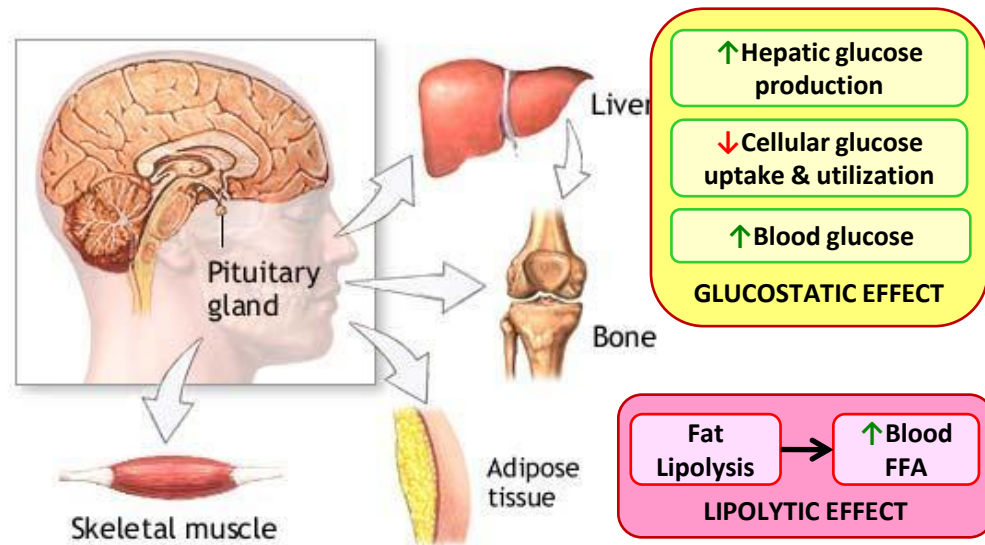


K Y Ho, et al. 1988., Wook-chul Choi et al. 2016



J Clin Endocrinol Metab, February 2005, 90(2):741-746

Growth Hormone (GH)



https://ib.bioninja.com.au/_Media/growth-hormone_med.jpeg

↑ GH

Plasma amino acids (Arginine)

↓ Blood sugar/Hypoglycemia/Fasting

↓ Blood FFA

Exercise/Excitement

Acute stress/Trauma

Deep sleep

GHRH

Sex hormones, Thyroid hormone

Ghrelin

↓ GH

↑ Blood sugar/Hyperglycemia/↑ FFA

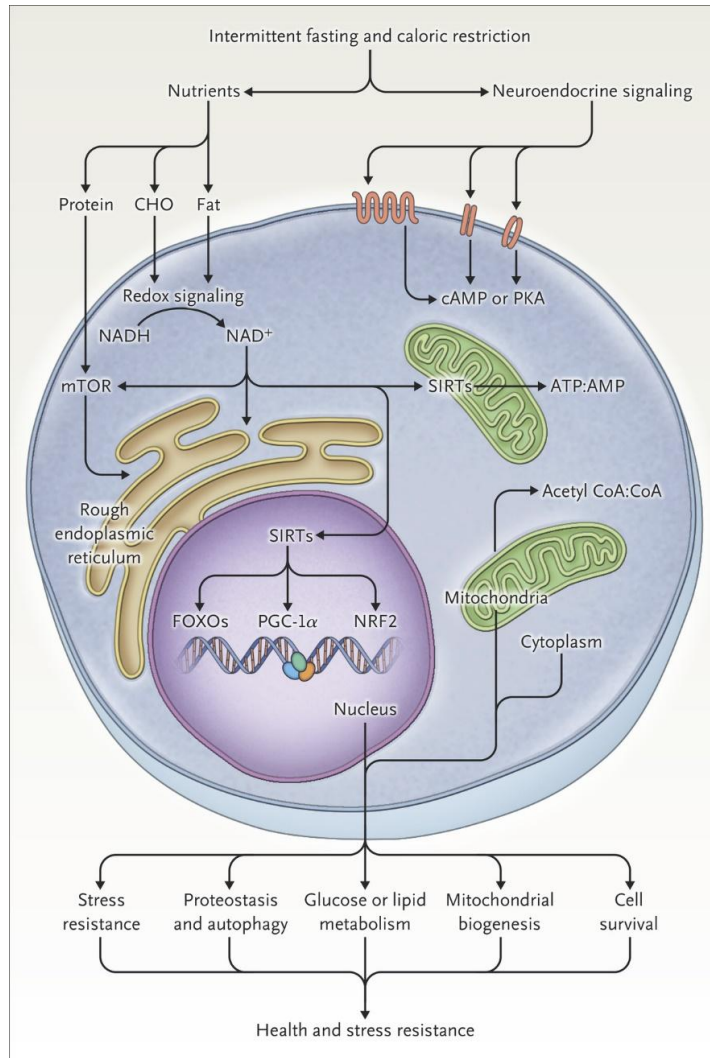
Aging/Obesity/Chronic stress

GHIH (somatostatin)/IGFs

The fasting state

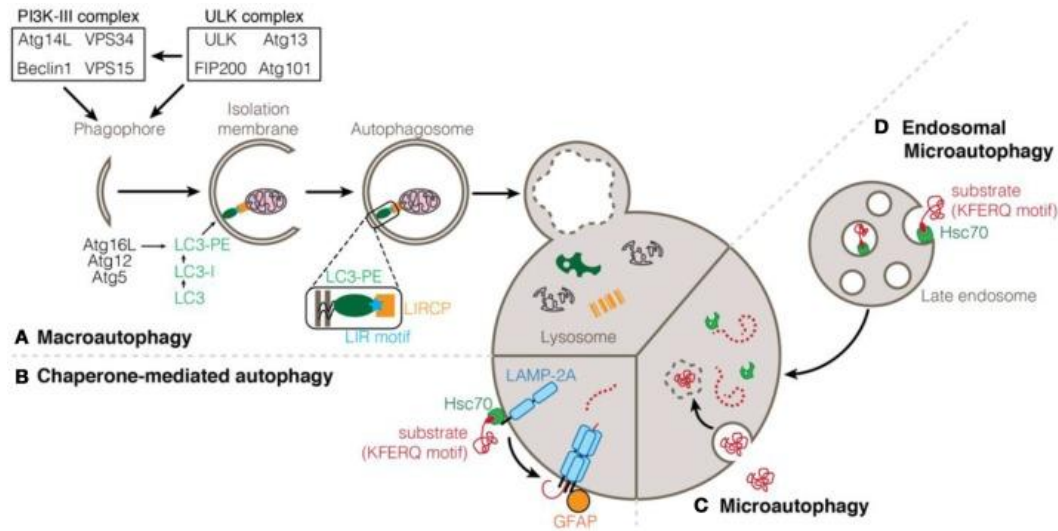
- ✱ Energy restriction for 10-14 hours or more
 - 🍃 Depletion of liver glycogen
 - 🍃 ↑ Lipolysis
 - 🍃 ↑ Production of ketone bodies
- ✱ β -hydroxybutyrate (β -HB) has signaling functions
 - 🍃 ↑ Transcription factors such as cyclic adenosine monophosphate (cAMP) response element-binding protein (CREB) and nuclear factor κ B (NF- κ B)
 - 🍃 ↑ Expression of brain-derived neurotrophic factor (BDNF) in neurons
- ✱ ↓ Glucose and amino acids during fasting
 - 🍃 ↓ Activity of the mammalian target of rapamycin (mTOR) pathway
 - 🍃 Up-regulation of autophagy
- ✱ Energy restriction stimulates
 - 🍃 Mitochondrial biogenesis
 - 🍃 Mitochondrial uncoupling

Cellular Responses to Fasting



- ✱ Intermittent fasting triggers neuroendocrine responses and adaptations.
- ✱ ↓ Circulating glucose, insulin, and amino acids
- ✱ ↓ Circulating amino acids → repress the activity of mammalian target of rapamycin (mTOR) → **inhibition of protein synthesis** → **stimulation of autophagy**
- ✱ Down-regulation of the insulin-like growth factor1 (IGF-1) signaling pathway
- ✱ Minimizing anabolic processes (synthesis, growth, and reproduction)
- ✱ Favoring maintenance and repair systems
- ✱ Enhancing stress resistance
- ✱ Recycling damaged molecules
- ✱ Stimulating mitochondrial biogenesis
- ✱ Promoting cell survival
- ✱ Improvements in health and diseases

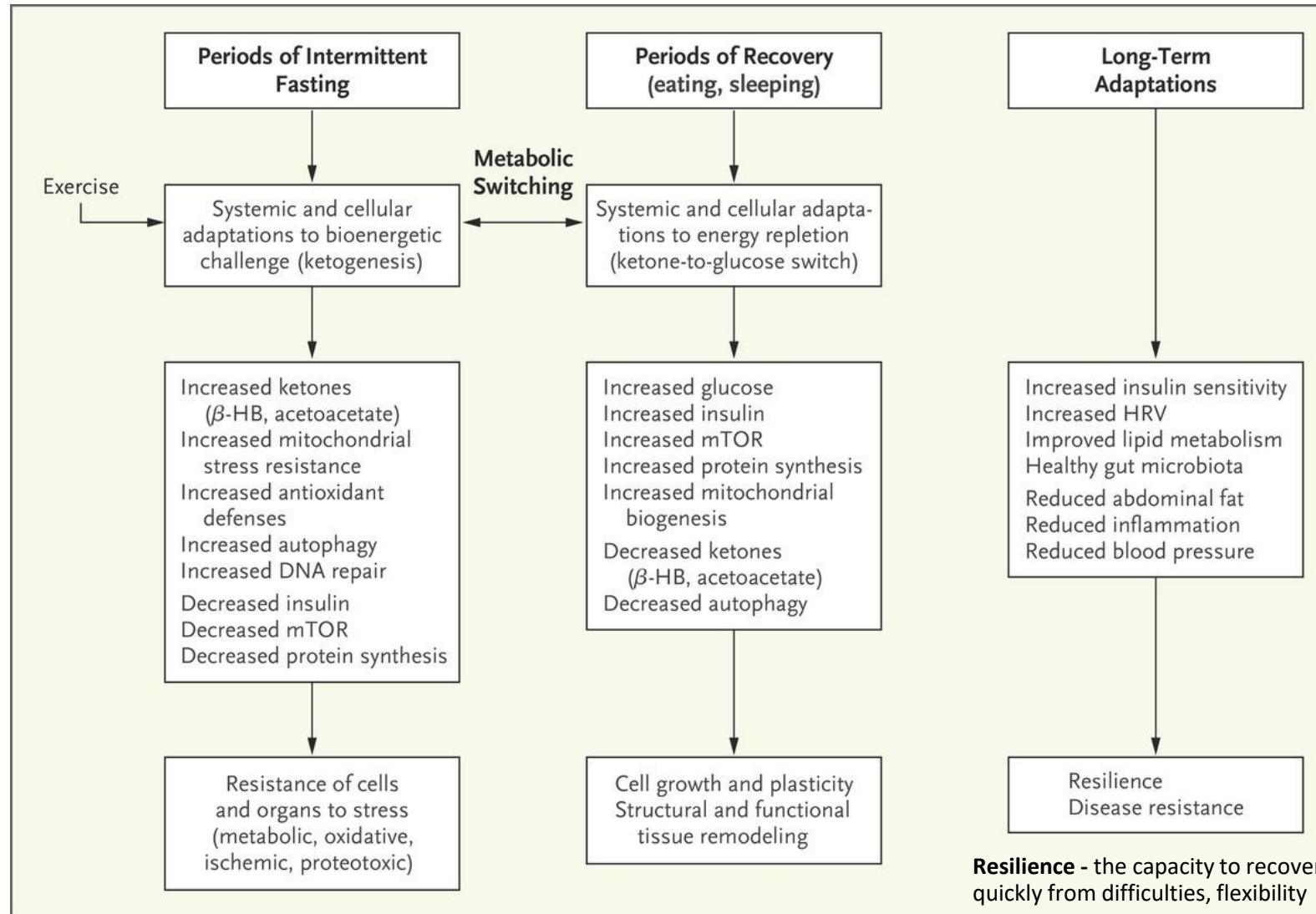
Autophagy



- ✿ Cellular self-digestion
- ✿ An adaptive response to stress, particularly in the condition of nutrient deprivation, allowing for cell and organism survival
- ✿ Cytoplasmic catabolic process that protects the cell against stressful conditions

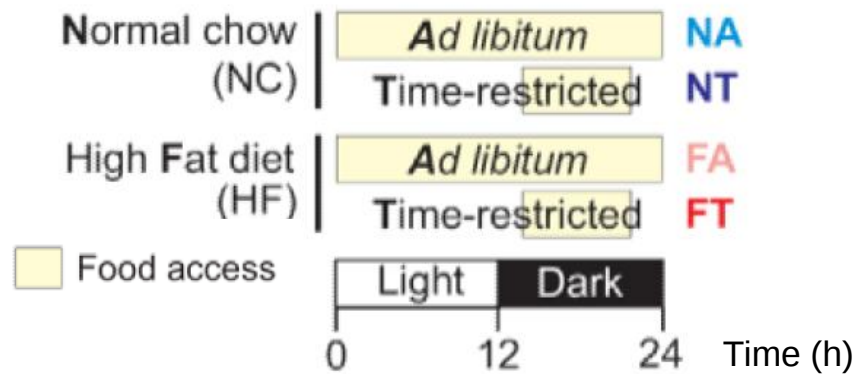
- ✿ Damaged cellular components are funneled by autophagy into the lysosomes, where they are degraded and can be re-used as alternative building blocks for protein synthesis and cellular repair.
- ✿ When nutrient resources are restricted, cells are able to break down and reprocess all sort of macromolecules including proteins, lipids, and carbohydrates which can then be reused as essential building blocks for the synthesis of new macromolecules and the production of energy.
- ✿ Autophagic dysfunction is associated with cancer, neurodegeneration, microbial infection, and ageing.

Cellular and Molecular Mechanisms Underlying Improved Organ Functions and Resistance to Stresses and Diseases with Intermittent Metabolic Switching

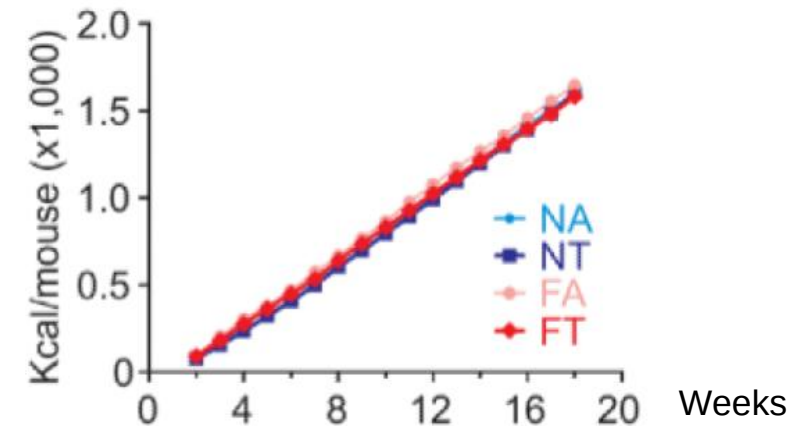


Time-restricted feeding (TRF) in mice

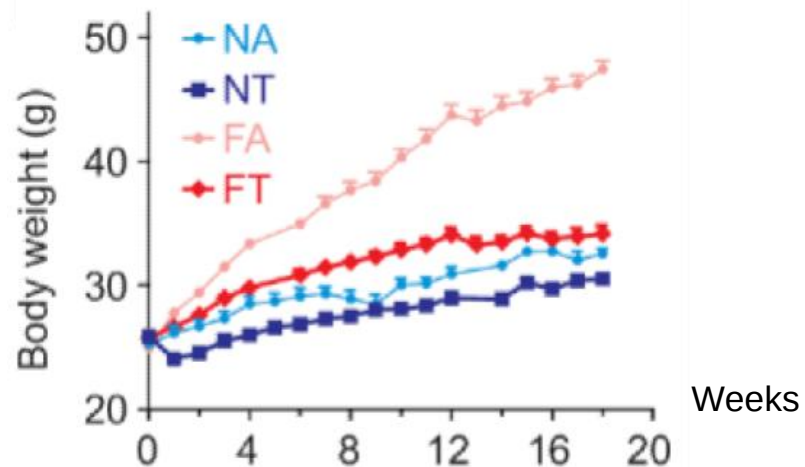
A) Four feeding regimens



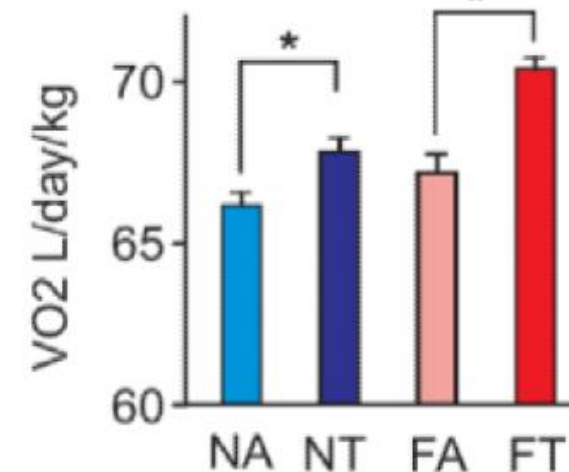
B) Cumulative average energy intake



C) Average body weight



D) O₂ Consumption

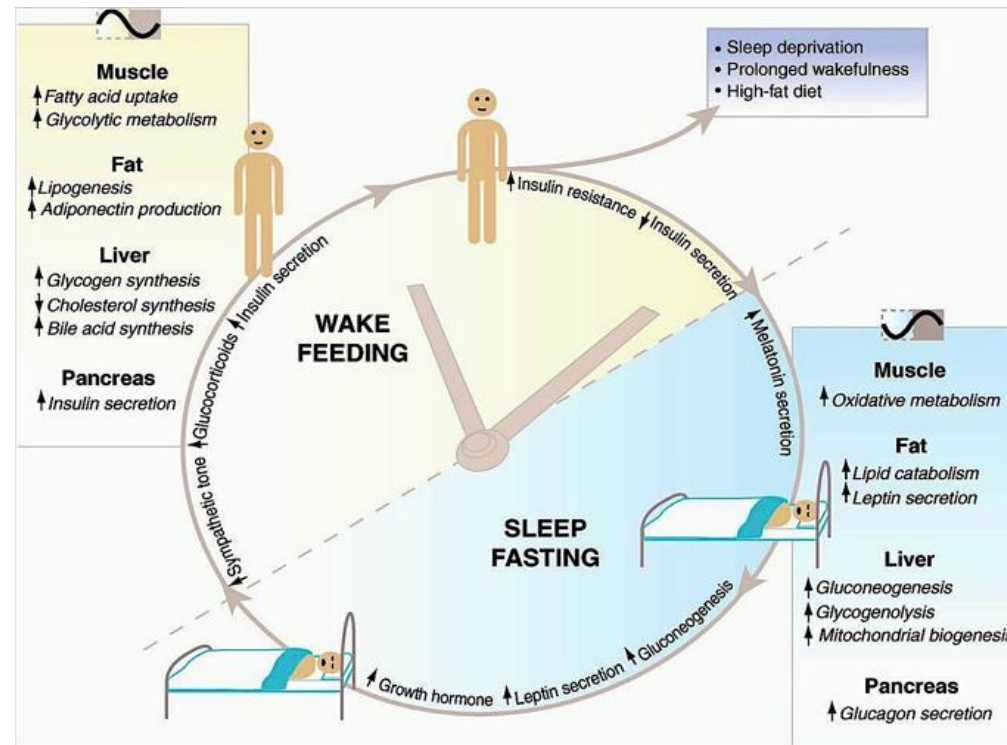


Time-restricted feeding (TRF) in humans

- ✿ Appears to depend on the time of day of the eating window
- ✿ **Restricting food intake to the middle of the day** (“mid-day TRF”)
 - 🍃 ↓ Body weight or body fat, fasting glucose and insulin level, insulin resistance, hyperlipidemia, inflammation
- ✿ **Restricting food intake to the late afternoon or evening** (“late TRF”)
 - 🍃 Produced mostly null results or worsened postprandial glucose levels, β -cell responsiveness, blood pressure, and lipid levels

Carlson et al., 2007; Gill and Panda, 2015; Moro et al., 2016; Stote et al., 2007; Tinsley et al., 2017;
Gill and Panda, 2015; Moro et al., 2016; Carlson et al., 2007; 9) Stote et al., 2007; Tinsley et al., 2017

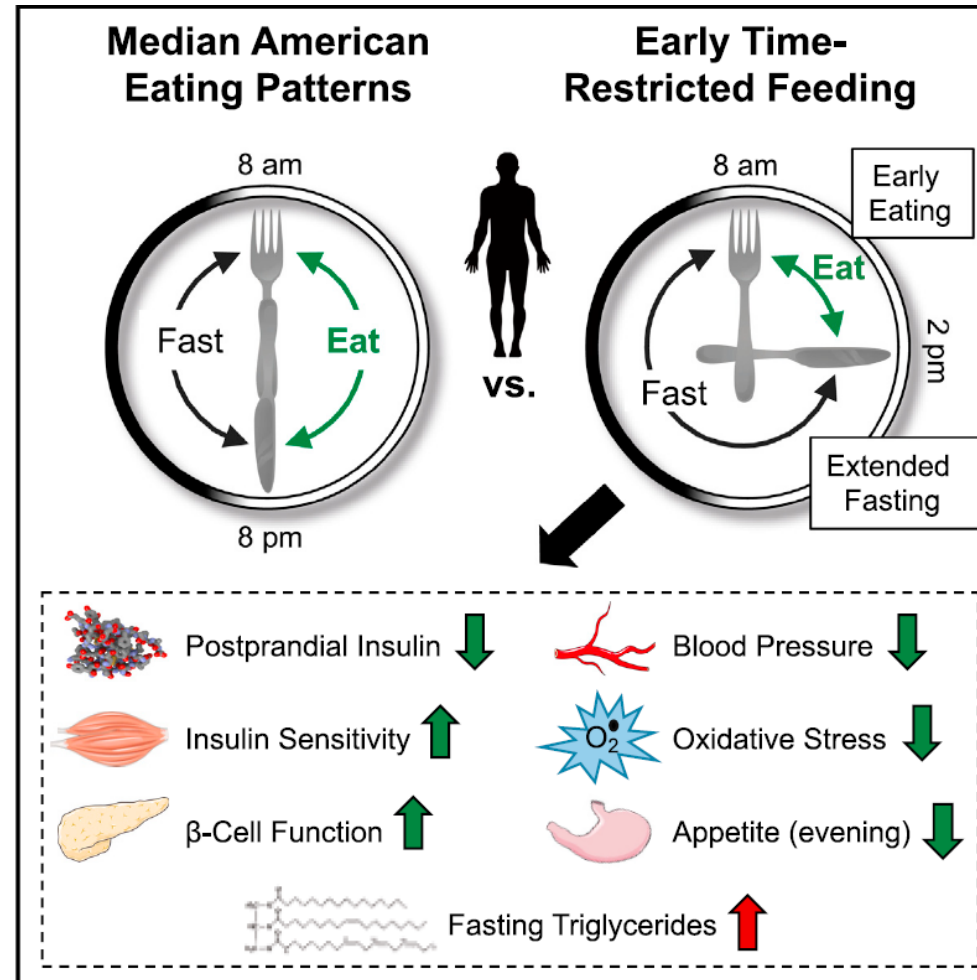
The circadian system



Joseph Bass, 2010

- ✿ In humans, ↑insulin sensitivity, beta cell responsiveness, fat oxidation, and the thermic effect of food in the morning than in the afternoon or evening
- ✿ Human metabolism is optimized for food intake in the morning.

Early Time-Restricted Feeding



Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes

Elizabeth F.Sutton¹RobbieBeyl¹Kate S.Early²William T.Cefalu¹³EricRavussin¹Courtney M.Peterson

Cell Metabolism Volume 27, Issue 6, 5 June 2018, Pages 1212-1221.e3

7. Ketogenic diet

- ✱ High-fats, moderate-proteins, and very-low-carbohydrates
- ✱ approximately **55-60% fat**, **30-35% protein**, and **5-10% CHO**
- ✱ The most common and relatively minor short-term side effects
 - 🌿 Nausea, vomiting, headache, fatigue, dizziness, insomnia, difficulty in exercise tolerance, and constipation, sometimes referred to as keto flu
 - 🌿 Ensuring adequate fluid and electrolyte intake → counter some of these symptoms
- ✱ Long-term adverse effects
 - 🌿 Hepatic steatosis, hypoproteinemia, kidney stones, and vitamin and mineral deficiencies

7. Ketogenic diet

✱ Most systematic reviews and meta-analysis

✱ Confounded by **low-CHO diets** that were likely not **ketogenic**

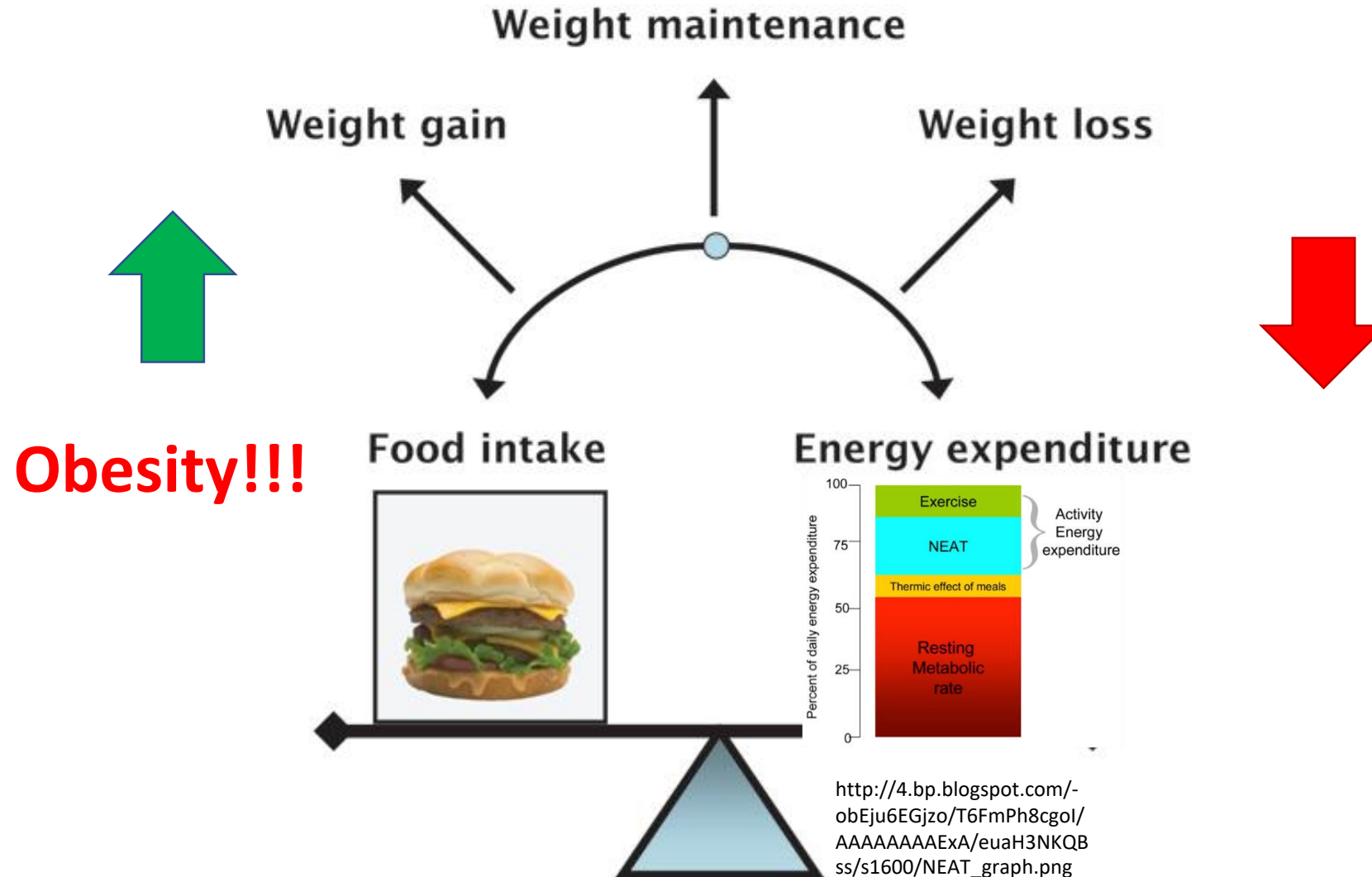
Saslow LR, et. al. PLoS One. 2014;9(4):e91027.

✱ ↓ Fat mass 66.15% and fat-free mass 33.85%

✱ No systematic reviews or RCTs examined mortality or cardiovascular disease

Can Fam Physician. 2018 Dec; 64(12): 906; Foster GD, et. Al. N Engl J Med. 2003;348(21):2082-90.; Dashti HM, et. al. Exp Clin Cardiol. 2004;9(3):200-5; Moreno B, et. al. Endocrine. 2016;54(3):681-90.; Yancy WS, Jr., et. al. Ann Intern Med. 2004;140(10):769-77.; Goday A, et. al. Nutrition & Diabetes. 2016;6(9):e230-e.; Jabekk PT, et. al. Nutrition & Metabolism. 2010;7(1):17.; Partsalaki I, et. al. Endocrinol Metab. 2012;25(7-8):697-704.; Saslow LR, et. al. Nutrition & Diabetes. 2017;7(12):304.; Westman EC, et. al. Nutrition & metabolism. 2008;5:36-.

Energy balance



Principle of Weight Management



ฉันทชา สิทธิจรูญ. ใน: ฉันทชา สิทธิจรูญ, บรรณาธิการ. ภาวะอ้วนและการลดน้ำหนัก.

พิมพ์ครั้งที่ 1. กรุงเทพฯ: บริษัท ไอที ออล ดิจิตอลพริ้นท์ จำกัด; 2565.

Principle of Weight Management

1. Inspiration and determination
2. Goal setting: short-term goal & long-term goal
3. Choosing a diet that's right for you
4. Increased energy expenditure
5. Self-monitoring
6. Sleep
7. Probiotics
8. Stress
9. Support
10. Positive attitude

Principle of Weight Management

1. Inspiration and determination

- ✱ The most important factor
- ✱ Drives behavior

2. Goal setting

- ✱ Short term-goal for goal achievement
- ✱ Long term-goal for optimum BW/BMI
- ✱ Limit setting

3. Choosing a diet that's right for you

- ✱ Could be done continuously in a long term
- ✱ Too hungry → over-eating!!!
- ✱ Method alternating

Weight loss diet regimens

1. **General Recommendation** (↓ Carbohydrate, ↓ Sugar, ↑ Protein, ↓ Fat, ↑ Vegetable/Fiber, ↑ Drinking water)
 - **Metabolism boosting meals** (High protein, Low fat, No carb with 1 day cheating/week)
 - **Plate method**
2. **Calories reduction**
3. **Paleolithic diet**
4. **Mediterranean diet**
5. **“Eating breakfast like a king, lunch like a prince, and dinner like a pauper”**
6. **Intermittent fasting** (including Time-restricted eating, TRF)
7. **Ketogenic Diet**

Principle of Weight Management

4. Increased energy expenditure

- * ↑EAT or exercise

 - ↑EE, lean mass, BMR, lipolysis, GH

- * ↑NEAT

- * Aerobic exercise

 - Moderate intensity 150 min/week (walking)

 - Vigorous intensity 75 min/week (running)

- * Muscle strengthening, all muscle groups

 - ≥2 days/week (8-12 repetitions, 2-3 sets)

- * Pedometer goal:

 - 5,000-10,000 steps/day

Moderate- and Vigorous-intensity Physical Activity

Moderate-intensity Physical Activity (Approximately 3-6 METs)	Vigorous-intensity Physical Activity (Approximately >6 METs)
Requires a moderate amount of effort and noticeably accelerates the heart rate.	Requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate.
Examples of moderate-intensity exercise include:	Examples of vigorous-intensity exercise include:
• Brisk walking	• Running
• Dancing	• Walking / climbing briskly up a hill
• Gardening	• Fast cycling
• Housework and domestic chores	• Aerobics
• Traditional hunting and gathering	• Fast swimming
• Active involvement in games and sports with children / walking domestic animals	• Competitive sports and games (e.g. Traditional Games, Football, Volleyball, Hockey, Basketball)
• General building tasks (e.g. roofing, thatching, painting)	• Heavy shovelling or digging ditches
• Carrying / moving moderate loads (<20kg)	• Carrying / moving heavy loads (>20kg)

http://www.who.int/dietphysicalactivity/physical_activity_intensity/en/

HR max = 208-0.7 x age

Heart rate reserve = HR max-HR basal

Moderate exercise intensity

- ✱ (Heart rate < 0.7 X Heart rate reserve, HRR)
 - ✱ Your breathing quickens, but you're not out of breath.
 - ✱ You develop a light sweat after about 10 minutes of activity.
 - ✱ You can carry on a conversation, but you can't sing.

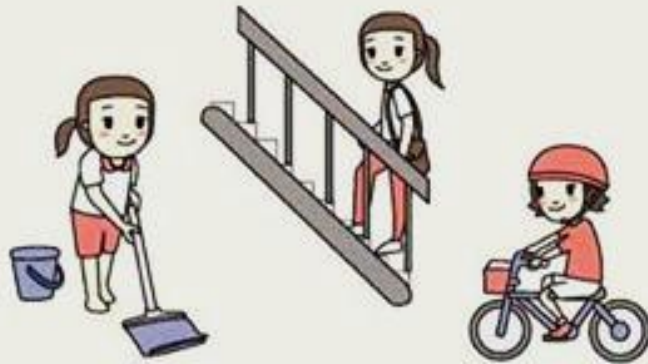
Vigorous exercise intensity

- ✱ (Heart rate 0.7- 0.85 X Heart rate reserve)
 - ✱ Your breathing is deep and rapid.
 - ✱ You develop a sweat after only a few minutes of activity.
 - ✱ You can't say more than a few words without pausing for breath.

<https://www.mayoclinic.org/healthy-lifestyle/fitness/in-depth/exercise-intensity/art-20046887>

Exercise

NEAT



is movement activities of the body caused by skeletal muscle causing energy consumption such as walking, cleaning the house, etc.

Exercise



is a subtype of physical activity that is structured, repetitive and intended to either strengthen a skill or maintain a fitness level, either or all.

**Exercise should be at least
30-45 minutes, 5-7 days/week.**

Principle of Weight Management

5. Self-monitoring

- * Weighing
 - * Bathroom scale
 - * Feedback (self-awareness)
 - * Fat → light weight → stepwise
- * Food Record
 - * Calories
 - * Response
 - * Feedback

6. Sleep

- * Deep sleep → GH → ↑lipolysis GH = growth hormone
- * Lack of sleep
- * Sleep deprived people → ↓leptin, ↑ghrelin → ↑appetite

Principle of Weight Management

7. Probiotics

- ✱ Faster gut & colonic transit time
- ✱ ↑ Stool frequency
- ✱ ↑ Stool consistency
- ✱ ↓ Flatulence
- ✱ ↑ recovery of tight junction between epithelial cells → prevent bacterial movement & ↓ inflammation from LPS → ↑ insulin sensitivity at hypothalamus → ↑ satiety
- ✱ ↑ GLP-1 & PPY in intestine → ↓ appetite, ↑ fullness

Principle of Weight Management

8. Adjust behavior when stressed

✱ Stress ➡ eat

9. Support

✱ Friend, family

✱ Social

✱ Environment

10. Positive attitude

✱ Don't give up

✱ Can always start over

Weight regain

Weight Regain

↑ Weight reduction 5-10% within 3-6 months

↑ Weight Regain

- * Obvious in ~6-12 months after weight loss

- * >25% within the first year

- * >50% within 2 years

- * >80% within 5 years

↑ Causes

- * ↓ Fat → ↓ Insulin & leptin → ↑ appetite

- * ↓ TEE (REE & non-REE) from ↓ body composition (↓ metabolically active component e.g. FFM)

- * ↓ FFM → **high risk** of weight regain or even ↑ BW

Weight Regain

↑ Causes

- * ↓ Thermogenesis not associated with BW & body composition called “**adaptive thermogenesis**” (AT) or ↓ EE > ↓ body composition

* Occurring

- * Eating less >2 weeks

- * Optimum ~10% weight loss of initial BW or after 12-20 weeks of losing weight

* ↓ T3

* ↓ SNS

* Unlimited eating → rapid weight regain

- * ↑ Energy intake

- * ↓ Energy expenditure from ↓ FFM and prolong AT

- * 4 weeks → normal BMR (new body composition)

AT = adaptive thermogenesis

EE = energy expenditure

BW = body weight

T3 = Triiodothyronine

SNS = sympathetic nervous system

FFM = fat-free mass,

BMR = basal metabolic rate

Diet break or Cheat days

Diet break or Cheat days

- * Eating less >2 weeks

- * ↓ RMR

- * Adaptive thermogenesis

- * Could be normal after diet refeed

- ↑ **Diet break or cheat days**

- * Eucaloric or ~5-10% a little bit ↑ or ↓ than current BW, not initial BW

- * Diet control, not over eating

- * Short term ~1-3 days

- * Or prolong >4 days to several weeks

- * Maintain BW to stimulate RMR & thermogenesis

- * More effectiveness in weight loss

Weight loss maintenance

Weight loss maintenance

- ✱ Voluntary weight loss at least **10%** of initial BW and maintain at least **1 year**
- ✱ Voluntary weight loss at least **5%** of initial BW and maintain at least **2 years**
- ✱ Generally, weight loss **~7-10%** of initial BW in **6 months** after that **~5-6%** of initial BW
- ✱ Within 5 years, **13-20%** of people can maintain weight loss

Factors associated with successful weight maintenance

1. Inspiration
2. Reaching a self-determined goal weight
3. Autonomy
4. Initial weight loss → more initial weight loss, more successful weight maintenance
5. Calorie Reduction and Portioning of food eaten
6. Eating breakfast regularly
7. Control of over-eating with eating restraint
8. Physically active lifestyle

Elfhag K, Rössner S. Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. *Obes Rev.* 2005;6(1):67-85.

Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. *Med Clin North Am.* 2018;102(1):183-97.

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Factors associated with successful weight maintenance

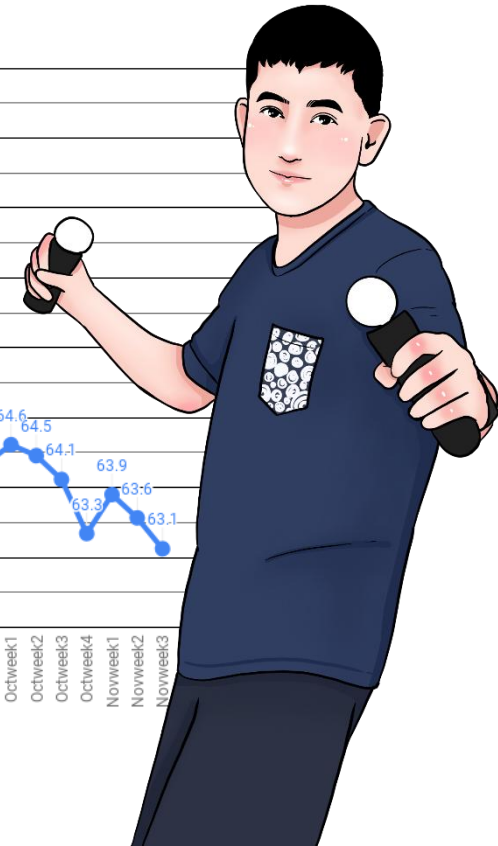
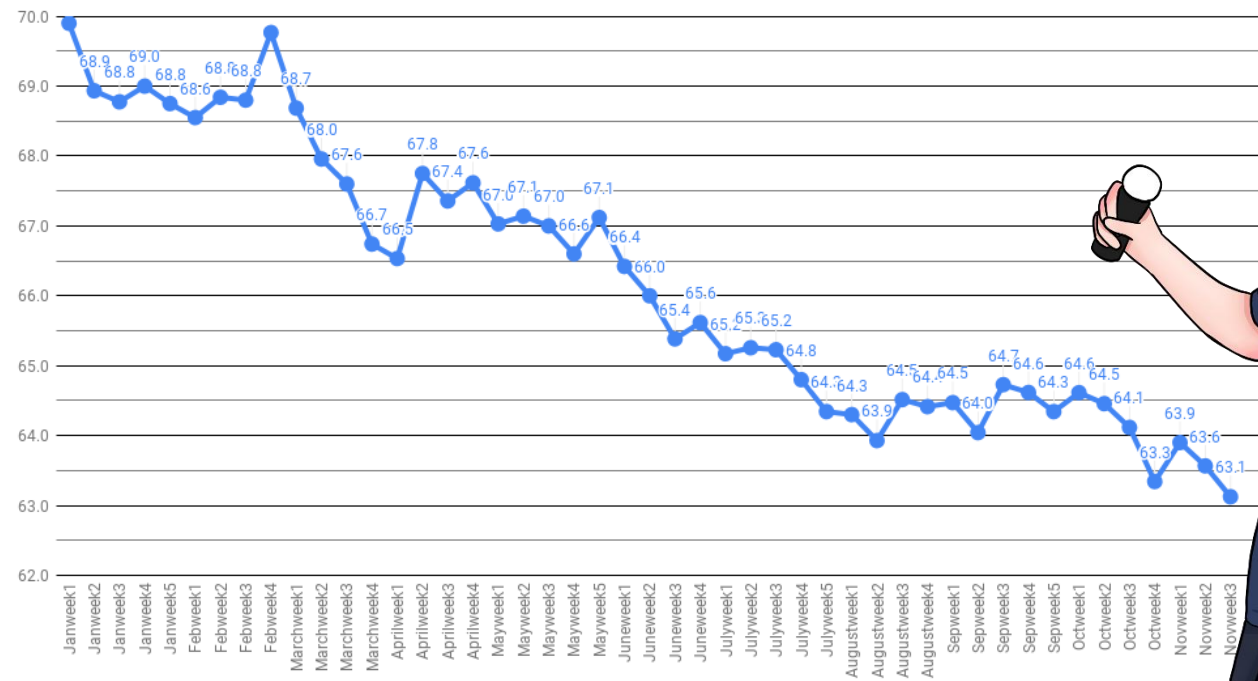
- 9. Self-monitoring → weighing & food record**
- 10. Psychological strength and stability**
- 11. Self-efficacy**
- 12. Ability to handle life stress & coping strategy**
- 13. Socialization & thinking flexibility**
- 14. Social support**
- 15. Being able to maintain weight after prolong weight loss**

Elfhag K, Rössner S. Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. *Obes Rev.* 2005;6(1):67-85.

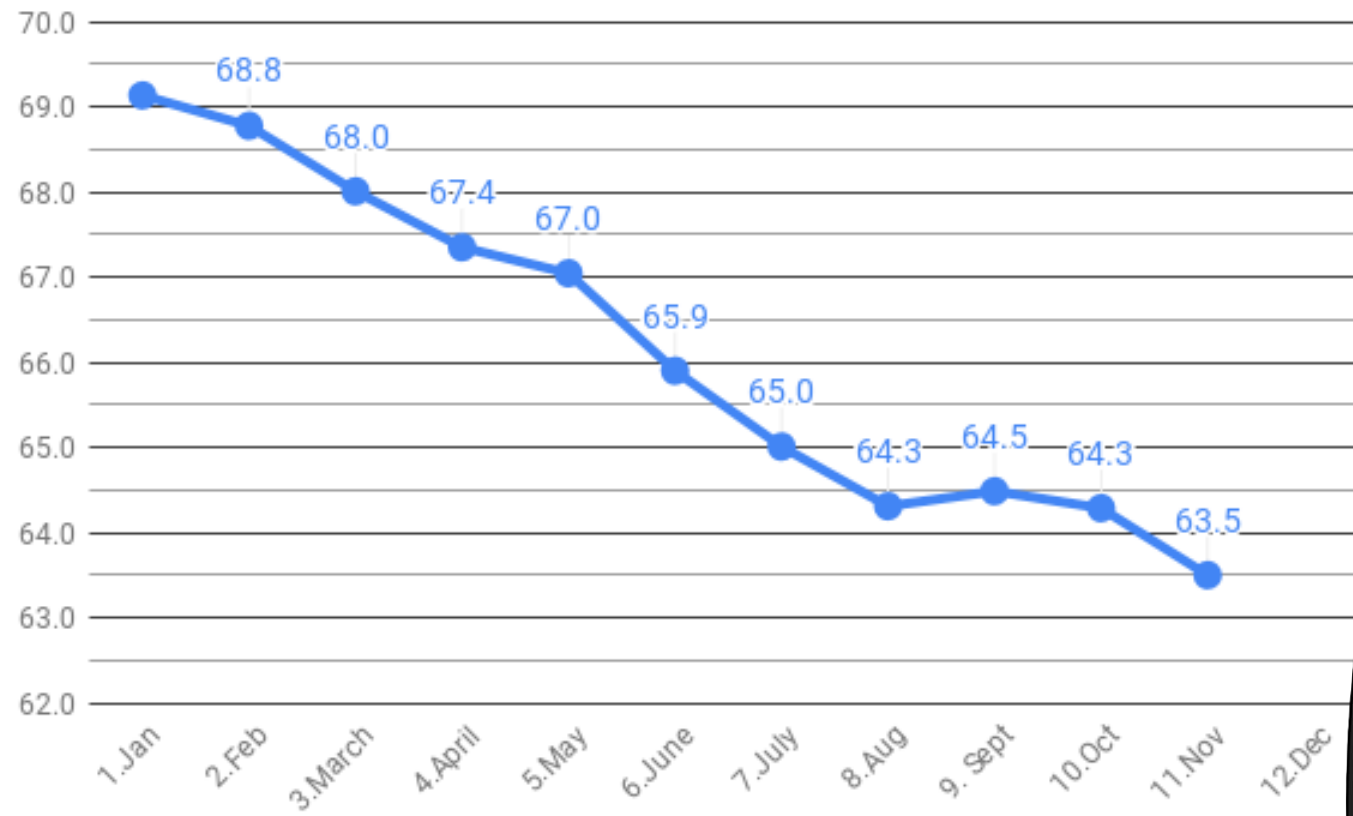
Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. *Med Clin North Am.* 2018;102(1):183-97.

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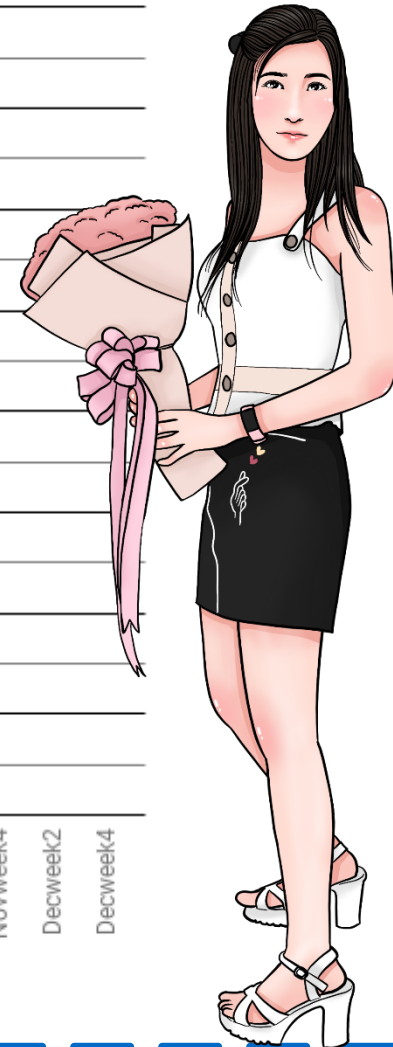
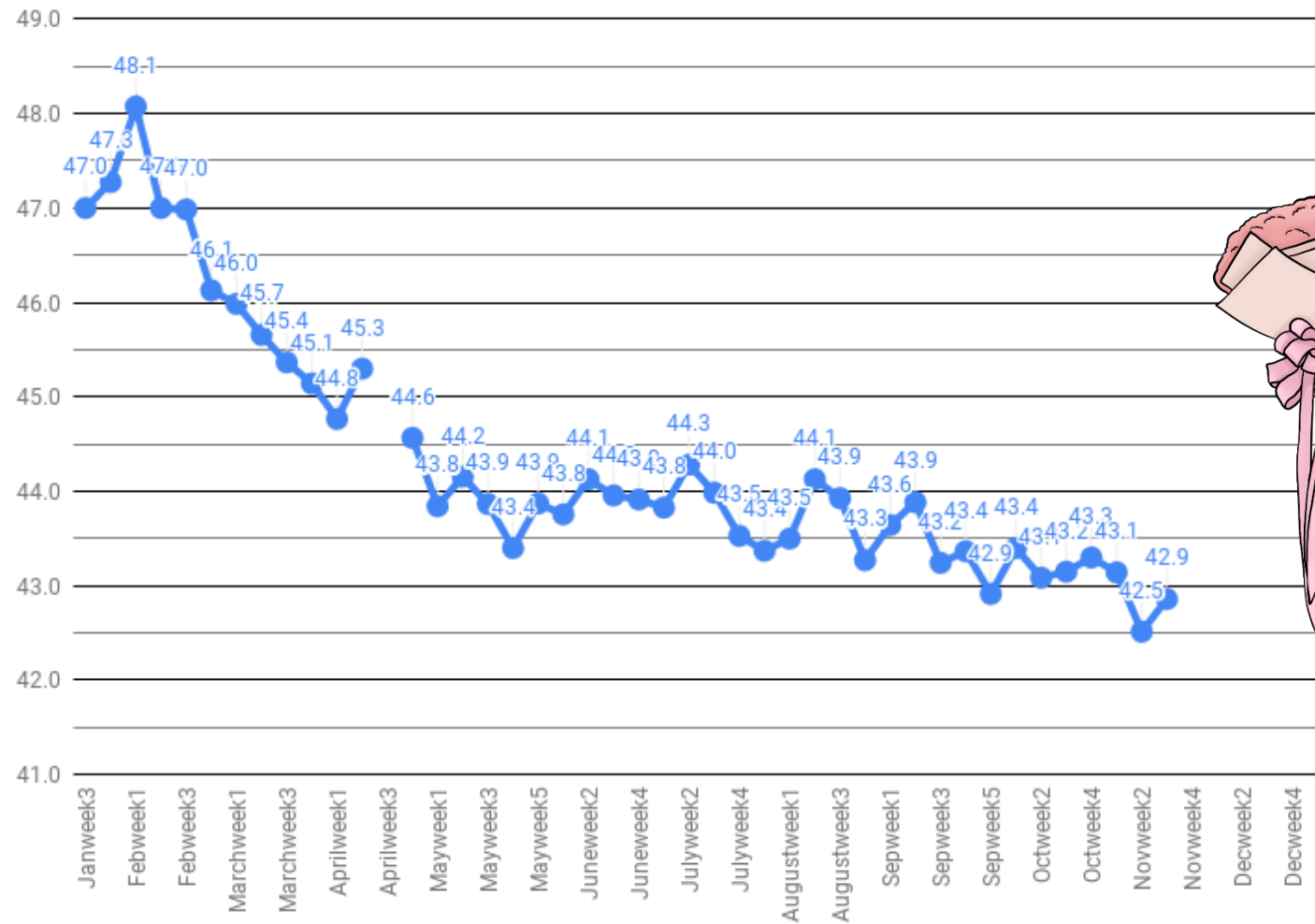
Example



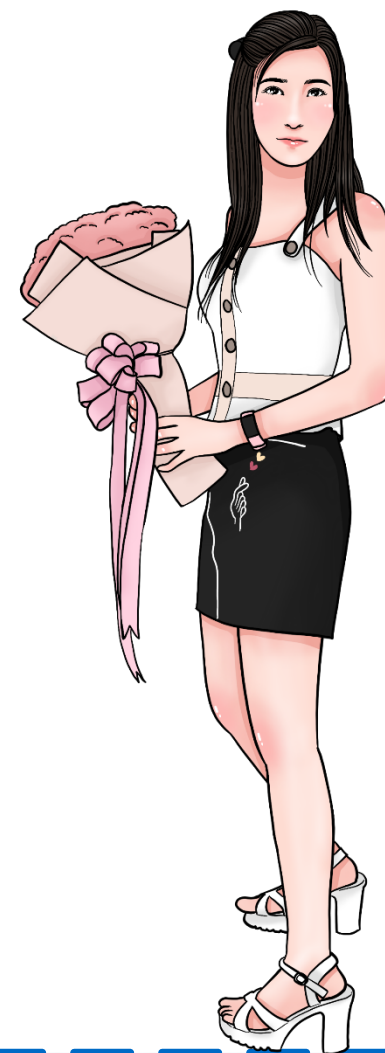
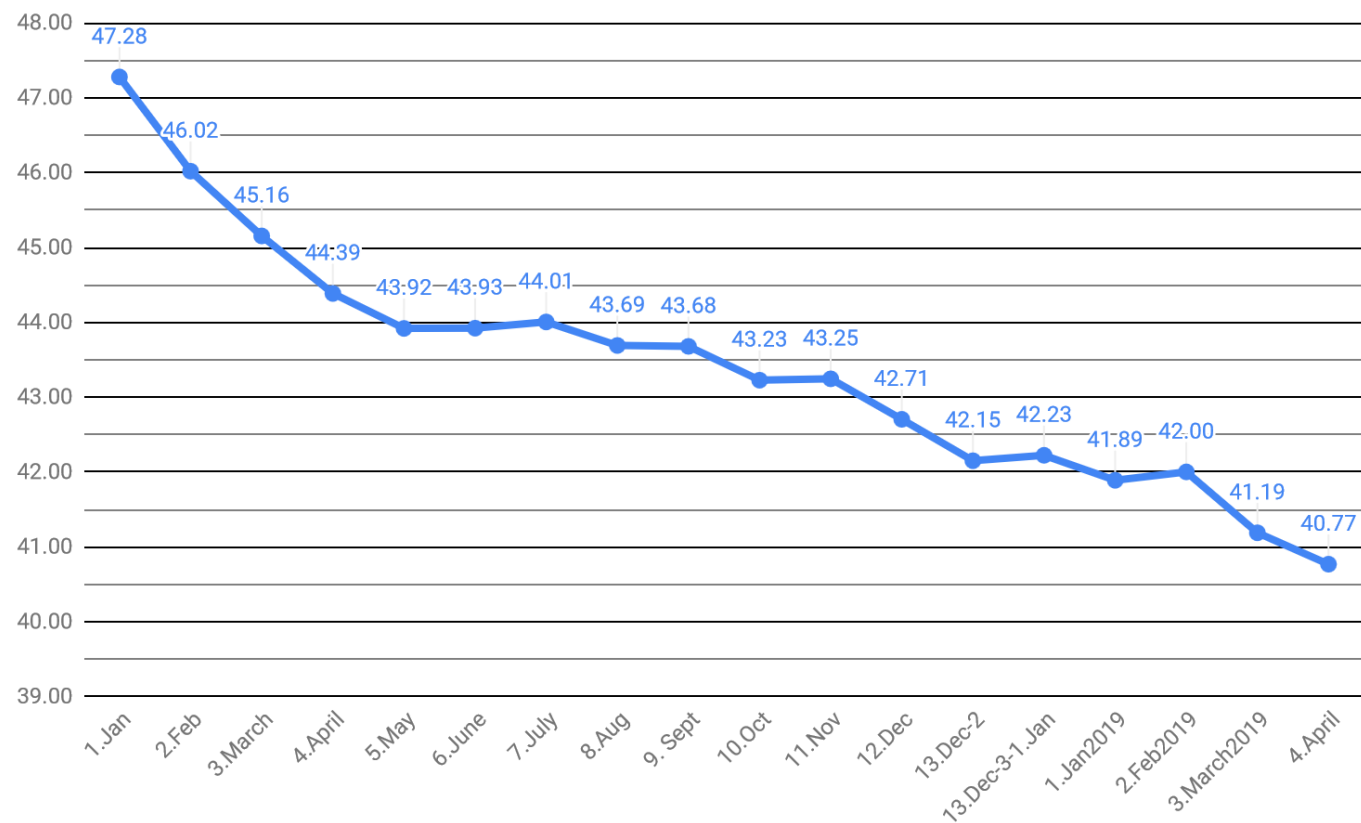
Example



Example



Example



Percentage of total weight loss

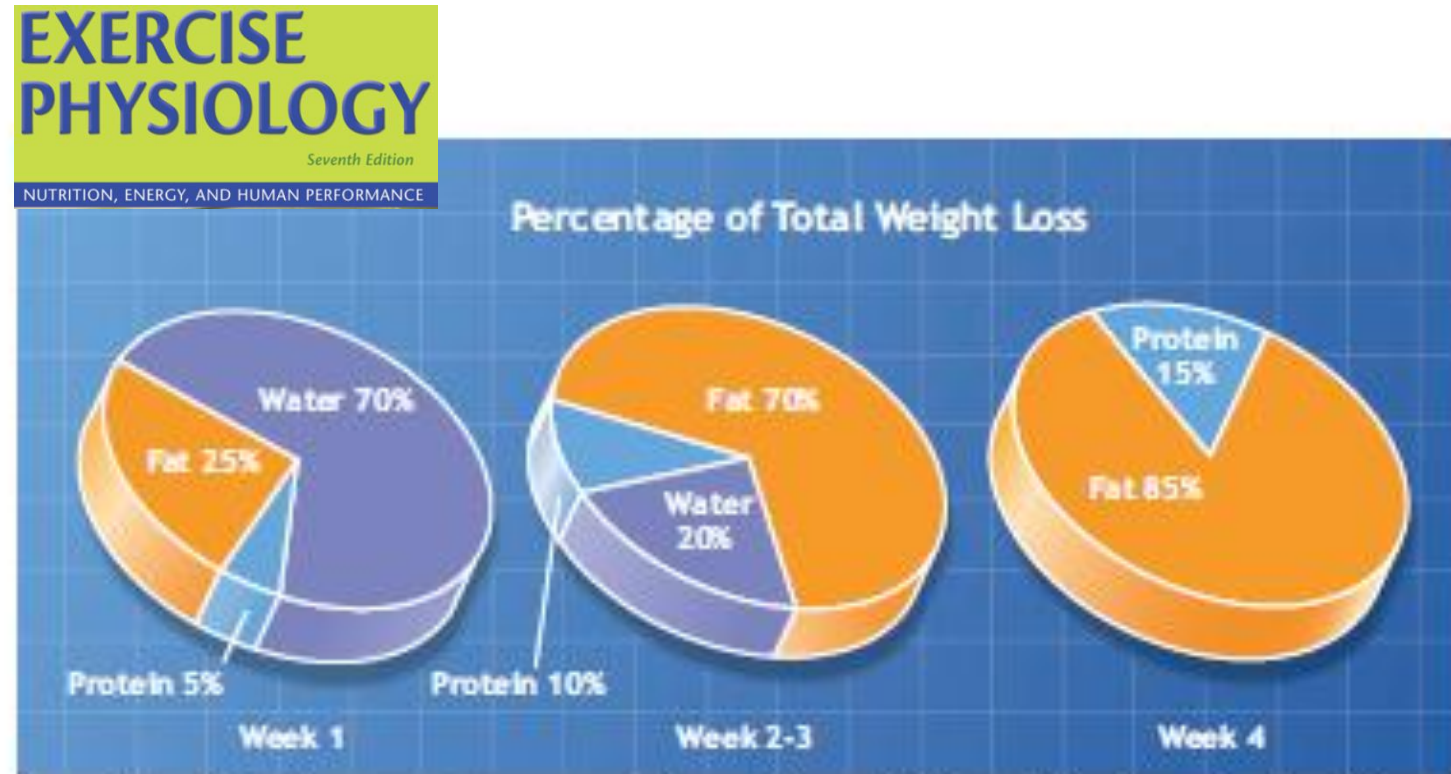
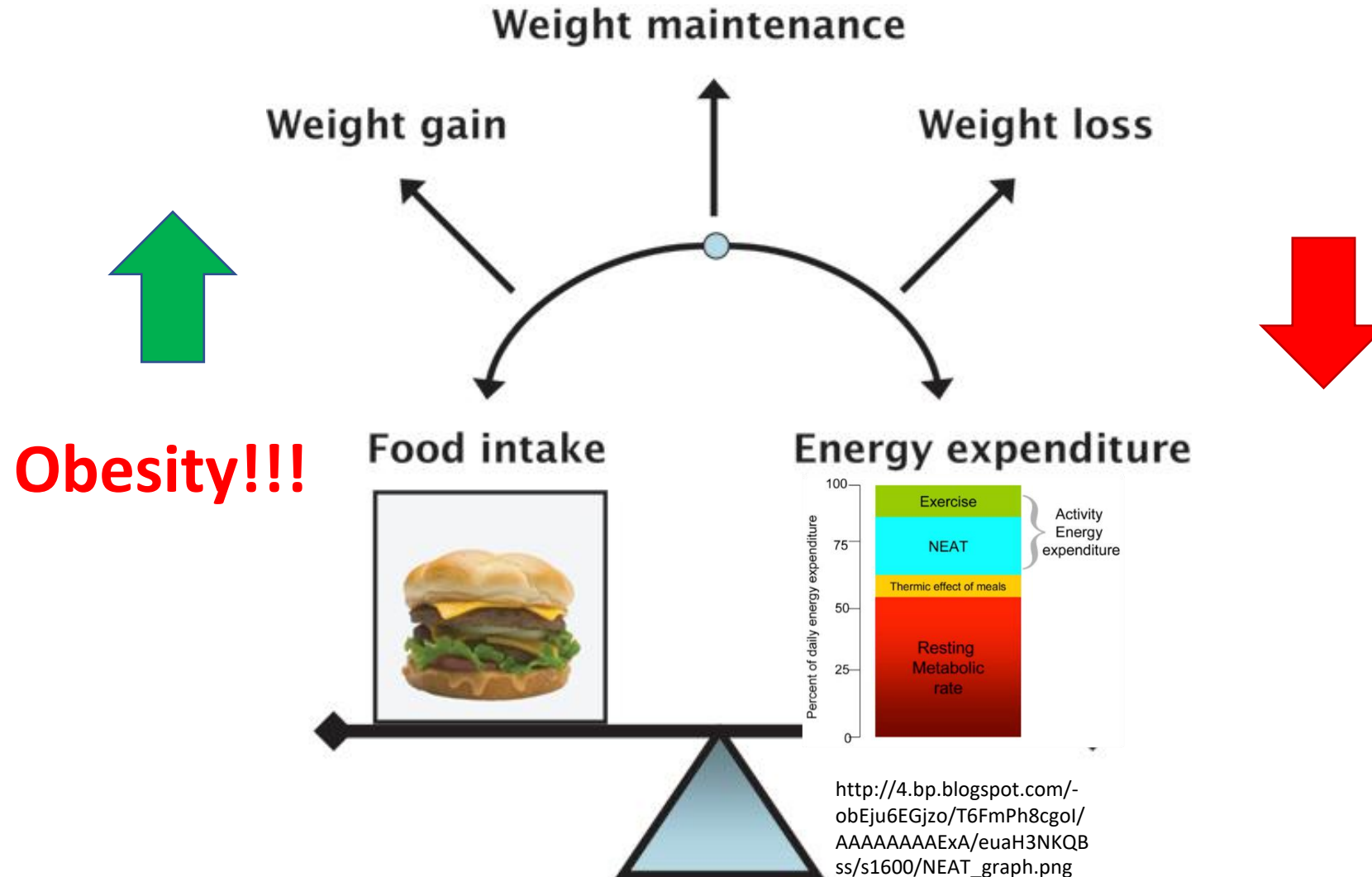


Figure 30.22 • General trend for the percentage composition of the weight lost during 4 weeks of caloric restriction.

The fasting state

- ✱ When fat reserves are gone.
 - ✱ Degradation of essential proteins begins
 - ✱ Loss of heart and liver function
 - ✱ Prolonged starvation → death
- ✱ **Stored fat** → provides adequate energy during fast or rigid diet, but vitamins and minerals must be provided.
- ✱ **Sufficient dietary glucogenic amino acids** are needed to replace those being used for gluconeogenesis.
- ✱ Rations for those on a **weight-reduction diet** are commonly fortified with **vitamins**, **minerals** and **amino acids** or **proteins**.

Energy balance



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