OBESITY& INFLAMMATION

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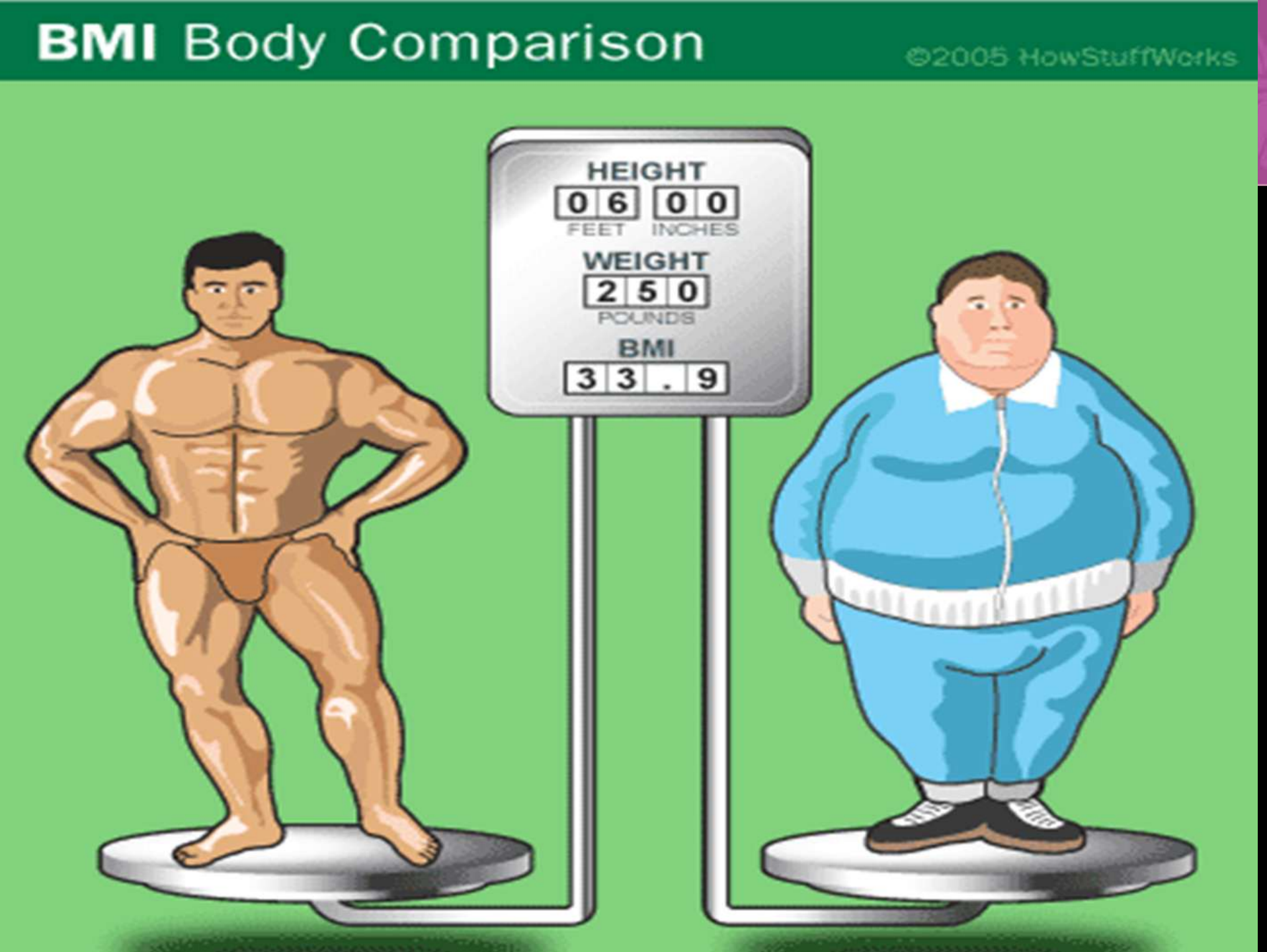
DEFINITION OF OBESITY

Obesity is defined as an excess of body fat sufficient to adversely affect health.

Body mass index (BMI) and waist circumference,are the most commonly used measures

WHO

- Worldwide obesity has more than doubled since 1980.
- In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 600 million were obese.
- 39% of adults aged 18 years and over were overweight in 2014, and 13% were obese..
- 41 million children under the age of 5 were overweight or obese in 2014.
- Obesity is preventabl


BMI Body Comparison
©2005 HowStuffWorks
HEIGHT
0 6 0 0
FEET INCHES
WEIGHT
2 5 0
POUNDS
BMI
3 3 . 9

OBESITY

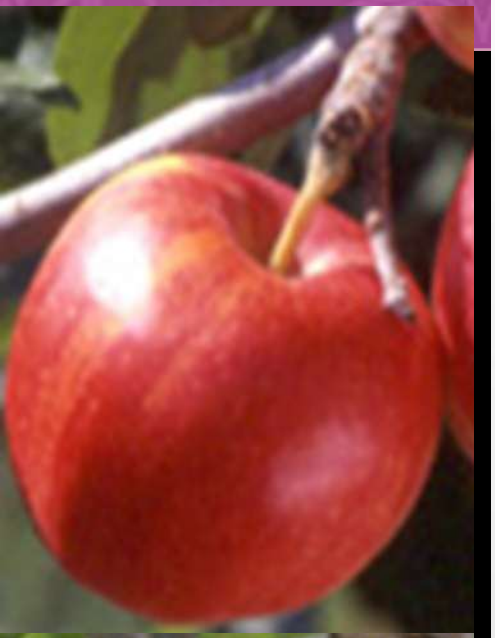
- BMI = (weight [kg]) / (height [m])2.

- Body fat percentage can be estimated using the Deurenberg equation.
- Body fat percentage = 1.2(BMI) + 0.23(age [y]) – 10.8(sex) – 5.4, with males coded as 1 and females as 0.
- This formula has a standard error of 4% and explains approximately 80% of the variation in body fat.

Central obesity may reflect increased visceral (intra-abdominal fat)

stores and/or ‘ectopic’ fat (fat stored in liver, muscle, pancreas, and epicardium)

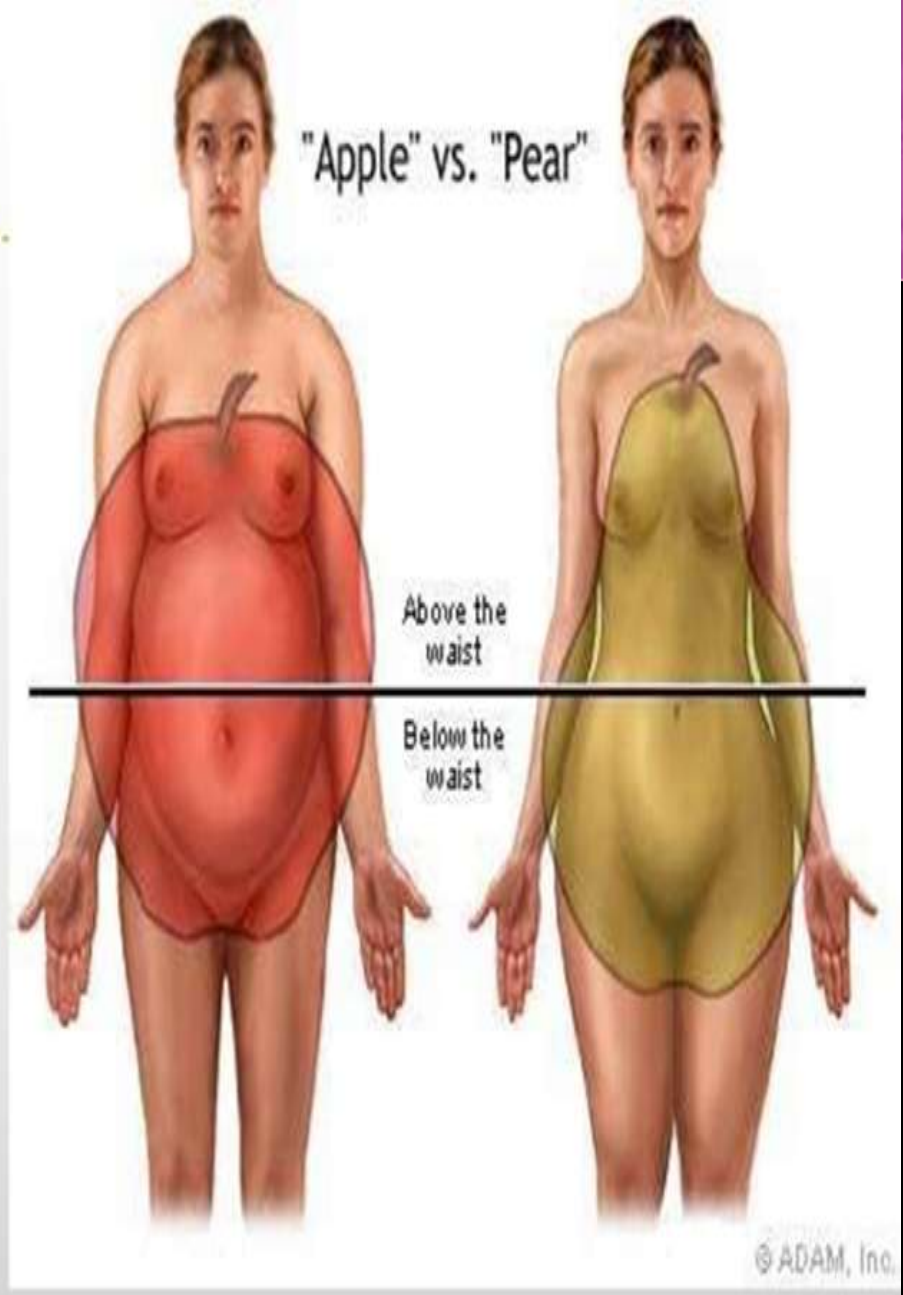
more directly linked to pathophysiology, such as insulin resistance.



Types of obesity

Android=Abdominal=Central= Apple shaped

Gynecoid=Peripheral=Pear shaped

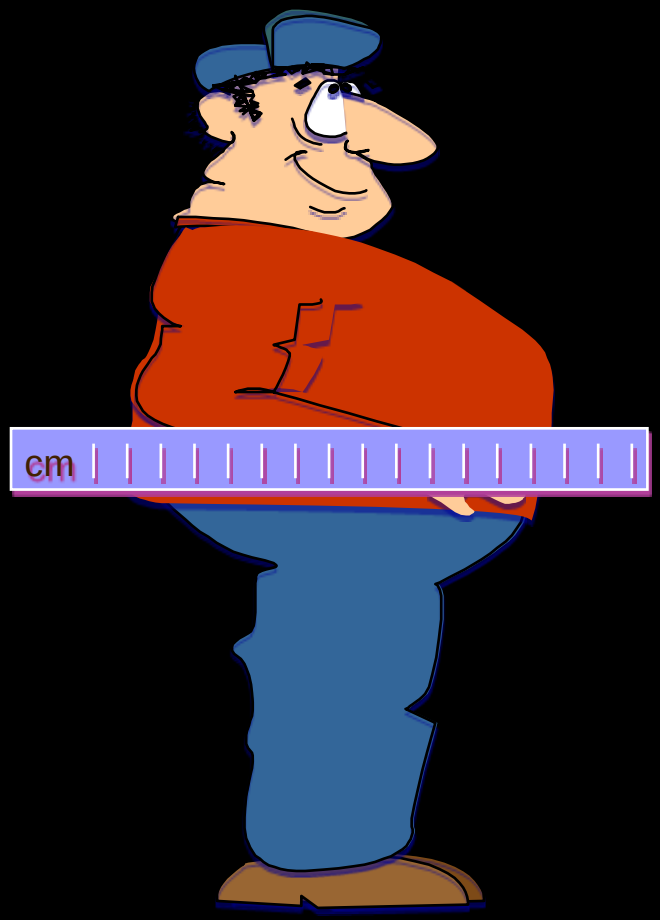


BMI TABLE WHO:

19–24,9	Normal weight
25–29,9	Overweight
30–34,9	Obesity level I
35–39,9	Obesity level II
≥ 40	Obesity level III

Women

>80 increased risk
>88 cm = Substantially increased risk



Men

>94 increased risk
>102 cm = Substantially increased risk

EDMONTON OBESITY STAGING SYSTEM
OXFORD UNIVERCITY

Stage 0

• No apparent obesity-related risk factors, physical symptoms, psychopathology, functional limitations, and/or impairment of well-being.

Stage 1

• Obesity-related subclinical risk factor(s) (borderline hypertension, impaired fasting glucose, elevated liver enzymes, etc.), *mild* physical symptoms (e.g. dyspnoea on moderate exertion), psychopathology, functional limitations, and/or impairment of well-being.

Stage 2

• Established obesity-related chronic disease(s) (hypertension, type 2 diabetes, sleep apnoea, osteoarthritis, reflux disease, polycystic ovary syndrome, anxiety disorder), moderate limitations in activities of daily living, and/or well-being.

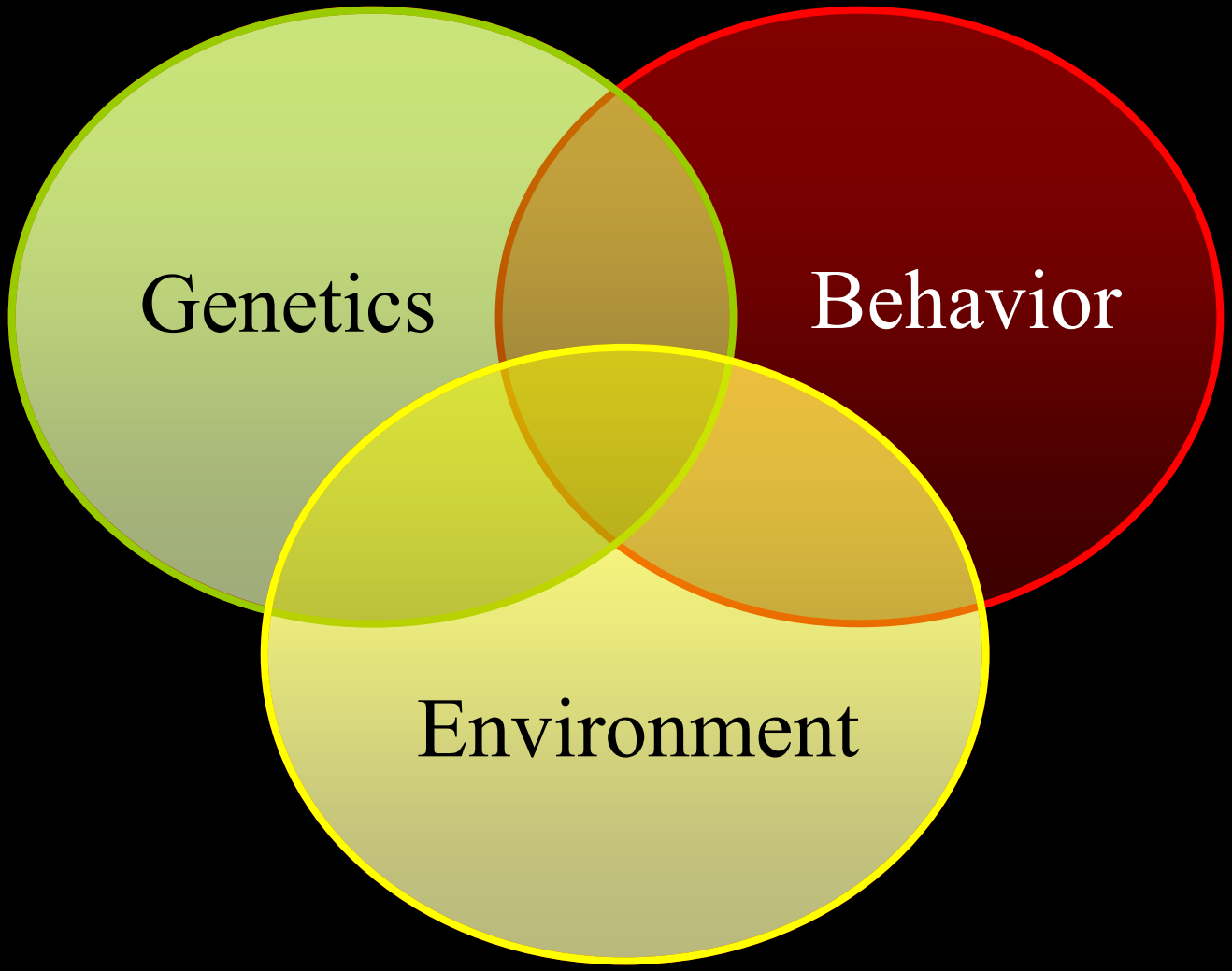
Stage 3

• Established end-organ damage (myocardial infarction, heart failure, diabetes complications, incapacitating osteoarthritis), significant psychopathology, functional limitation(s), and/or impairment of well-being.

Stage 4

• Severe (potentially end-stage) disability/ies from obesity-related chronic diseases, disabling psychopathology, functional limitation(s), and/or impairment of well-being.

AETIOLOGY OF OBESITY



AETIOLOGY OF OBESITY

Overweight and obesity results from a complex interaction between environmental

pressures and risks and genetic susceptibility. Heritability of

obesity is about 60%, but the rapid increase in obesity prevalence over

the past 30 years argues in favour of predominantly environmental drivers.

However, there is increasing interest in the possibility of epigenetic influences

on obesity related to maternal obesity, diet, gestational diabetes,

, and polycyclic aromatic hydrocarbons.and even possibly environmental pollutants such as polyfluorinated compounds

GENETIC FACTORS

Monogenic obesity

Mutations in genes (usually related to appetite control within the hypothalamus)

are associated with obesity of early childhood onset, usually

with hyperphagia. However, only about 5% of all severe childhood and

2% of adult obesity are associated with identified genetic causes. mutations in the melanocortin 4 receptor (MC4R) are the most frequent

and are associated with increased linear growth, fat and lean mass, hyperphagia

(moderate) and severe hyperinsulinaemia, but normal puberty and

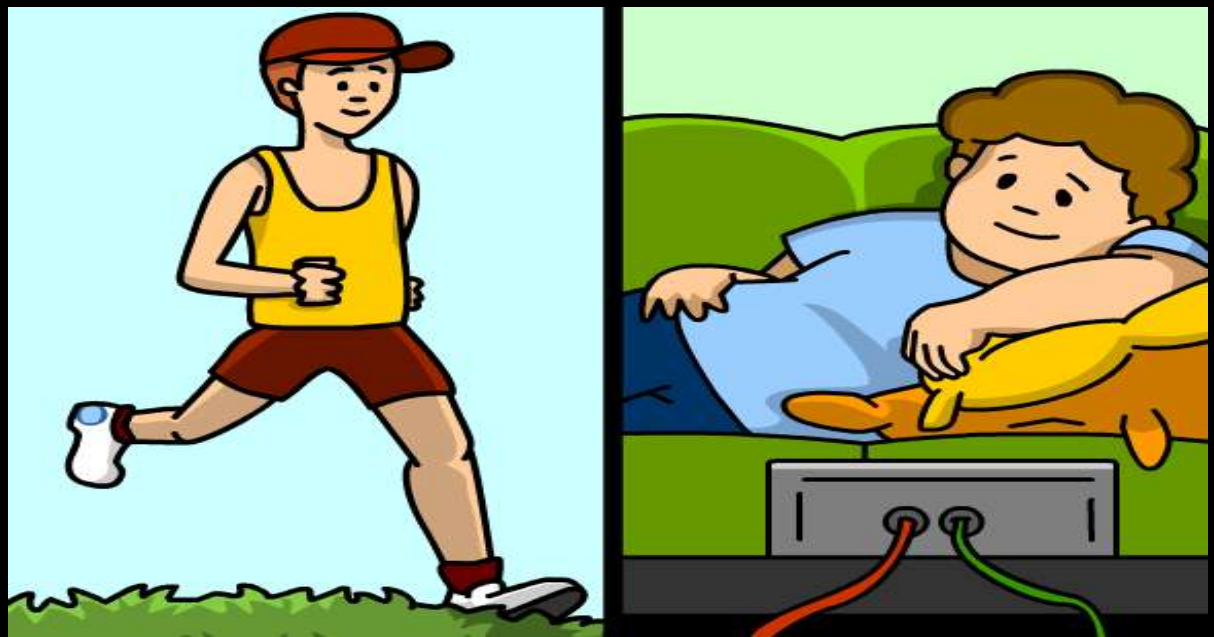
fertility.


www.StrangeCosmos.com

ENVIRONMENTAL FACTORS

increased energy (food) intake or decreased energy expenditure due to physical inactivity

increased availability of high caloric density foods and sedentary lifestyle.



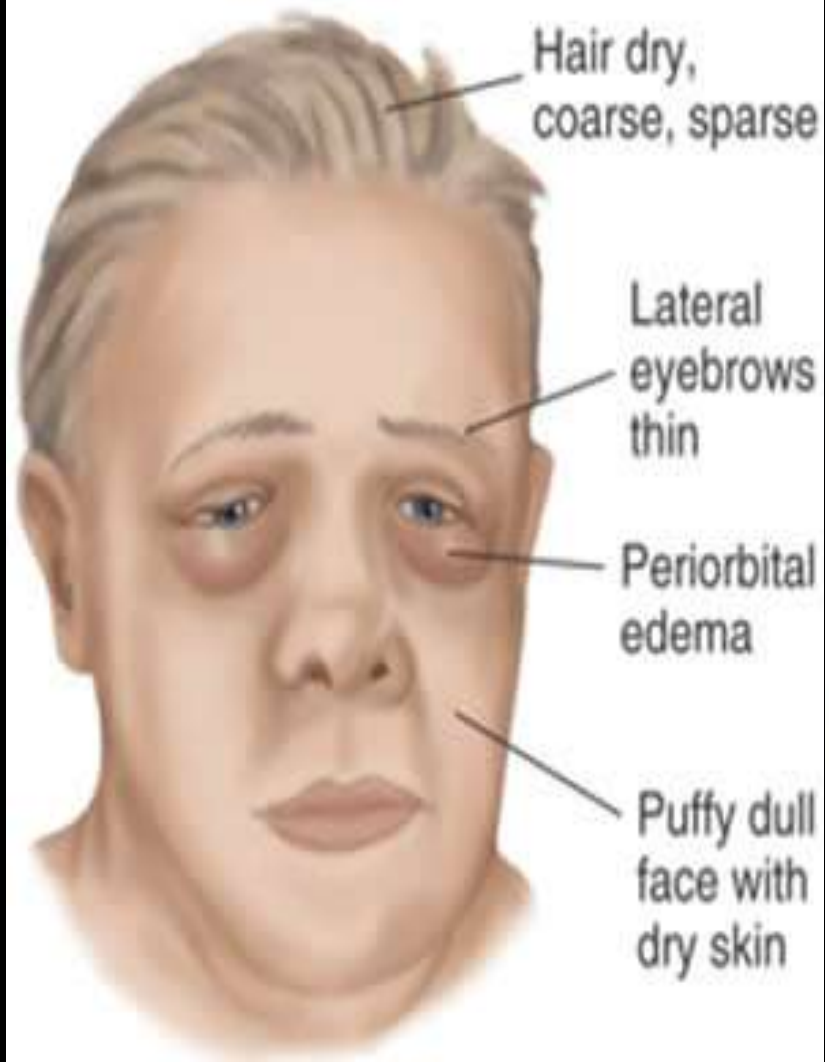
SECONDARY CAUSES

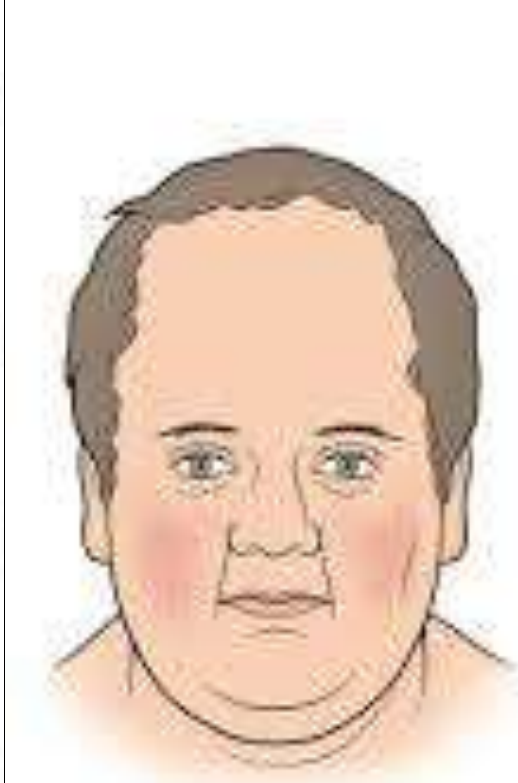
• Hypothyroidism: an important cause to exclude in children but rarely presents simply with weight gain in adults

• Cushing's disease/syndrome: rare, but an important cause to exclude in obese patients presenting with 'overlap' signs and symptoms :

include striae, depression, and hypertension

SECONDARY CAUSES





SECONDARY CAUSES

• Hypothalamic lesions: gonadal failure, visual disturbances, headache,

or raised intracranial pressure often predominate as presenting signs,

rather than weight gain and hyperphagia.

.

SECONDARY CAUSES

• Polycystic ovary syndrome (PCOS): strongly linked to overweight and obesity but mechanism unclear. Features of hyperandrogenism and Oligomenorrhoea may result from obesity itself.

• Iatrogenic: drugs, e.g. antipsychotic medication, hypoglycaemics (including insulin) glucocorticoids. Also recreational drugs, e.g. cannabis

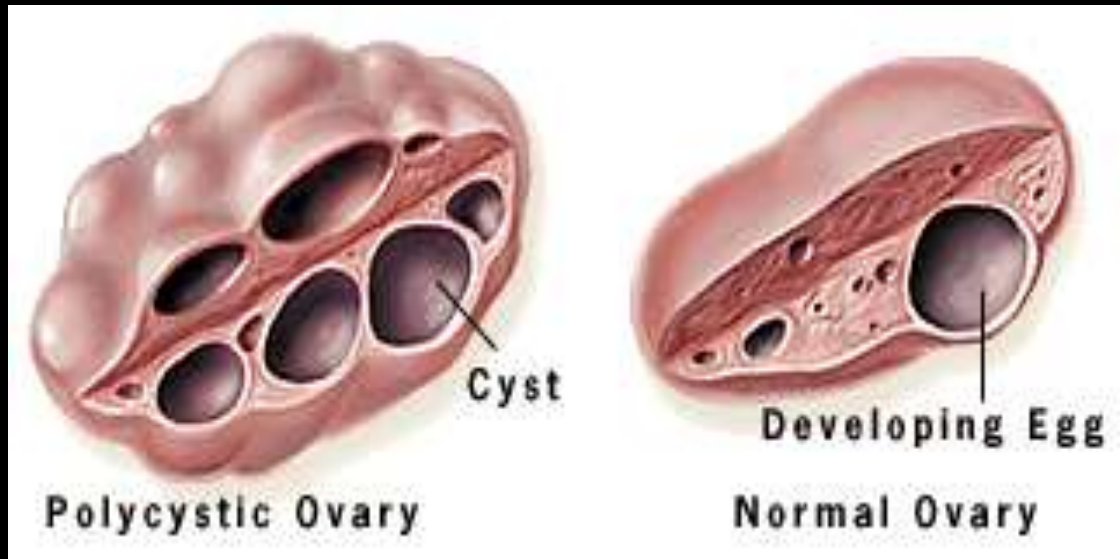


Figure 2

Secondary Causes of Obesity

1. Hypothyroidism
2. Cushing's syndrome
3. Insulinoma
4. Hypothalamic obesity
5. Polycystic ovarian syndrome
6. Genetic syndromes such as Prader Willi, Alstroms, Bardet Biedl, Cohens, Borjeson Forssman Lehmann and Frohlich's syndrome
7. Growth hormone deficiency
8. Oral contraceptive use
9. Pregnancy
10. Medication related: including phenothiazines, sodium valproate, carbamazepine, tricyclic antidepressants, lithium, glucocorticoids, megesterol acetate, the thiazolidine diones, the sulphonylureas, insulin, adrenergic antagonists, serotonin anatagonists especially cyproheptadine.
11. Smoking cessation
12. Eating disorders; especially binge eating disorder, bulimia nervosa and night eating disorder
13. Hypogonadism
14. Pseudohypoparathyroidism
15. Tube feeding related obesity

PATHOPHYSIOLOGY OF OBESITY
LEPTIN

- Synthesized in, and secreted by, adipose tissue (subcut > visceral).
- Encoded by *LEP* gene (chromosome 7q31.3).
- Hypothalamic receptors, activated through entry via arcuate nucleus (exposed to peripheral circulation), decrease food intake and increase energy expenditure (by sympathetic activation).
- Stimulated by glucocorticoids.
- Human obesity persists, despite high circulating levels of leptin (proportional to fat mass), suggesting resistance to effects or that, in human physiology, leptin signals low body fat stores, such as in starvation.
- Mutations in *LEP* lead to a rare syndrome of hyperphagia, obesity,

LEPTIN

hypogonadism, and impaired immunity. Features are reversed by recombinant leptin replacement.

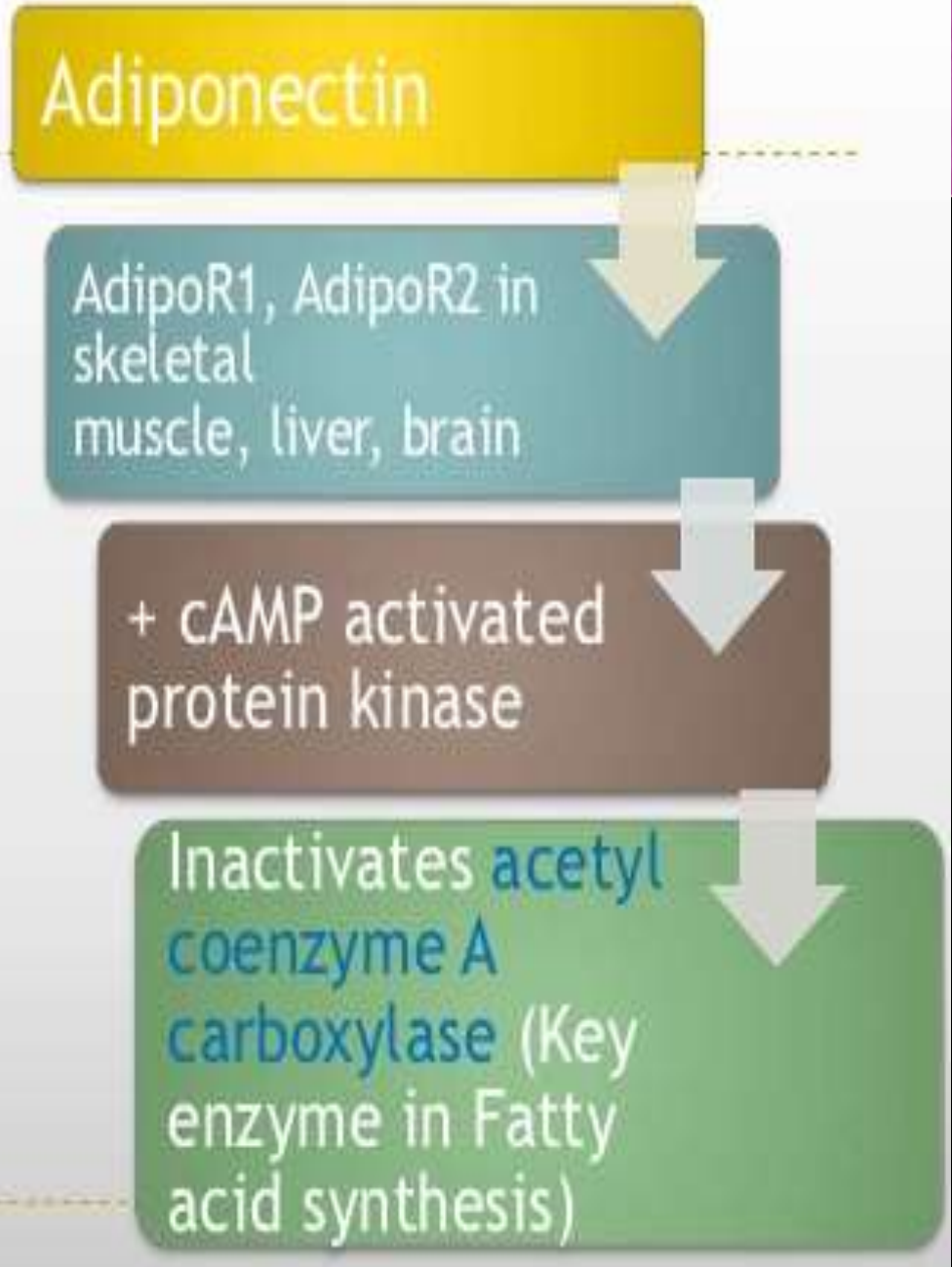
• In conditions of selective decrease in adipose tissue mass (lipodystrophy, HIV or HIV therapy-associated lipoatrophy, severe anorexia nervosa), leptin replacement therapy reverses insulin resistance.

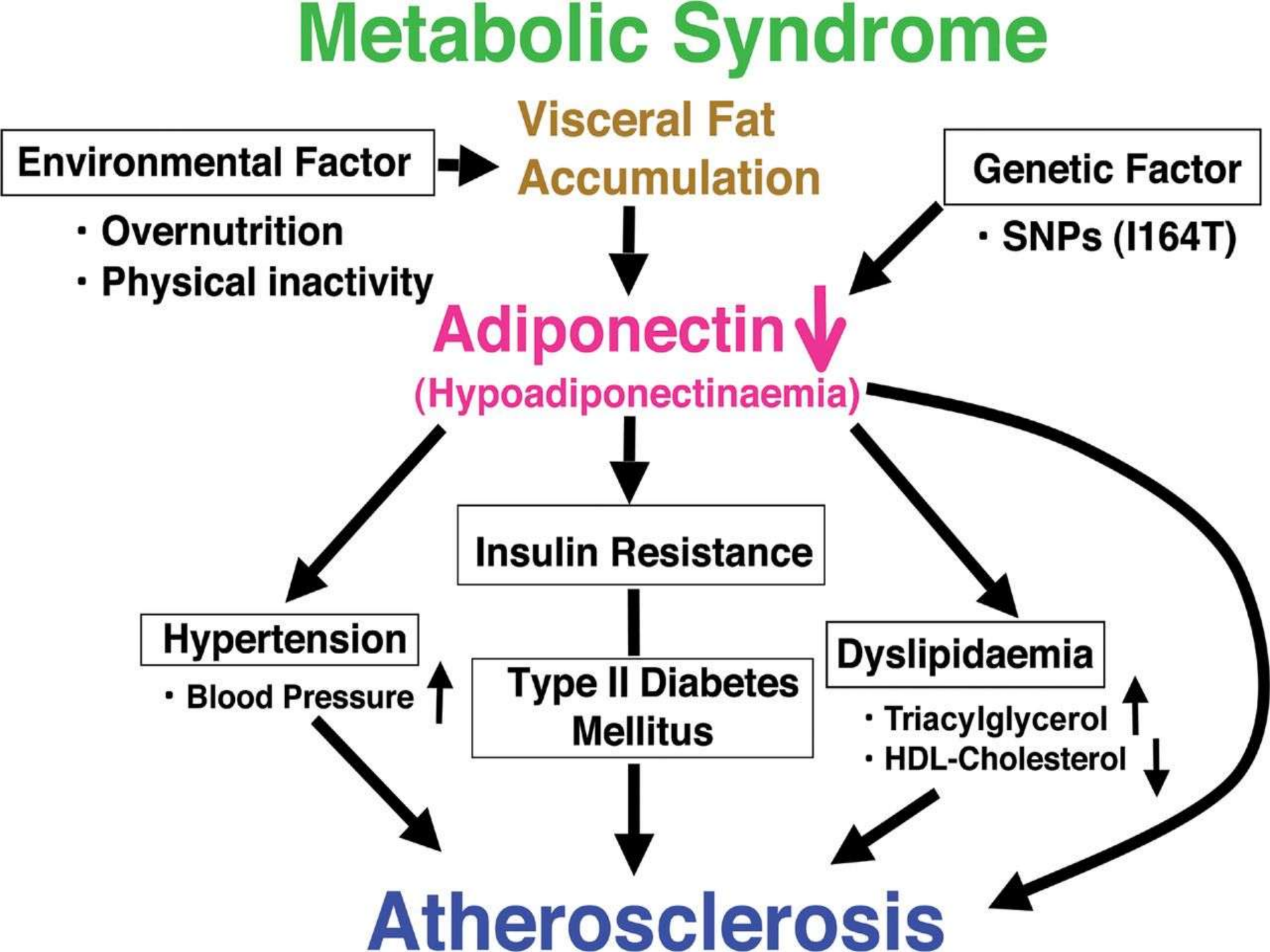
• In response to fasting, leptin levels fall rapidly before, and out of proportion to, changes in fat mass, triggering the neuroendocrine response to acute energy deprivation.

• Trials of leptin augmentation in common obesity do not lead to weight loss or maintenance of weight loss

Adiponectin

- Produced mainly by adipocytes
- Low levels in obesity
- Stimulates fatty acid oxidation
- "Fat-burning molecule"
- "Guardian angel against obesity"
- ↓ fatty acid influx in liver, liver glucose production
- ↓ Protects against Metabolic syndrome




Metabolic Syndrome
Visceral Fat Accumulation
Environmental Factor
• Overnutrition
• Physical inactivity
Genetic Factor
• SNPs (I164T)
Adiponectin ↓
(Hypoadiponectinaemia)
Insulin Resistance
Hypertension
• Blood Pressure ↑
Type II Diabetes Mellitus
Dyslipidaemia
• Triacylglycerol ↑
• HDL-Cholesterol ↓
Atherosclerosis

GUT PEPTIDE HORMONES LINKED TO WEIGHT REGULATION

Ghrelin

• The only known ‘hunger’ hormone.

• Derived from preproghrelin secreted in the stomach, cleaved to active form acyl ghrelin (28 amino acid peptide) and obestatin.

• Acts on hypothalamic GH secretagogue receptors (GHSR1a) to increase the release of GH from the pituitary.

• Peripherally injected ghrelin increases food intake through the stimulation of ghrelin receptors on hypothalamic neuropeptide Y-expressing neurons and agouti-related protein-expressing neurons.

.

• Levels in obesity not consistently elevated but are markedly reduced

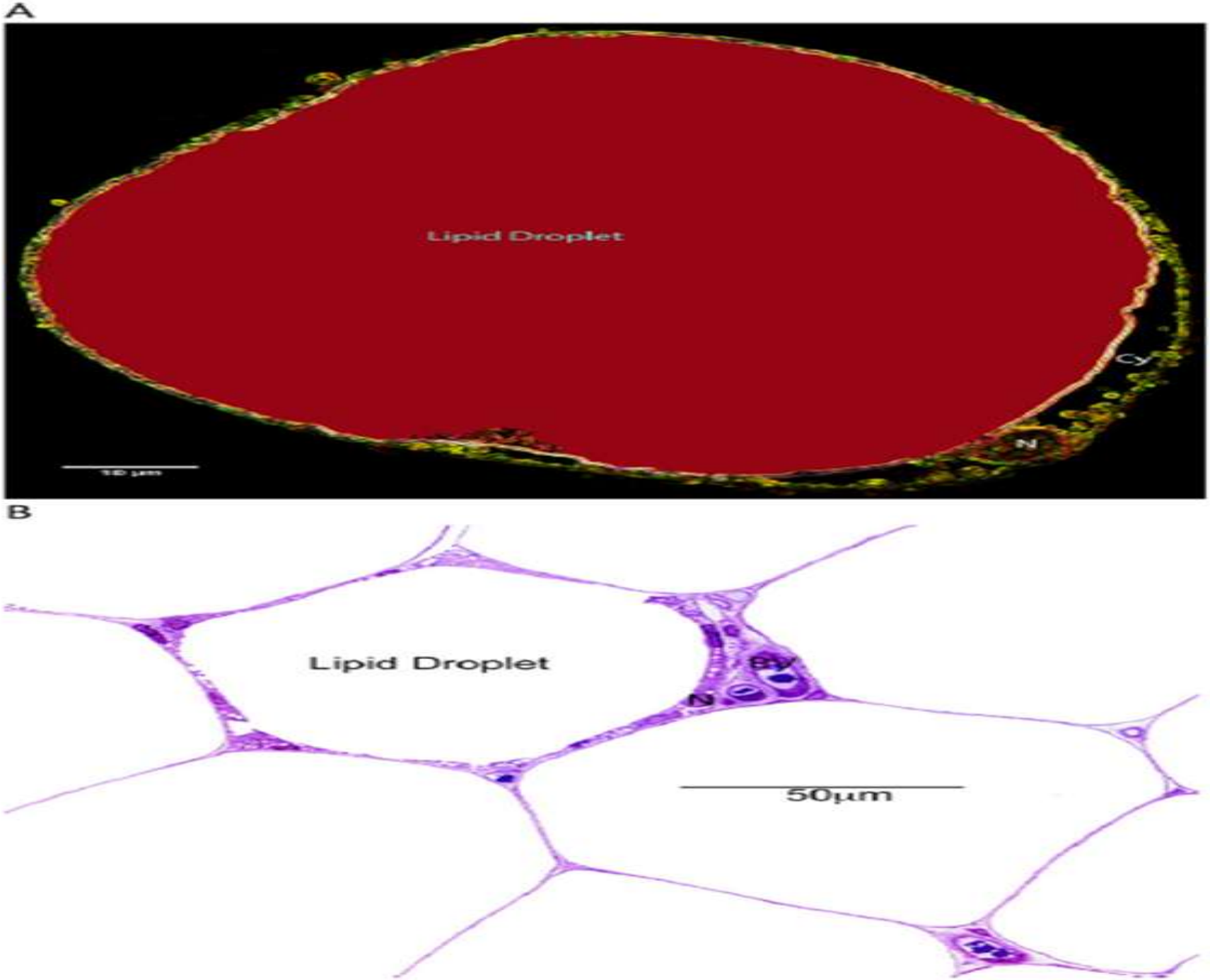
by bariatric surgery (sleeve gastrectomy and gastric bypass).

• Circulating ghrelin increases preprandially and decreases postprandially and is thought to regulate premeal hunger and meal initiation.

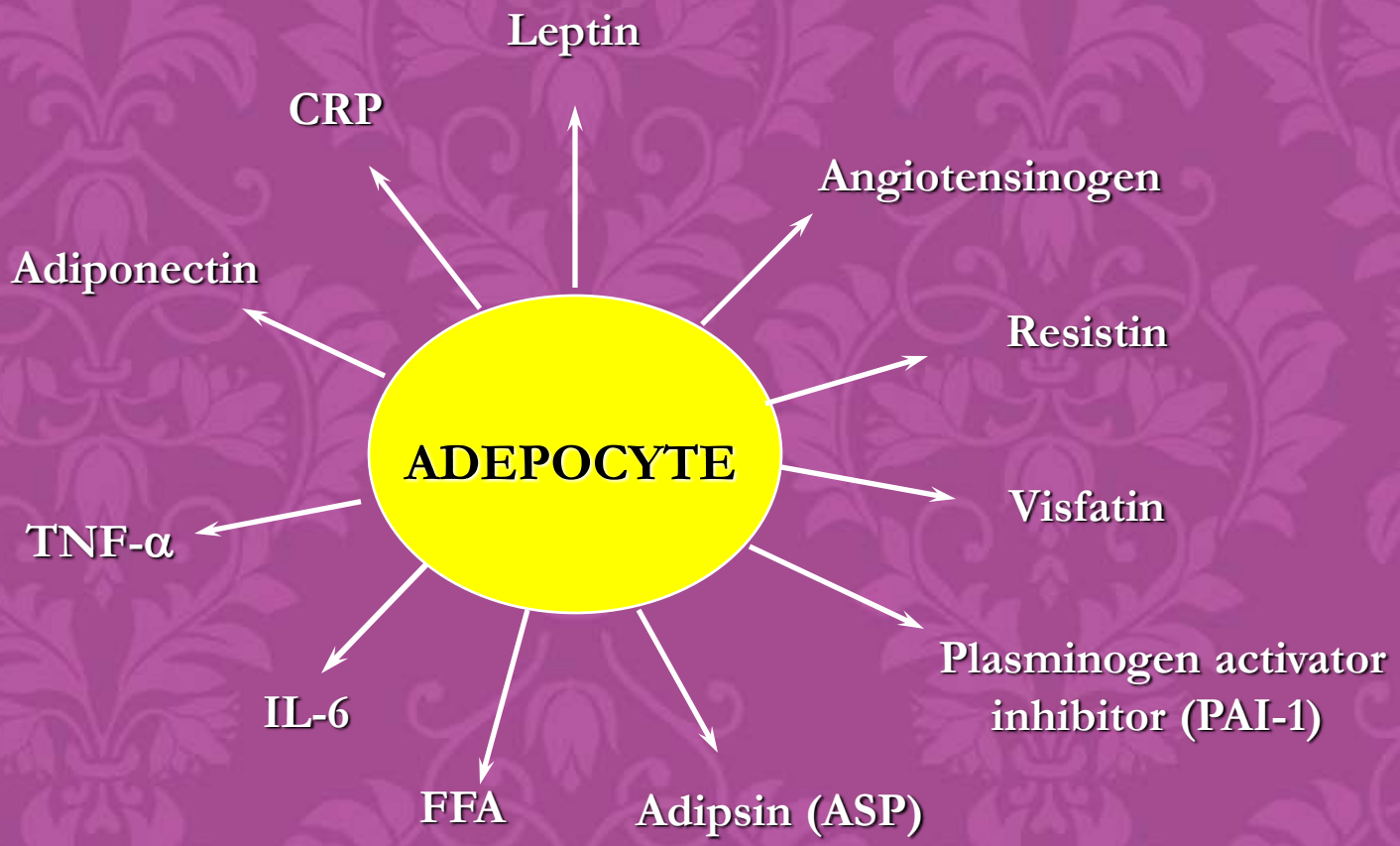
GLUCAGON-LIKE PEPTIDE-1 (GLP-1

)

• Secreted by L-cells in the distal intestine.
• Stimulates insulin secretion and (in animals) islet cell differentiation and proliferation.
• Inhibits glucagon secretion; inhibits gastric emptying.
• Unlike GIP, levels of GLP-1 are reduced in patients with diabetes.
• Levels raised preferentially by protein, accounting, in part, of protein's higher satiating effects compared to other macronutrients.
• GLP-1 analogues (exenatide and liraglutide) are associated with 75% weight loss.
• Liraglutide, in higher doses than used for diabetes treatment, produces sustained weight loss >10% in non-diabetic subjects.
•• Levels markedly elevated after bariatric surgery.

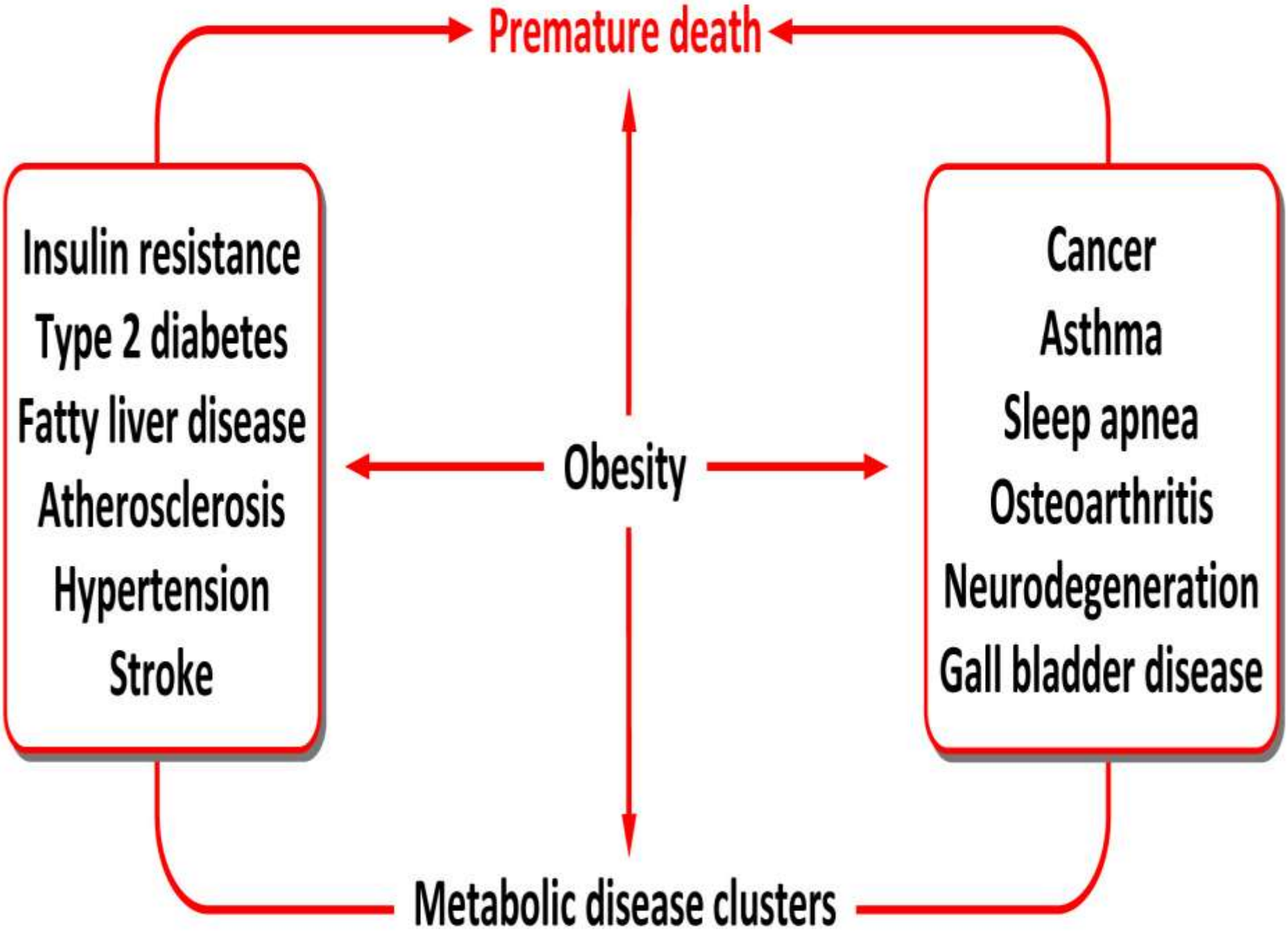

A
Lipid Droplet
Cy
N
10 µm
B
Lipid Droplet
Cy
N
50µm

ADIPOSE TISSUE



- Hypertrophy (enlargement) – overweight (BMI 25-29.9) and moderate obesity (BMI 30-34.9) characterized by adipocyte hypertrophy

- Hyperplasia (increase in number) – extreme obesity (BMI >40) characterized by hyperplasia as well as hypertrophy


Premature death
Insulin resistance
Type 2 diabetes
Fatty liver disease
Atherosclerosis
Hypertension
Stroke
Obesity
Cancer
Asthma
Sleep apnea
Osteoarthritis
Neurodegeneration
Gall bladder disease
Metabolic disease clusters

OBESITY ASSOCIATIONS AND CONSEQUENCES

Mortality rates rise steadily at BMI >5kg/m2.

'Mental'

Depression

Low self-esteem

Attention deficit disorder

Eating disorder

Cognitive impairment

‘Mechanical’

Sleep apnoea

Hypoventilation

Osteoarthritis

Chronic pain

Gastro-oesophageal reflux

Incontinence

Thrombosis

‘Metabolic’

Type 2 diabetes

Dyslipidaemia

Hypertension

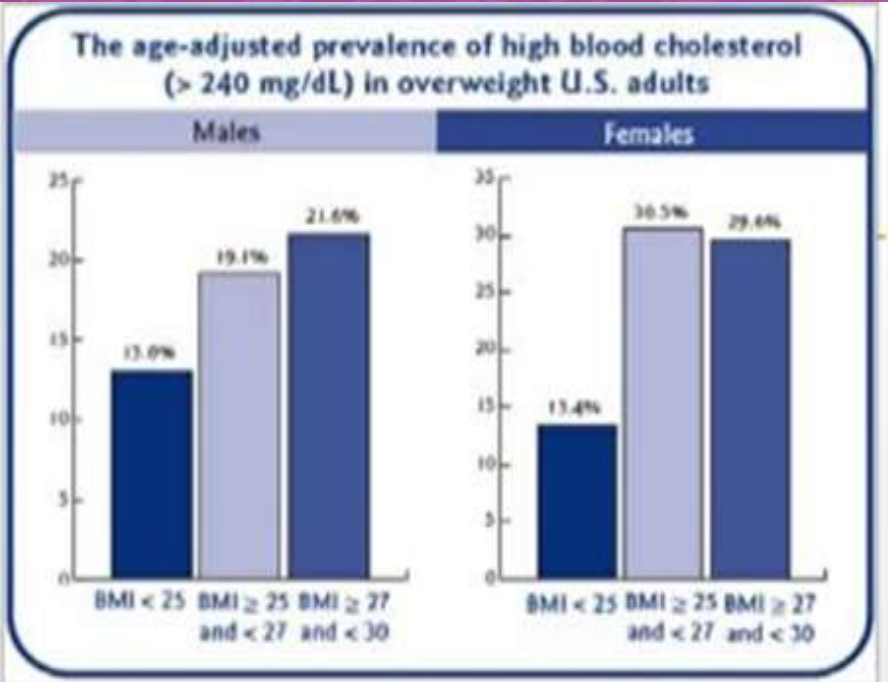
IHD

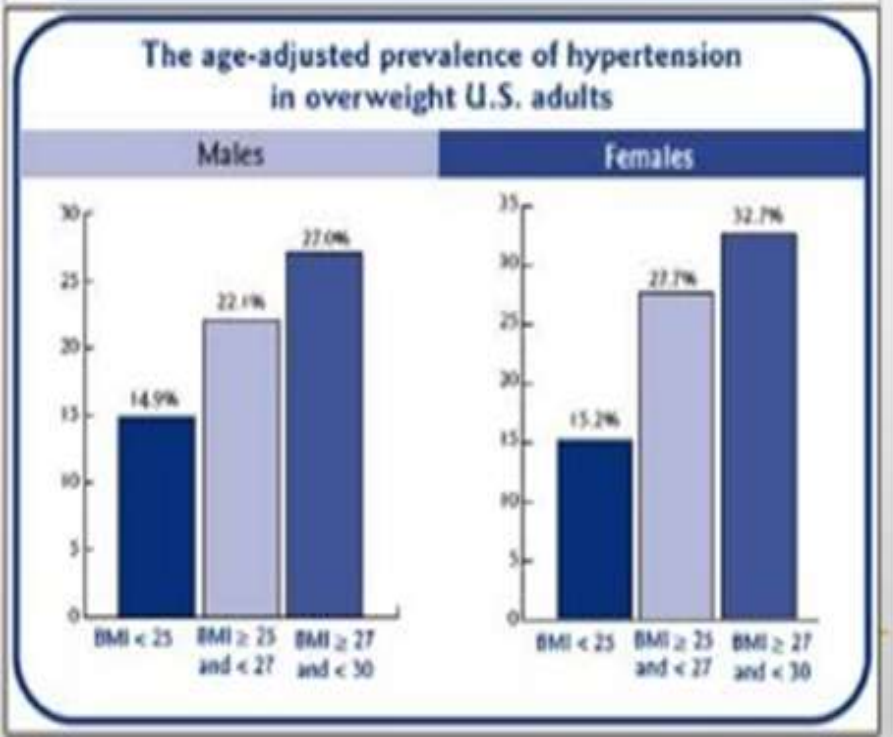
Gout

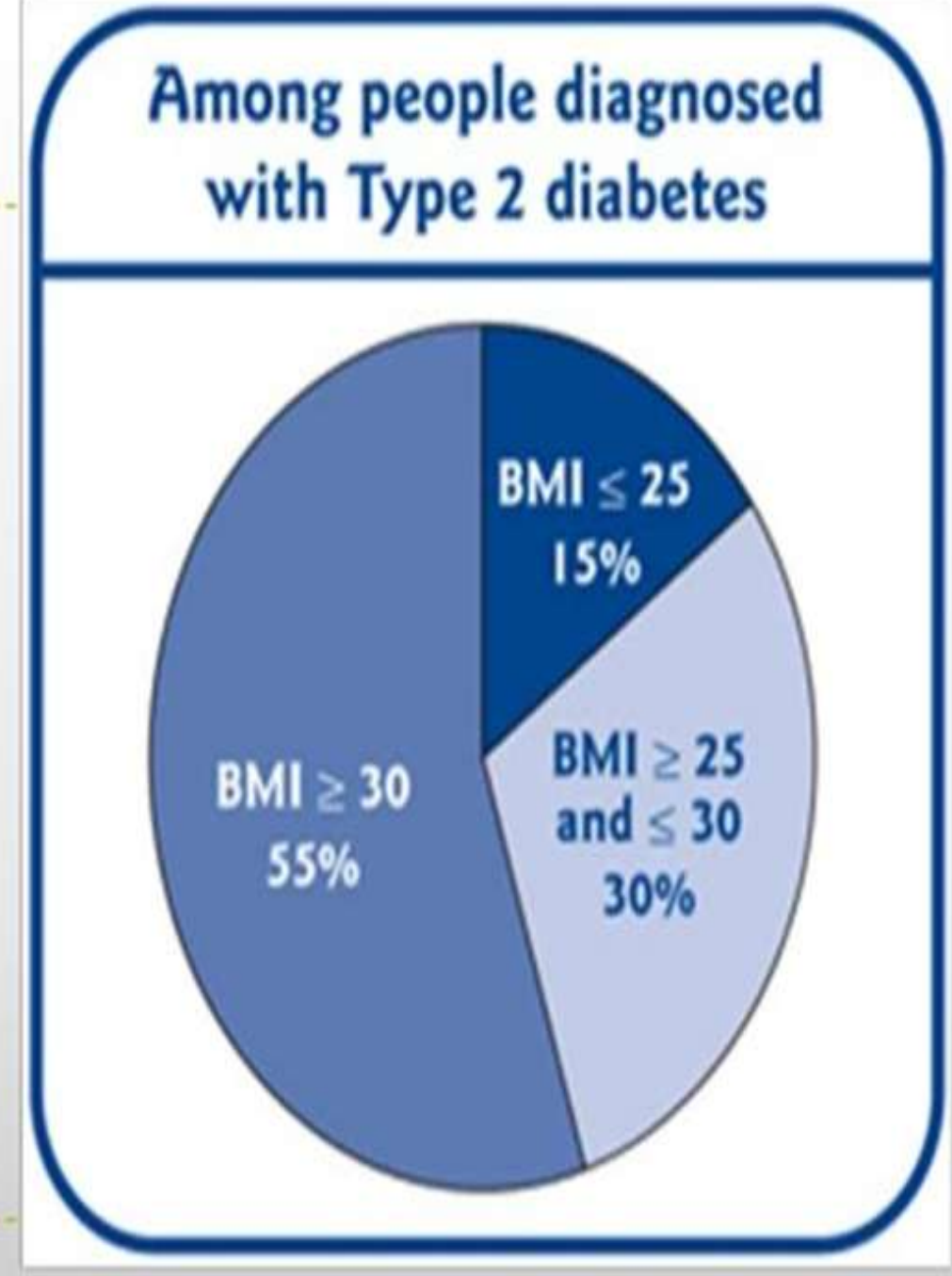
NAFLD and

NASH

Cancer


The age-adjusted prevalence of high blood cholesterol
(> 240 mg/dL) in overweight U.S. adults
Males
Females
13.0%
19.1%
21.6%
13.4%
30.5%
29.6%
BMI < 25
BMI ≥ 25 and < 27
BMI ≥ 27 and < 30


The age-adjusted prevalence of hypertension
in overweight U.S. adults
Males
Females
14.9%
22.1%
27.0%
15.2%
27.7%
32.7%
BMI < 25
BMI ≥ 25 and < 27
BMI ≥ 27 and < 30


Among people diagnosed with Type 2 diabetes
BMI ≤ 25
15%
BMI ≥ 25
and ≤ 30
30%
BMI ≥ 30
55%

Treating Obesity as a Disease

HISTORY

• Weight history from birth onwards (early onset may suggest genetic syndromes).

• Previous treatment/management strategies and their success.

• Current eating habits and triggers for eating/activity levels.

• Family history.

• Symptoms or previous diagnosis of obesity-related diseases, including

CVD, diabetes, psychological issues (eating disorder, depression, low

self-esteem), OA, obstructive sleep apnoea, PCOS.

• Symptoms of reflux.

• • Drugs that might exacerbate weight gain..

EXAMINATION

• Height, weight, fat distribution.
• General: evidence for syndrome (e.g. small hands and facies in Prader–Willi syndrome), mood.
• Skin: acanthosis nigricans and skin tags (insulin resistance), intertrigo, fat distribution (partial lipodystrophy).
• Cardiovascular: hypertension, heart failure, and other causes for breathlessness.
• Respiratory: airway, obstructive sleep apnoea (somnolence), pulmonary hypertension, cardiopulmonary fitness (consider 6-minute walk test).
• GI: hepatomegaly, herniae (may influence bariatric surgery).
• Musculoskeletal: mobility.
• Consider other diagnoses: hypothyroidism, Cushing's syndrome, haemochromatosis.

INVESTIGATIONS

- Blood count and iron studies (iron deficiency anaemia from reflux or GI bleeding; polycythaemia from hypoventilation).
- Renal function.
- Liver function (non-alcoholic steatohepatitis).
- Glucose, HbA1c, and possibly insulin (prediabetes, diabetes).
- Fasting lipid profile (raised triglycerides, total and LDL cholesterol, lowered HDL cholesterol).
- Vitamin D (often deficient in the obese).
- Thyroid function (hypothyroidism).
- ECG (atrial fibrillation, left ventricular hypertrophy

TREATMENT OPTIONS INCLUDE

- Dietary intervention.
- Physical activity.
- Psychological counselling.
- Anti-obesity medication.
- Bariatric surgery.

DIETARY INTERVENTION.

Dietary energy restriction produces greater weight loss than exercise..

A weight loss of 5–10% of the initial body weight reduces many

of the health risks associated with obesity and reduces cancer and

diabetes-related mortality;

a 5kg loss in adults with prediabetes reduces

progression to diabetes by 60%, maintained even if weight regain occurs. In

patients with a BMI >35kg/m_2, greater weight loss (>10kg or 15%) is likely

to be needed to produce a sustained improvement in comorbid diseases;.

ANTI-OBESITY DRUGS

In Europe, only orlistat is licensed; elsewhere, phentermine is widely

Prescribed

Orlistat

• Intestinal pancreatic lipase inhibitor; reduces fat absorption.

• Increases dietary fat loss to 30% (compared to <5% on placebo).

• Best used in those at medical risk from obesity: BMI >30kg/m_2 or BMI >27 with established comorbidities (e.g. diabetes, heart disease, dyslipidaemia).

•

- May have modest insulin-sensitizing effects over and above weight loss

(reduced portal triglyceride levels).

- Only use in patients who achieve at least 2.5kg weight loss in 4 weeks

using a dietary programme alone (NICE guidelines). This ensures

adequate dietary compliance with a low-fat diet (ideally <50g/day) and

minimizes GI side effects.

- Average weight loss of 8% at 1 year.

NICE GUIDELINES

:

- At 3 months, stop if <5% weight loss.
- At 6 months, stop if <10% weight loss (of initial weight).

• Contraindications: cholestasis, hepatic dysfunction, malabsorption, pregnancy, breastfeeding, concomitant use of fibrate, acarbose, renal impairment (creatinine >150micromol/L), anticoagulation (possible d vitamin K absorption with orlistat).

• Consider vitamin supplementation (especially vitamin D) if used beyond 1 year.

• Side effects (must warn patient): flatus (24%), oily rectal discharge, fatty stool (20%), faecal urgency (22%), fat-soluble vitamin deficiency,
incontinence (8%). Limited by dietary fat reduction (to <35% of energy).

BARIATRIC SURGERY

usually done laparoscopically.

The most compelling data for the success of bariatric surgery

at producing weight loss and improving the clinical outcomes for obese

patients come from the 20-year follow-up data

BARIATRIC SURGERY

bariatric surgery is associated with reduced all-cause mortality, including

deaths from CVD, diabetes, and cancer.

In patients with type 2 diabetes, benefit extends beyond weight loss. Up

to 80% of people with type 2 diabetes may experience remission of their

diabetes

GASTRIC BYPASS

Patients will lose approximately 50–75% of their excess weight (30–40% absolute weight loss) within 12–18 months of surgery. Routine supplementation of vitamins, minerals, and

vitamin B12 is required.

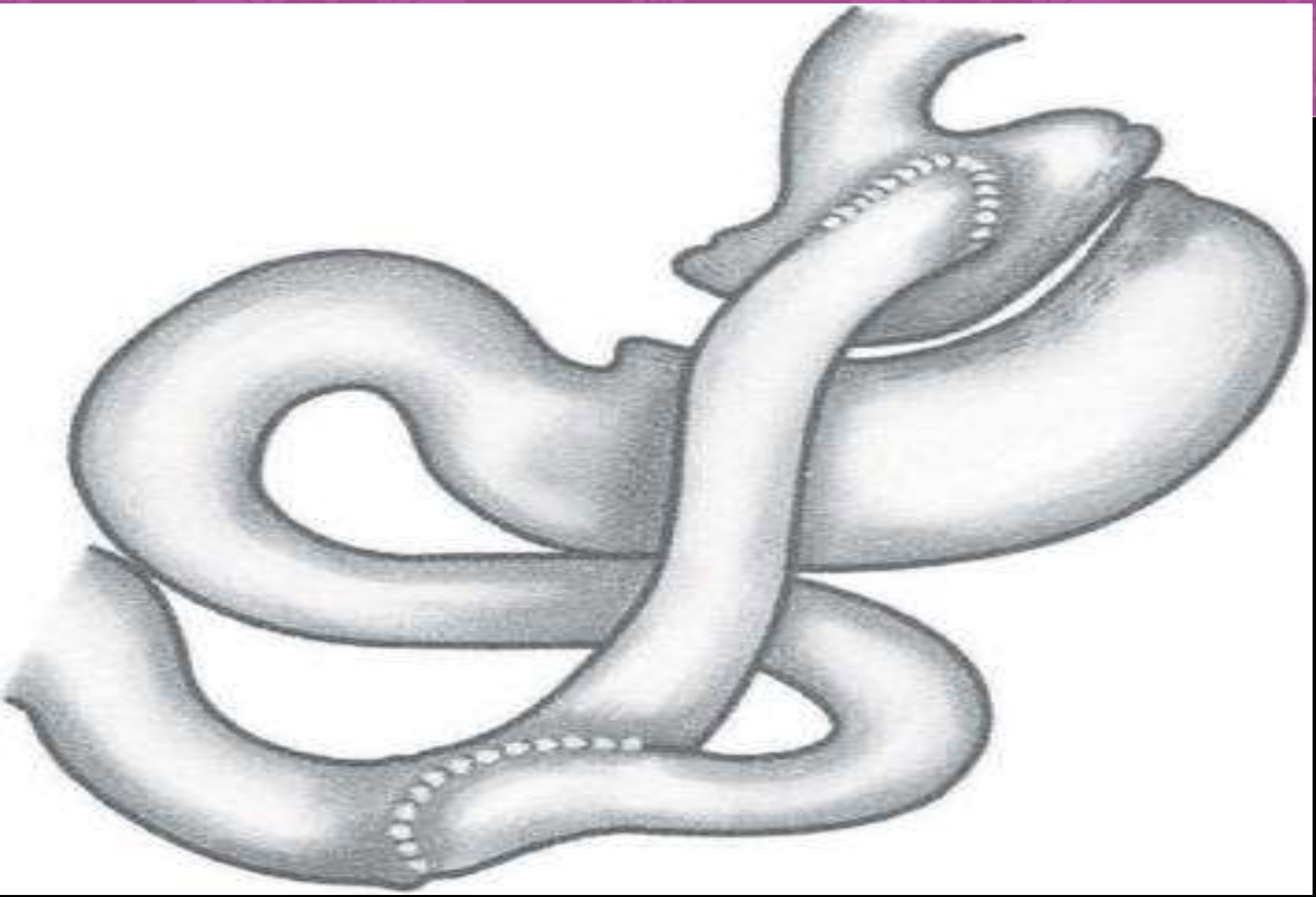
The gastric bypass works in the following way:

• There is a restriction in food intake, as the stomach is reduced to the size of a large egg.

- malabsorption.

• reduced ghrelin, increased and earlier release of GLP-1 and PYY).

• Other mechanisms, involving changes in gut flora and bile salt metabolism that affect appetite.



SLEEVE GASTRECTOMY

Patients will lose approximately 50–75% (30–40% absolute weight loss) of their excess weight within 12–18 months of surgery. Again, >80% have

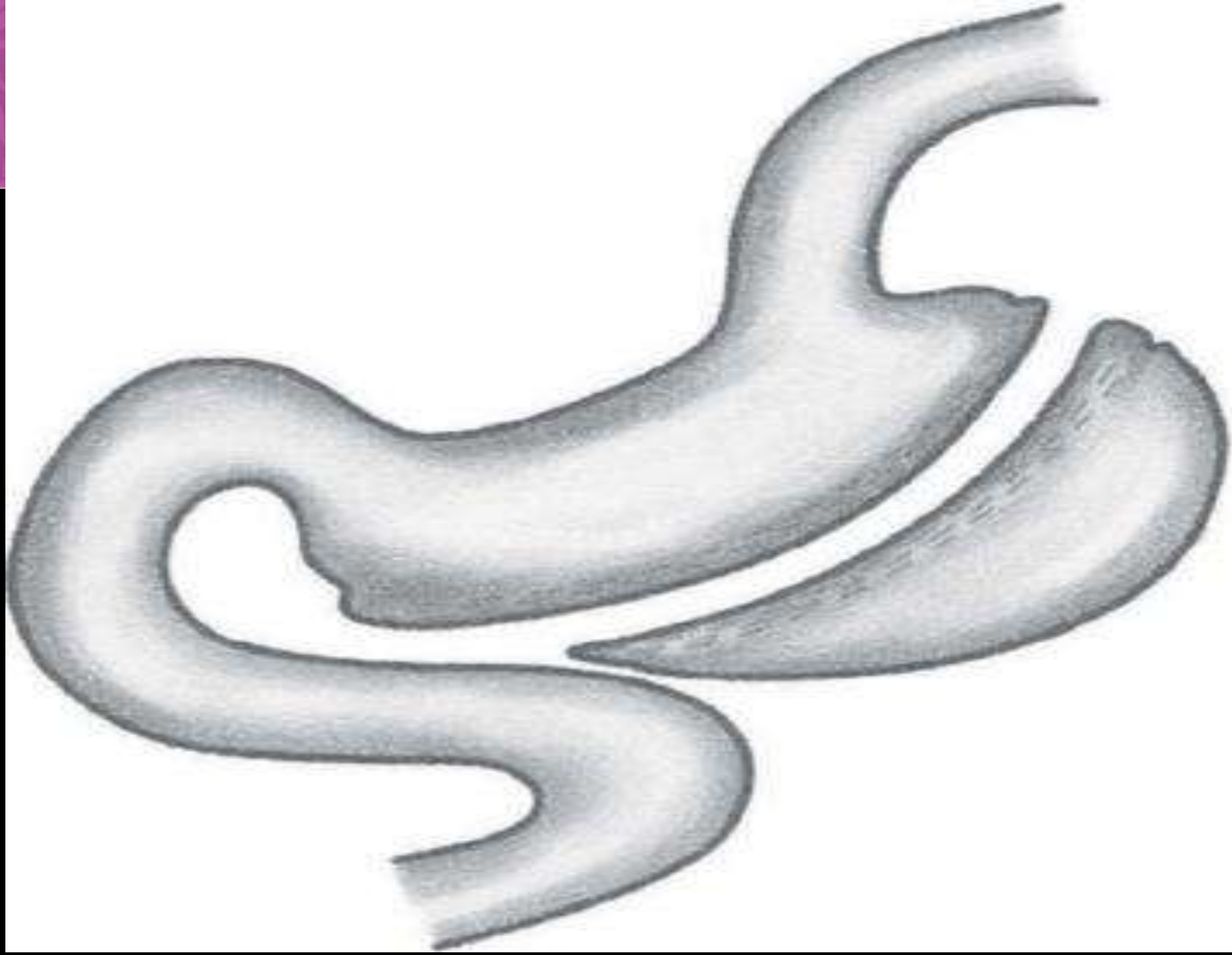
a significant improvement in weight-related illnesses and improved QoL.

Routine supplementation of vitamins is required for the first year.

The sleeve gastrectomy works in the following way:

• 75% of the stomach is removed, restricting the volume of food patients are able to eat in one sitting.

• Gastric emptying is faster which alters gut hormone profiles, resulting in satiety (reduced ghrelin, increased and earlier release of GLP-1 and PYY).



ADJUSTABLE GASTRIC BANDING

Patients will lose approximately 50% of their excess weight (30% absolute

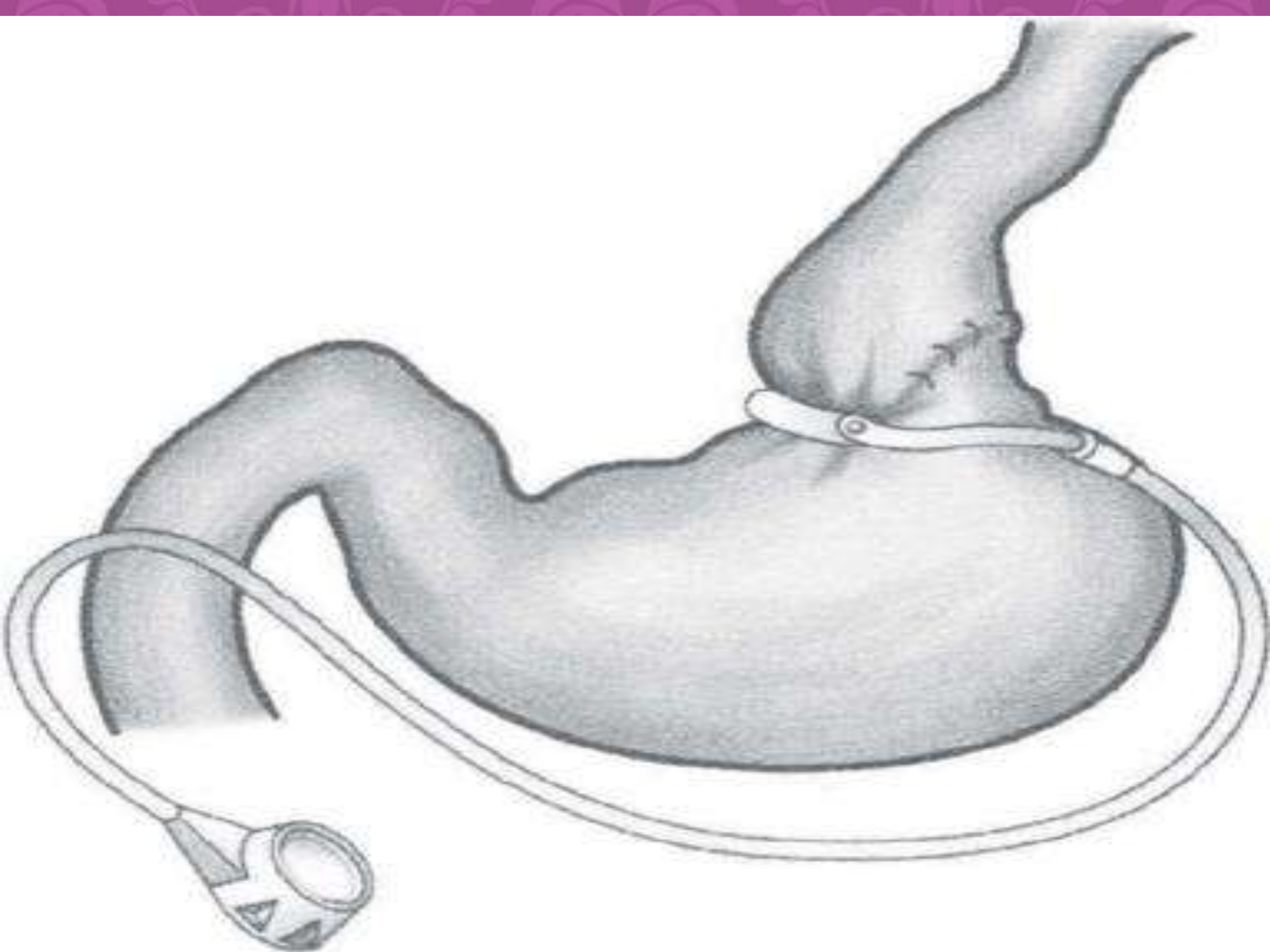
weight loss) within 2–3 years of surgery. Routine supplementation of vitamins,

minerals, and vitamin B12 is not usually needed beyond the first year.

The gastric band works in the following way:

• Gastric restriction is achieved by placing an adjustable silastic band around the upper gastric cardia that can be tightened or loosened by injecting saline into a tube that connects to a port under the skin. The restriction slows the speed of eating.

• Patients are required to attend clinic for band consultations every 2–3 months until the right degree of band adjustment is achieved



GASTRIC SLEEVE PLICATION SURGERY

the surgeons reduces the size of the stomach by creating an internal fold within the org

There is no removal of stomach tissue

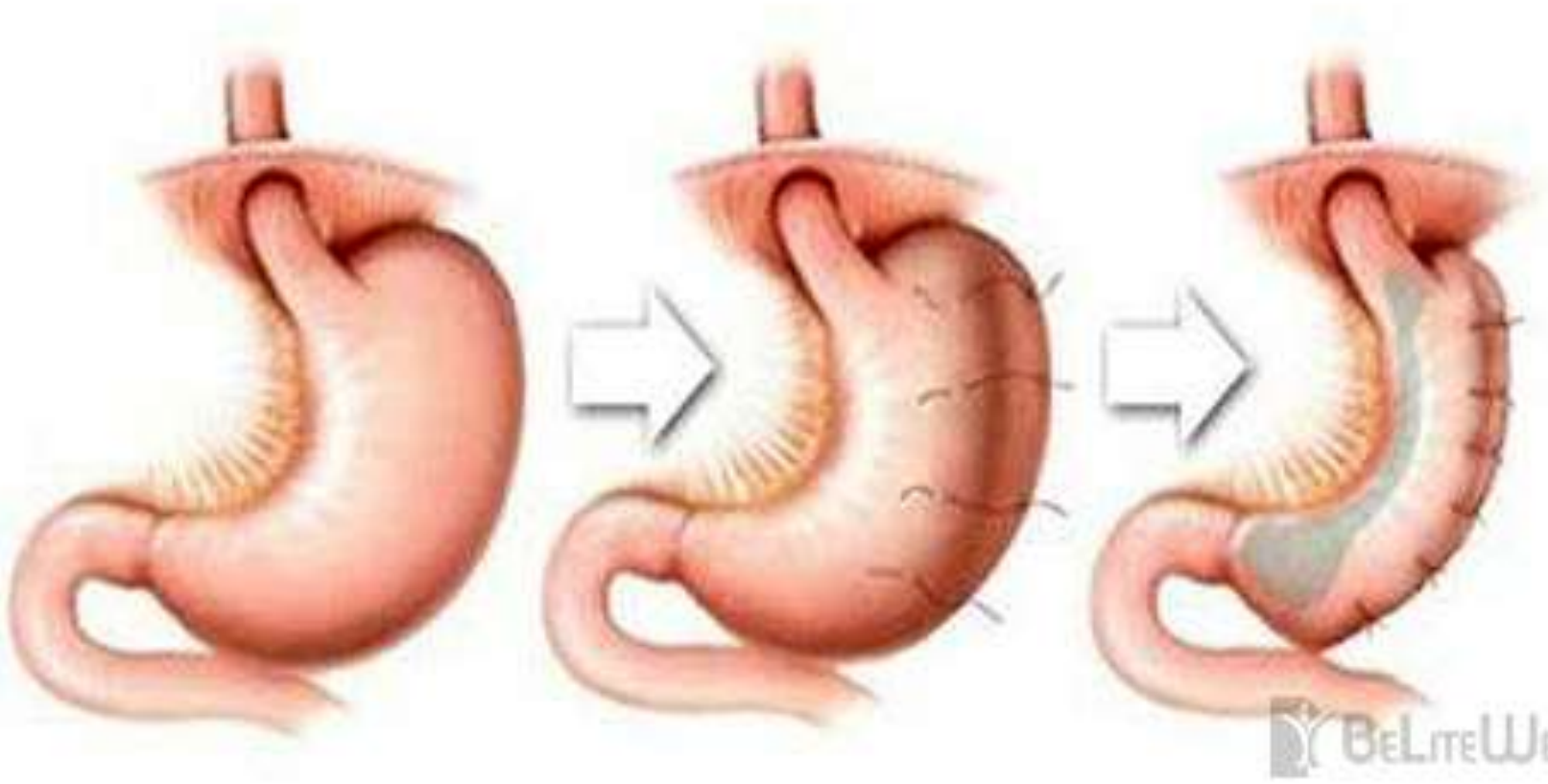
The procedure is completely reversible

The ability of the stomach to absorption nutrients is not compromised

The risk of short time complications is lower

The procedure doesn't require staples, meaning there is no possibility for leaking, bleeding, or rejection of a foreign object.

GASTRIC SLEEVE PLICATION



THANKS