OBESITY

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DEFINITION

- Obesity is defined as an accumulation of excess body fat (Adipose tissue) that is of sufficient magnitude to impair health.
- Obesity is regarded as a global pandemic, or 'syndemic' as it entails potentially disastrous consequences for human health.
- **Types of Obesity According to Body Fat Distribution**

1. **Central ('abdominal', 'visceral', 'android' or 'apple-shaped') obesity**: Increased accumulation of fat in the trunk and in the abdominal cavity/intra-abdominal (in the mesentery and around viscera). Associated with a greater risk for several diseases (e.g. type 2 diabetes, the metabolic syndrome and cardiovascular disease) than generalized obesity.
2. **Generalized ('gynoid' or 'pear-shaped') obesity**: Excess accumulation of fat diffusely in the subcutaneous tissue

ETIOLOGY

- Accumulation of fat results from a discrepancy between energy consumption and energy expenditure that is too large to be defended by the hypothalamic regulation of BMR

22.7 Secondary causes of weight gain

Endocrine factors

- Hypothyroidism
- Cushing's syndrome
- Insulinoma
- Hypothalamic tumours or injury

Drug treatments (worse in combination)

- Atypical antipsychotics (e.g. olanzapine)
- Antidepressants (e.g. amitryptyline, mirtazepine)
- Gabapentin, pregabalin
- Sulphonylureas, thiazolidinediones, insulin
- Pizotifen
- Glucocorticoids
- Sodium valproate
- β-blockers

22.5 Some reasons for the increasing prevalence of obesity – the 'obesogenic' environment

Increasing energy intake

- ↑ Portion sizes
- ↑ Snacking, grazing and loss of regular meals
- ↑ Energy-dense 'added-value' food (fat and sugars)
- ↑ Affluence
- Effective marketing

Decreasing energy expenditure

- ↑ Car ownership
- ↓ Walking to school/work
- ↑ Automation/domestic labour-saving
- ↓ Manual labour in occupations
- ↓ Sports in schools
- ↑ Time spent on computer games and watching TV
- ↑ Central heating, washing machines

GENETIC CAUSES

Children are at an increased risk for obesity if their parents are obese.

- one parent obese - 3-4 times more risk
- both parents obese - 10–12 times more likely to be obese.

POLYGENIC OBESITY

- Small contributions from different genes.
- Genes affected are PPARG (peroxisome proliferator activator receptor gamma), Adiponectin, and Leptin.

MONOGENIC OBESITY

- Single gene disorders.
- Mutations in the leptin gene and leptin receptor gene, mutations of POMC (Proopiomelanocortin), Mc4R (melanocortin-4 receptor) genes.

GENETIC SYNDROMES

- Alstrom syndrome
- Laurence – Moon - Biedl syndrome
- Carpenter syndrome
- Cohen syndrome
- Prader willi syndrome
- Downs syndrome
- Turner syndrome
- Frohlich syndrome
- Leptin/leptin receptor gene mutation
- Melanocortin 4 receptor gene mutation

ENVIRONMENTAL CONTRIBUTORS

FOOD

- Increased consumption of energy-dense foods
- larger food portion size
- increased variety of food
- increased availability
- reduced cost
- increased caloric beverages (soft drinks, juices)

PHYSICAL ACTIVITY

- (1) exercise (fitness and sports-related activities)
- (2) work-related physical activity
- (3) non-exercise, non-employment (spontaneous) activity.
- Increased sedentary behavior, reduced activities of daily living and decreased physical activity.

POTENTIALLY REVERSIBLE CAUSES

ENDOCRINE CAUSES

DISEASE	SYMPTOMS
CUSHING SYNDROME	Central obesity, hirsutism, moon face, hypertension
HYPOTHYROIDISM	Short stature, weight gain, fatigue, constipation, cold intolerance, myxedema
INSULINOMA	Nesidioblastosis, pancreatic adenoma, hypoglycemia, Mauriac syndrome
GH DEFICIENCY	Short stature, slow linear growth
STEIN-LEVENTHAL SYNDROME	
HYPOTHALAMIC DAMAGE (due to tumor, trauma)	
PSEUDOHYPOPARATHYR-OIDISM	Short metacarpals, subcutaneous calcifications, dysmorphic facies, mental retardation, short stature, hypocalcemia, hypophosphatemia

DRUG INDUCED CAUSES

- PSYCHIATRIC AND NEUROLOGIC MEDICATIONS : Atypical antipsychotics (eg: olanzapine), pizotifen, sodium valproate, flunarizine.
- STEROID HORMONES: Progestational steroids, corticosteroids, hormonal contraceptives.
- ANTIDIABETES AGENTS: Insulin (most forms), sulfonylureas, thiazolidinediones
- ANTIHYPERTENSIVE AGENTS: α-adrenergic and β-adrenergic receptor blockers

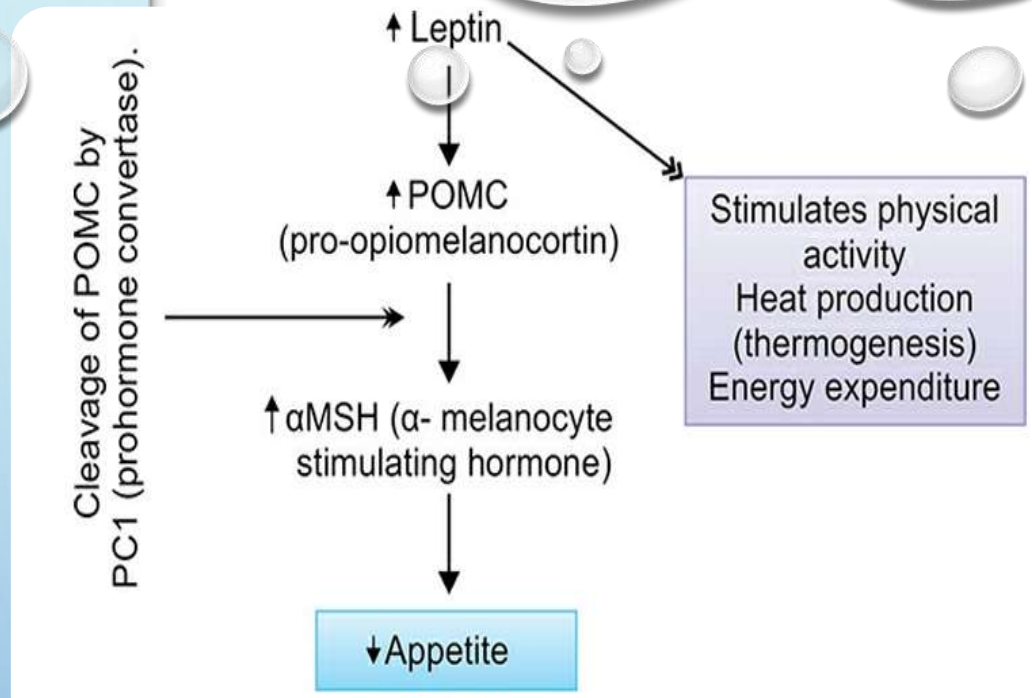
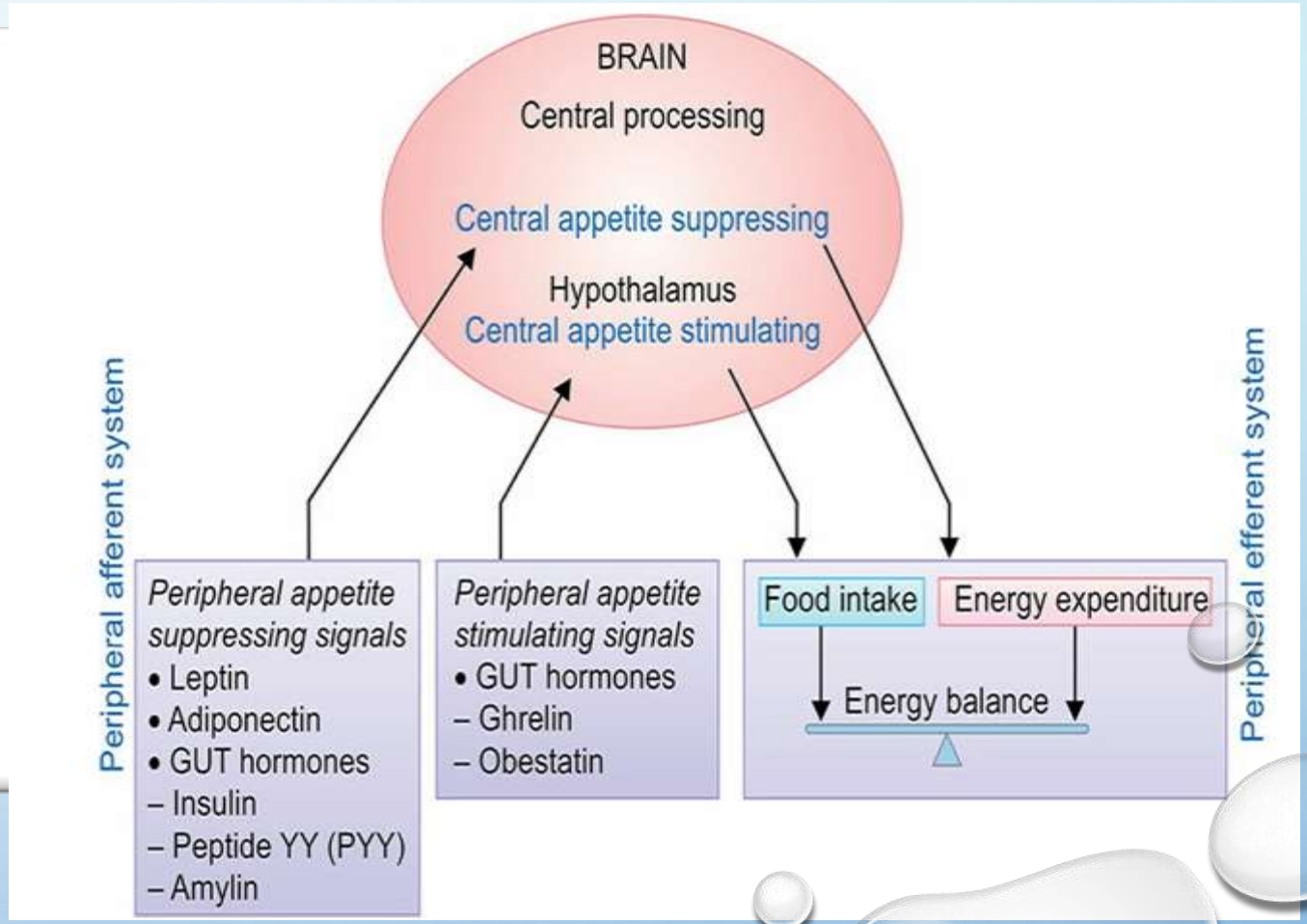


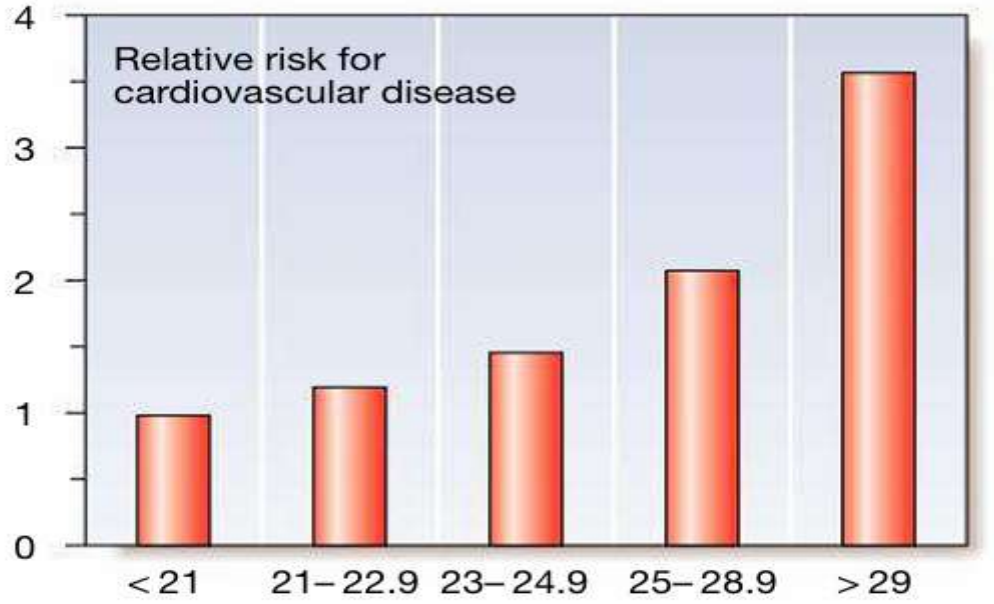
Fig. 1.11: Actions of leptin.

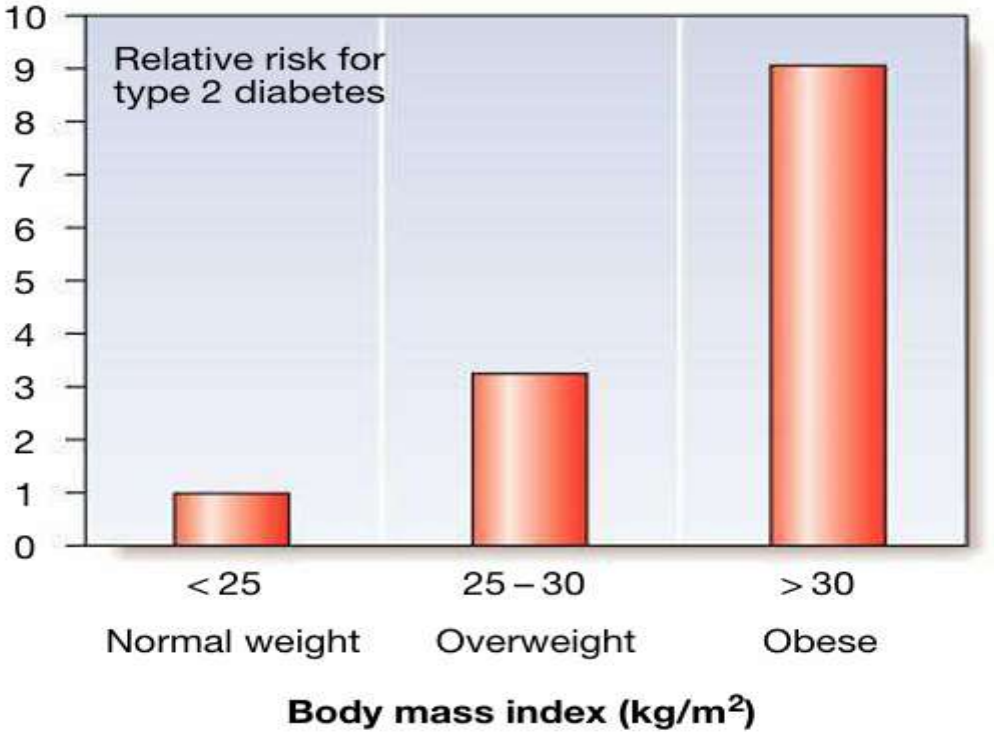


PATHOGENESIS

COMPLICATIONS

- Obesity affects both mortality and morbidity.
- Coronary heart disease is the major cause of death but cancer rates are also increased in the overweight, especially colorectal cancer in males and cancer of the gall bladder, biliary tract, breast, endometrium and cervix in females.





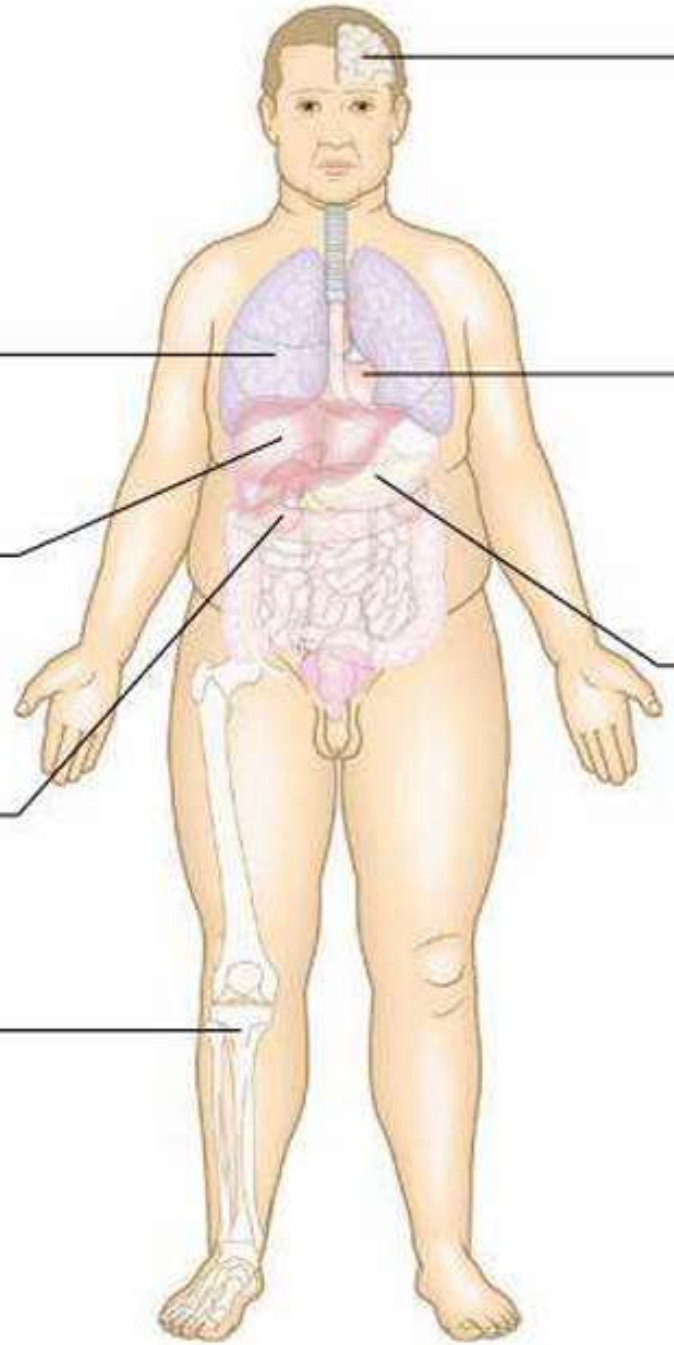
Psychosocial
Eating disorders
Poor self-esteem
Body image disorder
Social isolation and stigmatisation
Depression

Pulmonary
Exercise intolerance
Obstructive sleep apnoea
Asthma

Gastrointestinal
Gallstones
Gastro-oesophageal reflux
Non-alcoholic fatty liver disease
Colon cancer

Renal
Glomerulosclerosis
Renal cancer

Musculoskeletal
Ankle sprains
Flat feet
Tibia vara
Osteoarthritis
Back pain



Neurological
Pseudotumour cerebri
(idiopathic intracranial
hypertension)

Cardiovascular
Hypertension
Dyslipidaemia
Coagulopathy
Chronic inflammation
Endothelial dysfunction

Endocrine
Insulin resistance
Impaired fasting glucose
or glucose intolerance
Type 2 diabetes
Precocious puberty
Menstrual irregularities
Polycystic ovary
syndrome (females)
Hormone-related cancers
(breast, endometrium, prostate)

CLINICAL ASSESSMENT

HISTORY

- Family history of obesity and its complications
- Physical activity, dietary recall and periods of inactivity.
- Increased appetite in a child with recent onset - hypothalamic dysfunction
- History of neurologic infection, head trauma or neurosurgery
- intake of drugs such as steroids and antiepileptics

EXAMINATION

- Features of endocrinopathies, dysmorphic syndromes
- Sexual maturity and ocular examination.
- Hypogonadism is an important feature of obese children with Laurence-Moon-Bardet-Biedl and Prader-Willi syndromes

INVESTIGATIONS

- **BODY COMPOSITION**
  - Anthropometry
  - Bioelectrical impedance
  - Dual x-ray absorptiometry (DXA)
  - Magnetic resonance imaging (MRI)
- **MUSCLE FUNCTION AND GLOBAL NUTRITIONAL STATUS**
  - Hand grip strength (dynamometer test) – poor grip associated with increased mortality
- **OBESITY AND FAT DISTRIBUTION (ANDROID VS GYNOID)**
  - Waist circumference (useful up to BMI 35 kg/m) measured midway between superior iliac crest and lower border of rib cage.
- **BODY FAT CONTENT AND MUSCLE MASS**
  - Triceps skinfold thickness (when combined with mid-/ upper arm circumference estimates muscle mass
  - Triceps skinfold thickness. Lean patients 6–12 mm; obese patients 40–50 mm.

22.6 Quantifying obesity with BMI and waist circumference for risk of type 2 diabetes and cardiovascular disease[1]

BMI (weight in kg/height in m^2)	Classification[2]	Waist circumference[3]		
		Men < 94 cm Women < 80 cm	Men 94–102 cm Women 80–88 cm	Men > 102 cm Women > 88 cm
18.5–24.9	Reference range	Low	*Increased*	**Severe**
25.0–29.9	Overweight	Low	*Moderate*	**Very severe**
>30.0	**Obese**			
30.0–34.9	Class I	*Moderate*	**Severe**	**Very severe**
35.0–39.9	Class II	(not possible)	**Very severe**	**Very severe**
>40.0	Class III	(not possible)	**Very severe**	**Very severe**

[1]Lower cut-offs apply for people of South Asian ancestry, see note 2. High waist circumference is the more potent risk indicator, reflecting increase intra-abdominal and ectopic fat accumulation in vital organs. [2]Classification of the World Health Organization (WHO) and International Obesity Task Force. The Western Pacific Region Office of WHO recommends that, among South Asians, BMI > 23.0 is overweight and > 25.0 is obese. Lower cut-offs for waist circumference have also been proposed for South Asians but have not been validated. [3]When BMI is > 35 kg/m^2, waist circumference is difficult to measure because the waist descends under gravity, so does not add to the increased risk.

All obese patients should have thyroid function tests performed

Overnight dexamethasone suppression test or 24hour urine free cortisol if Cushing's syndrome is suspected clinically

Elevated serum transaminases occur in patients with non alcoholic fatty liver disease.

Blood pressure should be measured with a large cuff, if required. Associated type 2 diabetes and dyslipidaemia are detected by measurement of HbA1c and a serum lipid profile, respectively, ideally in a fasting morning sample.

PREVENTION AND MANAGEMENT

- Aims at reducing the imbalance between energy intake and output.
- A stepwise approach is suggested depending on the severity of obesity, presence of complications and the response of interventions.
- It includes:

1. Dietary interventions
2. Physical activity
3. Behavioral interventions
4. Pharmacotherapy
5. Surgery

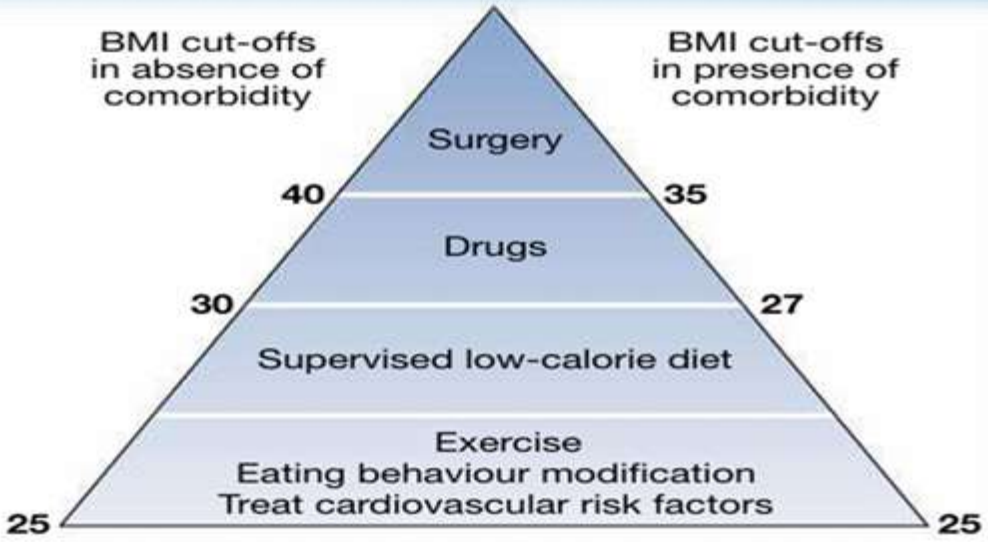


Fig. 22.8 Therapeutic options for obesity. Relevant comorbidities include type 2 diabetes, hypertension, cardiovascular disease, sleep apnoea, and waist circumference of >102 cm in men or 88 cm in women. This is an approximate consensus of the numerous national guidelines, which vary slightly in their recommendations and are revised every few years. (BMI = body masss index).

TABLE 15.21: Obesity—treatment according to BMI category (kg/m^2) for Asian Indians.

Treatment	≥23	≥25	≥27.5	≥32.5	≥37.5
Diet, exercise, behavior	+	+	+	+	+
Pharmacotherapy		With comorbidities	+	+	+
Bariatric surgery				With comorbidities	+

DIETARY INTERVENTION

- Effective modest weight loss (5–10 kg) ameliorates all the cardiogenic metabolic risk fators.
- An initial reasonable goal for most patients with BMI up to 30 kg/m is to lose 5%–10% of body weight using conventional diet and lifestyle modifications.
- With BMI above 30 kg/m 2 , or if type 2 diabetes or other serious complications are present, greater weight loss of over 10–15 kg is recommended, and more intensive intervention is indicated, with separate strategies for inducing and for maintaining weight loss of this order and reduces the incidence of type 2 diabetes.

TABLE 15.20: Types of diet in the treatment of obesity.

Fixed energy diet	*Low-calorie diet*	*Very low-calorie diet (VLCD)*
➢ 1,200–1,800 kcal ➢ Intake is limited by controlling portion sizes, menu choice and composition ➢ Minimal self-monitoring ➢ Lack of compliance to this rigid pattern	➢ 800–1,000 kcal ➢ Applicable to most of the patients ➢ Fewer restrictions than VLCD ➢ Supplementation of vitamins and minerals ➢ Reduction of 6–7 kg observed over a year	➢ 400–600 kcal ➢ Even below one's basal metabolic rate ➢ Used for period of 1–2 months under medical supervision ➢ 45–70% protein, 30–50% carbohydrates, and 2 g fat ➢ Supplementation of vitamins, minerals, and trace elements ➢ Greater weight loss compared to restrictive diets

- A minimum content of 40–50 g protein daily minimises muscle degradation , with sufficient magnesium to avoid constipation, and fluid intake of at least 2.5 L/day to avoid dehydration which can cause orthostatic hypotension, headache, constipation and nausea.
- Medical supervision is needed for patients whose glucose lowering and antihypertensive medications need withdrawal or reduction with rapid weight loss

LIFESTYLE MODIFICATION

- Behavioural modification -- cornerstone of long term control of weight.
- Adopting more disciplined eating patterns, and pre planned meals, is advised.
- Advising modest extra activity to increase physical activity level (pal) ratios may be successful for younger people, but this must be sustainable and regular as a daily routine.
- Regular support, and positive strategic encouragement from a dietitian or weight loss group is very valuable.

PHARMACOTHERAPY

- Drug therapy should only be used as an adjunct to optimal, evidence based, lifestyle advice and support, which should be continued throughout treatment.
- **Orlistat** inhibits pancreatic and gastric lipases. The standard dose of 120 mg taken with each of the three main meals reduces dietary fat absorption by about 30%. Adverse effects relate to fat malabsorption : loose oily stools, faecal urgency, flatus and malabsorption of fat soluble vitamins.
- The combination of the opioid antagonist naltrexone and the noradrenaline (norepinephrine)/dopamine re-uptake inhibitor bupropion is similarly effective, and approved in both the United States and Europe. Main adverse effects -- dry mouth and constipation.

- **GLP 1 RECEPTOR AGONIST** The most effective medications for obesity treatment, usually at higher doses than are used to treat type 2 diabetes. These drugs are remarkably safe, their main drawback being high cost. Main side effects are gastrointestinal symptoms.
- Liraglutide is approved for obesity treatment for high risk obese patients, at a daily subcutaneous dose up to 3 mg.

SURGERY

- It is usually reserved for those with severe obesity (BMI > 40 kg/m 2),
- Or those with a BMI >35 kg/m2 and significant complications, such
- As type 2 diabetes or obstructive sleep apnoea, although some evidence based guidelines now suggest surgery can be considered at a lower weight with recent onset diabetes and a BMI > 30 kg/m 2.
- **COMPLICATIONS**

1. Pouch and distal oesophageal dilatation with loss of effectiveness
2. Persistent vomiting
3. 'Dumping' syndromes
4. Micronutrient deficiencies, particularly of folate, vitamin B 12 and iron, which are of special concern to women contemplating pregnancy; this should be delayed for at least 2 years following surgery.

- Cosmetic surgical procedures **apronectomy** is a major operation to remove an overhang of unsightly, infected or ulcerated abdominal skin, a common problem in obese women after the menopause.

i 22.8 Effectiveness and adverse effects of laparoscopic bariatric surgical procedures*

Procedure	Expected 2-year weight loss (kg)	Adverse effects
Gastric banding	19–25	Band slippage, erosion, stricture Port site infection Mortality <0.2% in experienced centres
Sleeve gastrectomy	20–30	Iron deficiency Vitamin B_{12} deficiency Mortality <0.2% in experienced centres
Roux-en-Y gastric bypass	20–40	Internal hernia Stomal ulcer Dumping syndrome Hypoglycaemia Iron deficiency Vitamin B_{12} deficiency Vitamin D deficiency Mortality 0.5%

*Weight regain is a frequent problem beyond 5 years after all bariatric surgery, particularly banding and sleeve gastrectomy.

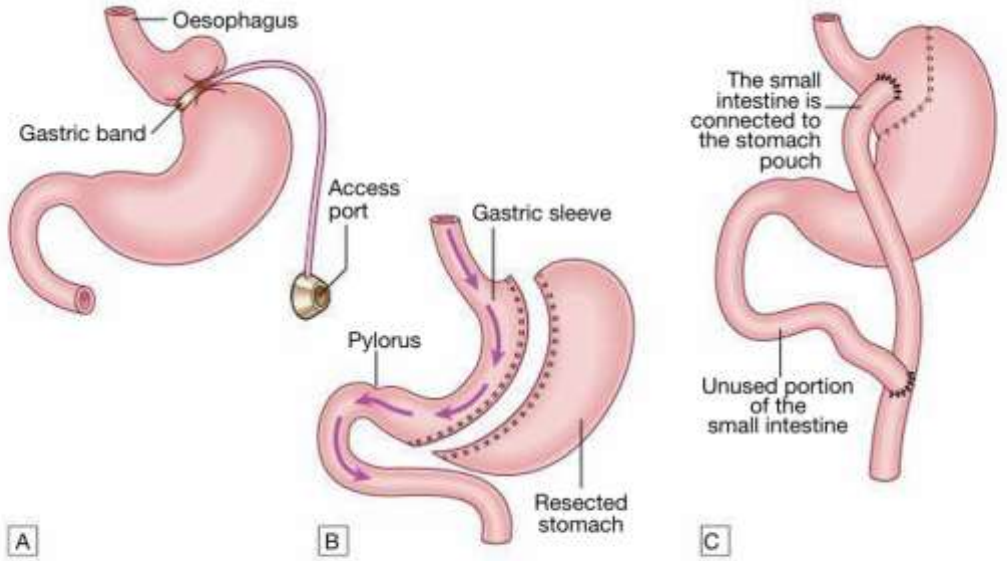


Fig. 22.9 Bariatric surgical procedures. A Laparoscopic banding, with the option of a reservoir band and subcutaneous access to restrict the stomach further after compensatory expansion has occurred. B Sleeve gastrectomy. C Roux-en-Y gastric bypass.

OTHERS

- Treatment of additional risk factors
- Obesity must not be treated in isolation.
- Other risk factors must be addressed, including smoking, excess alcohol consumption, diabetes, hyperlipidaemia, hypertension and obstructive sleep apnoea.

THANK YOU

REFERENCE

- DAVIDSON 24TH EDITION
- ARCHITH BOLOOR EXAM PREP MANUAL FOR UG MEDICINE