

What is Obesity?

A degree of overweight that is associated with an increase in morbidity and mortality











Causes of Obesity

- Excessive intake of calories in relationship to energy expenditure over a prolonged period
- Genetic background explains only an estimated 40% of the variance in body mass
- Environmental factors and reduced physical activity e.g..
 - More meals eaten outside home
 - Greater availability of convenience and snack foods
 - Larger serving sizes
- Reduced physical activity due to sedentary lifestyles
- Children who became obese after 6 years of age had a more than 50% risk of becoming
 obese adults. Children with obese parents are at higher risk of becoming obese adults.

Genetic Causes of Obesity

- · Monogenetic causes: Rare
 - E.g.
 - · Leptin gene mutations
 - · Leptin receptor mutations
 - Prohormone convertase 1 gene mutation
 - POMC gene mutation
 - Melanocortin 4 Recetor mutation
 - SIM1gene mutation
- Polygenetic causes: More than 250 genes, markers and chromosomal markers linked with obesity

Energy metabolism

- Total energy expenditure (TEE) per day:
 - Resting energy expenditure (REE): 70%
 - Energy expenditure in physical activity: 20%
 - Thermic effect of food: 10%
- Diet induced weight loss decreases REE, which promotes weight gain (Set point theory)

How Much Energy in Fat?

- Fat: 9.3 kcal/g = 37 kJ/g
- To burn 1 kg of additional fat you will have to run at 12 km/h for 10 hours if you weigh 68 kg
- For crash dieters you will need to run for 4.74 min with 1 ton on your back at 100 km/h to burn 1 kg of fat.
- The energy content of a 100 g slab of chocolate is 2000 kJ (running at 12 km/h for 32 min if you weight is 68 kg)

Prevalence of Obesity

- US 61% of the adult population 20 to 74 years of age are considered to be overweight or obese (2000)
- South Africa: Men 29.2% are overweight or obese and for Women 56.6% (1998)

Clinical Features and Complications of Obesity

- · Endocrine and Metabolic disease
 - Insulin resistance syndrome
 - Insulin resistance and DM2
 - Dyslipidaemia ↑TG, ↓HDL
 - Hypertension
 - Diabetes Mellitus type 2
 The risk of Diabetes increases linearly with Obesity
 - Dyslipidemia
 - \uparrow TG, \uparrow sd LDL, \downarrow HDL

Clinical Features and Complications of Obesity

· Cardiovascular disease

- Hypertension
 Linear relationship between HT and BMI
- Coronary heart disease
 - AHA classified obesity as a major preventable risk factor for CHD
- Cerebrovascular and thromboembolic disease
- Ischaemic strokes is approximately twice as great in obese than
 in lean subjects
- Risk of DVT and PE is increased in obese individuals especially those with abdominal obesity

Clinical Features and Complications of Obesity

- · Pulmonary disease
 - Restrictive lung disease
 - Increased pressure on the chest wall which restricts pulmonary function
 - Obesity hypoventilation syndrome
 Inshility of recrirectory myseles to meet
 - Inability of respiratory muscles to meet the demand imposed by mechanical effects of obesity
 - Obstructive sleep apnoea
 - Large neck girth: Males > 43, Females > 40.5 cm

Clinical Features and Complications of Obesity

- Musculoskeletal
 - Gout
 - Osteoarthritis
- Cancer
 - Increased risk of cancer of the esophagus, gallbladder, colon, breast, uterus, cervix, and prostate
- · Genitourinary disease in women
 - Irregular menses, amenorrhea, infertility, pregnancy related complications

Clinical Features and Complications of Obesity

- Neurological
 - Increase risk of stroke
 - Idiopathic intracranial hypertension
- Gastro-intestinal
 - Esophageal reflux
 - Gallstones
 - Non-alcoholic fatty disease

Risk Related to Obesity

Greatly increased (relative risk much greater than 3)	Moderately increased (relative risk 2–3)	Slightly increased (relative risk 1–2)
Type 2 diabetes	CHD	Certain cancers
Gallbladder disease	Hypertension Osteoarthritis Hyperuricemia and gout	Reproductive hormone abnormalities
Dyslipidemia		
Insulin resistance		Polycystic ovarian syndrome
Dyspnea/Hypoventilation		Impaired fertility
Sleep apnea		Low back pain
		Increased anesthetic risk
		Fetal defects

Benefits of Intentional Weight Loss

- Type 2 Diabetes mellitus
- Dyslipidaemia
- Hypertension
- Cardiovascular disease
- Pulmonary function
- Reproductive and urinary tract function in women



Obesity Therapy

- Dietary intervention
- Physical activity
- Behaviour modification
- Pharmacotherapy
- Surgical therapy







NA agents

- · Amfepramone, Cathine, Phentermine, Phendimetrazine
- Registered for short term use (< 12 weeks)
- Studies showed a moderate effectivity (between 2 and 10 kg over 12 weeks better than placebo)
- · Side effects: insomnia, dry mouth, constipation, euphoria, palpitation, hypertension
- · Significant abuse potential

Serotonergic agents

- Increase release or inhibit the reuptake of serotonin
- Fenfluramine, Dexfenfluramine
- Withdrawn from the market due to pulmonary hypertension and valvular heart disease
- Note that SSRI antidepressants have a short term appetite suppressant effect, but is not registered for use of weight loss.

Mixed NA/ Serotonergic Agents

- Only one drug: Sibutramine (Recordial)
- Only one drug: Stouramine (Repetch)
 Inhibits the reuptake of both NA and Serotonin
 In conjunction with a reduced calorie diet followed for 6 months a veight loss of 5 8% of the pre-intervention budy weight, in comparison to 1 4% in the placebo treated group
 Side effects: inclusion placebo treated group
 Side effects: inclusion placebo treated and blood pressure, incomparison
- constipation

Nutrient Absorption Inhibitors

- Only one registered Orlistat (Xenical)
- · Moderate effectivity
- Side effects: flatulence, fecal urgency, fecal incontinence, increased frequency of defecation
- Decrease absorption of fat-soluble vitamins

Other Drugs not Yet Registered

- Topiramate
- Buproprion
- · Neuropeptieds
- · Cannabinoids
- Gastro-intestinal peptides

Bariatric Surgery

- Indications:
 - -BMI > 40
 - BMI 35 39.9 and one or more severe medical complication of obesity (HT, heart failure, DM2, sleep apnea)
- 2 types of surgery
 - Gastric restriction
 - Induce nutrient maldigestion and malabsorbtion

Gastric Restriction

<u>Gastroplasty or gastric</u> <u>banding</u>

- Loss of $\sim 40\%$ excess weight
- Complications:
 - Staple line disruption
 - Stomal stenosis
 - GE reflux



Gastric Bypass

- Roux-en-Y gastric bypass Gastric restriction and • malabsorbtion due to bypass of duodenum and proximal jejenum
- Complications:
- Marginal ulcers
 - Stomal stenosis
 - Dilatation of bypassed stomach
 - Staple line disruption
 Internal hernias

 - Malabsorbtion of nutrients
 - Dumping syndrome





