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Review article on newer concepts of obesity

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Abstract
Obesity can be described as the "New World Syndrome". The increasing prevalence of medically significant obesity raises great concern. The rapid spread of urbanisation and industrialisation and dramatic lifestyle has led to the pandemic of obesity, even in developing countries. The prevalence of obesity has also risen in children and adolescents. Diseases commonly associated with obesity in adults, such as T2DM, hypertension, hyperlipidemia, gallbladder disease, non-alcoholic steatohepatitis, sleep apnoea, and orthopaedic complications, are now increasingly observed in children. Hence, prevention of obesity during childhood should be considered a priority, as there is a risk of persistence to adulthood and also we require a strong and adherent strategies focussing on those with existing weight problems and also on those at high risk of developing obesity. This article highlights various preventive and treatment aspects of obesity.

Keywords: obesity, newer concepts

Introduction
Obesity has been described long back in *Charak Samhita*: (Sutrasthana: Ch XXI v. 3-4) in the context of body phenotypes with obese phenotype having the following 8 defects: shortening of lifespan, hampered movement, difficulty in sexual intercourse, debility, foul smell, over sweating, excessive much hunger, and excessive thirst. [1]

Prevalence
In the United States alone, the consequences of obesity account for an estimated 300,000 deaths per year.[2, 3] The medical expenses and cost of lost productivity due to obesity are greater than $100 billion per year.[2, 4] Obesity is emerging as an important health problem in India. It is estimated that 22 million Indians are obese, especially
Abdominally obese. [1]
Prevalence of obesity increases progressively from 20 to 50 years of age but then declines after 60 to 70 years of age. The prevalence of obesity has also risen in children and adolescents [2, 5]
The most widely used method to gauge obesity is the *body mass index* (BMI), which is equal to weight/height 2 (in kg/m 2). Based on data of substantial morbidity, a BMI of 30 is most commonly used as a threshold for obesity in both men and women. Large-scale epidemiologic studies suggest that all-cause, metabolic, cancer, and cardiovascular morbidity begin to rise (albeit at a slow rate) when BMIs are ≥25. Other approaches to quantifying obesity include anthropometry (skinfold thickness), densitometry (underwater weighing), CT or MRI, and electrical impedance, waist-to-hip ratio, with a ratio >0.9 in women and >1.0 in men being abnormal. [6]

Table 1: Classification of Overweight and Obesity by Body Mass Index (BMI) for Asian Indians

Obesity Class	BMI (kg/m2)
Underweight	<18.5
Normal	18.5 to 22.9
Overweight	23.0 to 24.9
Obesity I	25.0 to 29.9
Obesity II	30.0 to 34.9

Table 2: BMI cut-offs for Asian Indians. *According to* WHO and IOTF guidelines

Body mass index	
Overweight:	23 kg/m2 (as opposed to 25*)
Obese:	25 kg/m2 (as opposed to 30*)

Waist circumference
Measurement method to be clearly mentioned
Action level 1: 78 cm (M), 72 cm (F), to be further reached
Action level 2: 90 cm (M), 80 cm (F), accepted
Waist-to-hip ratio
0.88 (men), 0.80 (women)
* Reproduced with permission from: J Assoc Physicians India 2009; 57: 163-70.api [1]

Physiologic Regulation of Energy Balance
A complex physiologic system regulates energy homeostasis by integrating signals from peripheral organs with central coordination in the brain. [2, 7] The hypothalamus functions as the main cerebral center in which these signals converge. [2, 8] Activation of neurons secreting neuropeptide Y (NPY) and agouti-related protein (AgRP) promotes food intake, whereas

that of neurons secreting pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) has an anorexigenic effect. Studies demonstrated that the cannabinoid system has an important role in the regulation of ingestive behavior in animals and humans. [2, 9] The stomach and the duodenum secrete the orexigenic peptide ghrelin, which increases before eating and decreases after feeding. Glucagon-like peptide 1 (GLP1 exerts pleiotropic effects, including slight anorexic effects. [2, 10]

Etiology of obesity: [11]
Potentially reversible causes of weight gain
Endocrine factors
- Hypothyroidism
- Cushing's syndrome
- Insulinoma
- Hypothalamic tumours or injury

Drug treatments
- Tricyclic antidepressants
- Sulphonylureas
- Oestrogen-containing contraceptive pill
- Corticosteroids
- Sodium valproate
- -blockers

Some reasons for the increasing prevalence [11]
Of obesity—the 'obesogenic' environment
P Increasing energy intake
- Portion sizes
- Snacking and loss of regular meals
- Energy-dense food (mainly fat)
- Affluence

Decreasing energy expenditure [11]
- Car ownership
- Walking to school/work
- Automation; ↓manuallabour
- Sports in schools
- Time spent on computer games and watching TV
- Central heating
  Davidson

A study found that one microbe called Akkermansia muciniphila helps ward off obesity, diabetes, and heart disease by lowering blood sugar, improving insulin resistance, and promoting a healthier distribution of body fat.
A. muciniphila is associated with a fiber-rich diet, and fiber has long been recognized for its beneficial effects on health and weight. It's still not known whether A. muciniphila produces these effects all on its own, or whether it helps promote other beneficial bacteria. According to the Authors of this study, this needs further research.

Pathologic Consequences of Obesity [11]
Obesity has major adverse effects on health. Obesity is associated with an increase in mortality, with a 50–100% increased risk of death from all causes compared to normal-weight individuals. [6]

Risk factors	Out comes
'Metabolic syndrome'	Type 2 diabetes Hypertension Stroke Hyperlipidaemia Coronary heart disease
Liver fat accumulation	Non-alcoholic steatohepatitis Cirrhosis
Restricted ventilation	Exertional dyspnoea Sleep apnoea Respiratory failure (Pickwickian syndrome)
Mechanical effects of weight	Urinary incontinence Osteoarthritis Varicose veins
Increased	Hormone-dependent cancers
Peripheral steroid interconversion in adipose tissue	Polycystic ovary syndrome (infertility, hirsutism)
Others	Psychological morbidity (low self-esteem, depression)
	Socioeconomic disadvantage (lower income, less likely to be promoted) Gallstones Colorectal cancer Skin infections (groin and submammary candidiasis; hidradenit

Energy Balance Davidson
Goals of Weight Loss and Management
The overall goals of weight loss management are: to prevent further weight gain, to lose weight to achieve a realistic target BMI and to maintain a lower body weight over the long term. The initial goal of weight loss therapy is to reduce body weight by approximately 10% from baseline. A reasonable time period for a 10% reduction in body weight is 6 months of therapy.

Dietary therapy
The diet should be nutritionally adequate. It must be tailored to a person's tastes and habits. It should create a deficit of 500 to 1000 kcal per day. The fat content should be 30% or less of total calories. Emphasis should be on greater intake of fruits, vegetables and foods high in fibre.

Exercise and physical activity
Sustained physical activity is most helpful in the prevention of weight regain. Most global guidelines recommend that adults participate in at least 30 minutes of moderate-intensity physical activity on most, and preferably all, days of the week. Exercise should be initiated slowly, and the intensity should be increased gradually. The patient can start by walking 30 minutes for 3 days a week and can build to 45 minutes of more intense walking for at least 5 days a week.

Behavioural therapy
Behavioural therapy forms the cornerstone of any weight loss programme. This includes food intake diaries analysed periodically, and new modes of eating can be suggested, including not eating between meals, eating only three times a day, watching the portions of food eaten, and eating slowly with concentration [1].

Pharmacotherapy
Conventional obesity therapy is associated with a high rate of recidivism. Pharmacotherapy should not be considered a

short-term approach for weight loss, because patients who lose weight with drug therapy usually regain weight when the therapy is discontinued. [2, 12, 13]. Treatment outcome is less successful when pharmacotherapy is administered alone than when pharmacotherapy is administered as part of a comprehensive weight-loss program that includes diet, exercise, and behaviour modification [2, 14].

Drug treatment is advised only for subjects with BMI > 27 and with associated risk factors or with a BMI > 30 [15, 16] and thus at medical risk because of their obesity.

Most available weight loss medications are "appetite–suppressant" medications. The initial drugs used for appetite suppression were amphetamine [15, 17] metamphetamine and phenmetrazine (Preludin) and are no longer used in treatment of obesity because of their high potential for abuse.

Inhibitors of 5-hyroxytryptamine (5-HT) reuptake, fenfluramine and dexfenfluramine were licensed for obesity but proved to cause pulmonary hyper tension and increased valvular heart disease [15, 18] and have been withdrawn from the market. Drugs like phendimetrazine (Plegine), diethylpropion (Tenuate), phentermine (Lonamin) etc., are being marketed but have been classified as controlled substances and are recommended for short-term use only.

The newest agents available for weight loss are sibutramine (Meredia) and orlistat (Xenical). They are the only weight loss medications approved by the US Food and Drug Administration (FDA) for long-term use [19] in significantly obese patients, although their safety and effectiveness have not been established for use beyond one year.

Sibutramine is the serotonin and norepinephrine re-uptake inhibitor, which induces decreased food intake and increased thermogensis [20, 21, 22]. In clinical trials, sibutramine showed a statistical improvement in amount of weight lost versus placebo [20]. It limits decline of metabolic rate that typically accompanies weight loss [23]. However, this agent is contraindicated in-patient with known seizure disorders, high blood pressure, congestive heart failure (CHF) a history of myocardial infraction and arrhythmias.

Orlistat is a potent and irreversible inhibitor of gastric, pancreatic lipases. It blocks the digestion of approximately 30% of the ingested dietary triglycerides. Studies proved that it produces 5% more weight loss than in control groups [24]. It is now available on prescription as Xenical® (Orlistat-120 mg). The most commonly reported side effects include oily stools, soft stool [24], and increased defecation and decreased absorption of fat-soluble vitamins (A, D, E and K). Hence, patient may be recommended intake of fat-soluble vitamins [25] along with it. When used in conjugation with diet it was found to improve glycemic control and cardiovascular disorders [26, 27].

Drugs Approved by the U.S. Food and Drug Administration for the Treatment of Obesity

Year Approved Generic Name Trade Name

1959 Phendimetrazine tartrate Bontril, Plergine, Prelu-2, X-Trozine

1959 Phentermine Ionamine, Adipex-P, Fastin, Oby-trim

1959 Diethylpropion hydrochloride Tenuate, Tenuate Dospan

1960 Benzphetamine HCl Didrex

1973 Mazindol Sanorex, Mazanor

1997 Sibutramine HCl Meridia

1999 Orlistat Xenical, Ally (over the counter) [6]

List of some important drugs under clinical trials for weight reduction. [27]

Drugs in phase II trials	Drugs in phase III trials
Bupropion (dopamine reuptake inhibitor)	Mazindol (adrenergic agonist)
Linitript (cholecystokinin A antagonist)	Sertraline (selective serotonin uptake inhibitor)
Pegylated leptin	Posatirelin (thyrotrphin-releasing hormone analogue)
Dipeptidyl peptidase IV inhibitors	Cannabinoid antagonists
Human growth hormone factor AOD9604	Lipase inhibitor, ATL-962
Phytostanol	

Surgery: Bariatric surgery considered for patients with severe obesity (BMI ≥40 kg/m 2) or those with moderate obesity (BMI ≥35 kg/m 2) associated with a serious medical condition. Weight-loss surgeries fall into one of two categories: restrictive -

Laparoscopic adjustable silicone gastric banding (LASGB) has replaced the VBG as the most commonly performed restrictive operation.

Restrictive-malabsorptive. The three restrictive-malabsorptive bypass procedures Include Roux-en-Y gastric bypass (RYGB), biliopancreatic diversion (BPD), and biliopancreatic diversion with duodenal switch (BPDDS).RYGB is the most commonly performed and accepted bypass procedure. Surgical mortality rate from bariatric surgery is generally 1%. [6]

Conclusion

Obesity is steeply increasing in India. Primary reasons are imbalanced foods and physical inactivity. Asian Indians have, more intra-abdominal and truncal subcutaneous fat conducive to the development of type 2 diabetes and cardiovascular disease. Morbidities occur at lower levels of BMI and WC in Asian Indians. More aggressive and early intervention according to revised guidelines will result in prevention of diseases in Asian Indians.

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