AN OVERVIEW ON OBESITY

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Abstract

Obesity is a medical condition that can reduce life expectancy with increase in health problems because excess fat has been accumulated to the body. Body Mass Index is a measurement which compares weight and height. It defines a person as overweight when their BMI is between 25-30 kg/m^2,and obese when it is greater than 30 kg/m^2. Individual susceptibility to obesity is recognized by genetic inheritance. Recently, genes responsible, such as the β_3-adrenergic receptor leptin, have been identified that may contribute to the inheritance of body fat mass. Overeating, alcoholism and inactive lifestyles which has an important impact on life style-related diseases such as coronary heart disease, dyslipidemia, glucose intolerance, diabetics, hypertension and some cancers. Several factors, including lack of exercise, sedentary lifestyles and the consumption of energy rich diets are contributory to the etiology of obesity.

Key words

Obesity, Dyslipidemia, Hyperuricemia, Thermogenesis,Meralgia paresthetica,
Molecular genetics.

INTRODUCTION

Obesity is a chronic metabolic disorder caused by an imbalance between energy intake and expenditure. Persons whose body weight becomes more than 120% of the ideal weight, is called as an obese body. Obesity is one of the greatest health threats of this century. It has an important impact on lifestyle related diseases such as coronary heart disease, dyslipidemia, glucose intolerance, diabetics, hypertension, atherosclerosis and some cancers. There are many factors which contribute to the etiology of obesity such as, lack of exercise, sedentary lifestyles, consumption of energy rich diets &

Agents known to suppress food intake

Anorectics, Bombesin, Cholecystokinin, Corticotropin-releasing hormone, Estrogen, Fluoxetine, Glucagon, High blood glucose, High-fat diet, High-protein diet, Histidine, Mazindol, Neurotensin, Pain, Phenylethylamines, Serotonin, Somatostatin, Thyrotropin releasing hormone, Tryptophan [6,7].

OBESITY RELATED PROBLEMS IN DIFFERENT ORGAN OR SYSTEMS

Cardiopulmonary problems

alcoholism [1-4]. An estimation of an obese patient's absolute risk status requires an assessment of associated conditions for example: Height and weight: calculate BMI, Waist circumference, Neck circumference, double chin. High blood pressure and resting pulse rate, Any evidence of cardiac valvular disease, Any evidence of pulmonary hypertension, congestive cardiac failure, Signs of dyslipidemia, Signs of thyroid disease, Diabetic retinopathy in a diabetic patient, Any evidence of diabetes mellitus, Coronary artery disease (CAD), Other atherosclerotic diseases, Type 2 diabetes, Sleep apnoea, Gynaecological abnormalities, Osteoarthritis [5].

Hypertension, Dyspnea, Congestive heart failure, Obstructive sleep apnoea, Hypoventilation syndrome, Varicose veins, Pickwickian syndrome, Pulmonary embolism, Asthma, Coronary artery disease.

Gastrointestinal & endocrine problems

Gastroesophageal reflux disease, Metabolic syndrome, Nonalcoholic fatty liver disease, Type 2 diabetes mellitus, Cholelithiasis, Dyslipidemia hernias, Polycystic ovary syndrome, Colon cancer, Amenorrhea, Infertility, Menstrual disorders.

Genitourinary & musculoskeletal problems
Urinary stress incontinence, Hyperuricemia and gout obesity-related glomerulopathy, Immobility end-stage renal disease, Osteoarthritis (knees and hips), Hypogonadism (male), Low back pain breast and uterine cancer, Carpal tunnel syndrome pregnancy complications.

Neurological problems

Striae distensae, Stasis pigmentation of legs & idiopathic intracranial hypertension, Lymphedema, Meralgia paresthetica, Cellulitis dementia, Intertrigo, Carbuncles.

Psychological problems
Acanthosisnigricans depression and low self-esteem, Acrochordon (skin tags) body image disturbance, Hidradenitis suppurativa social stigmatization [8].
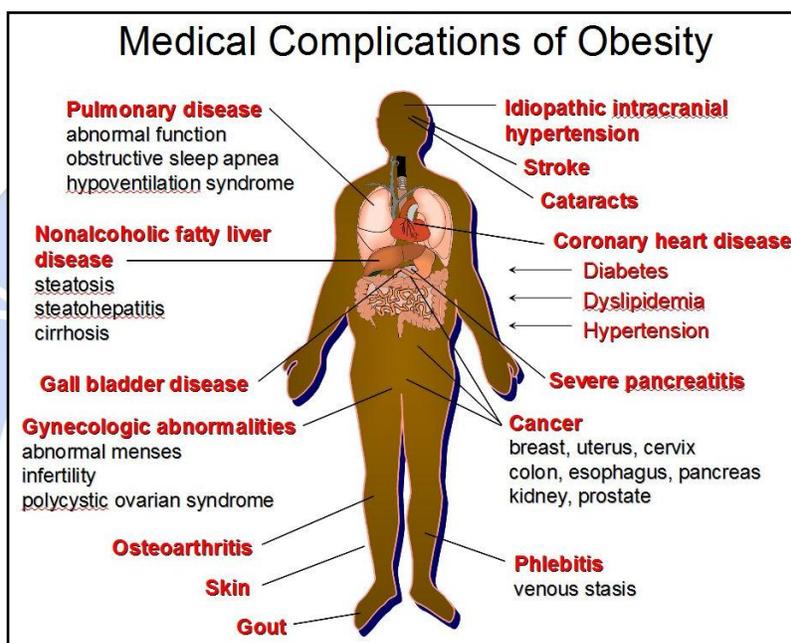

Fig.1: Medical Complications of Obesity

EPIDEMIOLOGY
The current status of obesity has been reported in several but not all regions globally. But it has been observed to be increased in both developed and as well as developing countries throughout the world. Today worldwide, at least 2.8 million people die each year as a result of being overweight or obese and an estimated 35.8 million (2.3%) of global DALYs (disability-adjusted life years) are caused by

PATHOPHYSIOLOGY
Molecular genetics of obesity
Generally obesity mainly caused by dietary and lifestyle factors but from different studies it has been found that genetics also play a major role to cause obesity [13].One of the first approaches in understanding obesity was the discovery of ob/ob mice. Due to a genetic defect, these mice eat excessively and weigh 3 to 4 times as much as their heterozygous siblings. Normal body weight can be restored, however, by joining an ob/ob mouse's circulatory system with that of its healthy counterpart [14]. This indicates that the ob/ob mouse is lacking a

overweight or obesity. The biomedical roots of epidemiology lead most epidemiologists to examine individuals as units of analysis, typically in one population and one place .The highest rate of obesity has been reported in the Pacific Islands and the lowest rates have been seen in Asia. The rates in European and North American are generally high, while the rates in African and Middle Eastern countries are variable [9-12].

blood-borne weight regulating factor that can be replaced by the healthy mouse. The factor is the peptide leptin, (derived from Greek root, Leptos meaning thin). Leptin is secreted from adipose cells and act primarily through the hypothalamus. Its level of production provides an index of adipose energy , high leptin levels, decreases food intake and increases energy expenditure [15]. Leptin has also been discovered to be synthesised from gastric chief cells and P/D1 cells in the stomach. It acts on the receptors in hypothalamus of the brain, where it inhibits appetite, counteracting the effects of neuropeptide Y(a potent feeding stimulant secreted by

cells in the gut and in the hypothalamus), it counteracts the effects of anandamide (another potent feeding stimulant that binds to the same receptors as THC) and it promotes the synthesis of α-MSH, an appetite suppressant. This appetite inhibition is long-term, in contrast to the rapid inhibition of eating by cholecystokinin (CCK) and the slower suppression of hunger between meals mediated by PYY3-36. Absence of leptin (or its receptor) leads to uncontrolled food intake and resulting obesity [16]. However, leptin resistance might also be a consequence of impaired signal-transduction by the leptin receptor, analogous to the post-receptor mechanisms of insulin resistance [17].The leptin receptor (OB-R) is a member of the class 1 cytokine receptor family and has a widespread tissue distribution in several alternatively spliced isoforms in rodents and humans. In mice, only the Ob-Rb isoform with a long cytoplasmic tail appears fully functional and is thought to mediate the hypothalamic actions of leptin. Since most obese humans also have elevated blood leptin levels, it is possible that defects in the *OB-R* gene contribute to obesity in humans. Four leptin receptor isoforms have been identified so far in humans-a long isoform of 1165 amino acids homologous to mouse Ob-Rb and three shorter isoforms (huB219.1–3) generated by alternative splicing from a single gene located on chromosome 1p . Messenger RNA for the shorter isoforms has been identified in circulating haemopoietic cells and lymph glands [18].

Energy balance

Obesity can also result from increased energy intake, decreased energy expenditure, or a combination of the two [19].The high occurrence rate of obesity and physical inactivity is a worldwide public health issue, but the mechanisms of energy imbalances and obesity is

Peripheral storage and thermogenesis

Positive energy balance leads to obesity in humans and other mammals in which excess energy is stored as triglycerides in adipose tissue. Whereas White adipose tissue (WAT) functions as a storage depot for lipids, releasing energy between meals, Brown adipose tissue (BAT) provides a mechanism for thermogenesis, dissipating energy as

heat. The coordinated storing and burning of lipids is crucial for energy homeostasis, and the contribution of thermogenesis is demonstrated in mice, in which those lacking functional BAT become obese [23]. The sympathetic nervous system is thought to be the efferent pathway by which the brain regulates adaptive thermogenesis. The evidence for this is as follows: 1)

still unclear [20].Humans take in energy through the intake of food and drink, and expend energy through the resting metabolic rate (RMR)-the thermic effect (TEF) of food and physical activity. The RMR is the energy expenditure required for maintaining normal body functions and homeostasis. The RMR is proportional to body mass, in particular fat-free mass. TEF refers to the energy required to absorb, digest and metabolize the food consumed and typically accounts for 8–10 % of daily energy expenditure. People who have a low level of physical activity have trouble achieving energy balance because they must constantly use food restriction to match energy intake to a low level of energy expenditure. So, Dr.Hill said, "What we are really talking about is changing the message from 'Eat Less, Move More' to 'Move More, Eat Smarter". The energy expended due to physical activity (EEact) accounts for energy that is expended in addition to the RMR and TEF, including voluntary exercise, shivering, postural control and voluntary movement. The more sedentary the individual is, the lower the effect of physical activity. This may be as low as 100 calories per day, whereas elite athletes may expend 3,000 calories per day of physical activity. The decline in energy expenditure that occurs with advancing age is mainly the results of declining lean body mass, which reduces TEF and EEact. Disturbances in energy balance causes change in body mass. A positive energy balance, in which energy intake exceeds expenditure causes weight gain, with 60–80 % of the resulting weight gain being attributable to body fat. In negative energy balance, when energy expenditure exceeds intake, the resulting loss in body mass is also accounted for by 60–80 % body fat [21,22].

cold exposure and diet increase sympathetic nerve activity 2) exogenous administration of norepinephrine and epinephrine stimulates energy expenditure, both *in vivo* and in isolated tissue preparations, 3) the thermogenic target tissue, brown adipose tissue, is heavily innervated by sympathetic nerves, and 4) thermogenic activity in brown adipose tissue is completely dependent upon intact sympathetic stimulation [24].Adipose tissue generally is divided into two major types, white and brown. The primary function of white adipose tissue is lipid manufacture, storage, and release. Lipid storage occurs in response to insulin with lipid release occurring during periods of calorie restriction, when insulin levels are suppressed. Brown-type tissue is notable for its ability to dissipate energy via a process of uncoupled mitochondrial respiration [9].

Adipose tissue is highly innervated by the sympathetic nervous system, and adrenergic stimulation is known to activate lipolysis in fat cells as well as increase energy expenditure in adipose tissue and skeletal muscle. These properties provide a potential pharmacologic evidence for altering energy balance and changing weight status. A major focus of research in obesity pharmacotherapy has centered on the activity of adrenergic receptors and their effect on adipose tissue with respect to energy storage and expenditure or thermogenesis [10]. All three subtypes of β-adrenergic receptors (β1, β2, and β3) appear to be active in fat cell function. The β3-receptor appears to be less responsive than β1 and β2 with respect to activation via norepinephrine.

This has led to the development of specific β3-adrenoceptor agonists. However, apparent differences in selectivity and responsiveness between animal and human β3-receptors have complicated the drug development process. In vivo studies in humans suggest that the β3-receptor may be largely responsible for adipose tissue adrenergic-mediated increases in thermogenesis [11].

Genetic polymorphisms have been identified in both the β2- and β3-receptor systems that are associated with obesity or excess weight gain [12].

Thus genetic susceptibility for excess weight status may in part be related to adrenergic dysfunction. The development of effective pharmacotherapies involving these receptor systems may be delayed pending definitive identification of receptor subtype contribution [25].
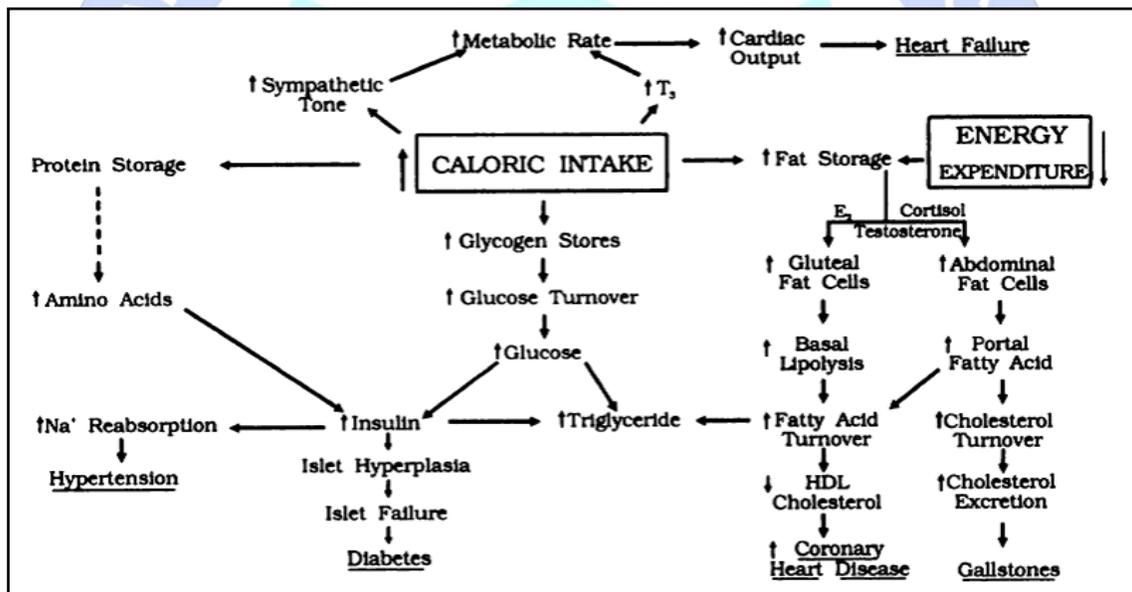

Fig.2: Pathophysiology of Obesity

Fig.2- This Figure explained that the consequences of increased food intake or reduced physical activity. The effects of increasing food intake and / or decreasing physical activity on the adipose tissue organ. On carbohydrate metabolism, the metabolism of protein and amino acid and the control of metabolism through thyroid hormone and sympathetic nervous system [25].

DIAGNOSIS
Tests to diagnose obesity include
Body Mass Index (BMI)
A BMI of 25 to 29.9 is considered overweight and 30 or higher is considered obese. Waist circumference, sagittal diameter, and waist-to-hip ratio-Simple

measurements that estimate the amount of fat deposited in the skin and inside the abdominal cavity. Waist-to-hip ratio greater than 1 in men or greater than 0.85 in women is considered obese. Waist circumferences that exceed 102 centimeters (40 inches) men or exceed 88 centimeters (35 inches) in women are associated with an increased risk of heart disease.

Skin fold caliper
Most fat is deposited beneath the skin. This test measures fat just beneath the skin, but cannot measure fat accumulated inside the abdomen.

Water displacement tests
Fat floats; the rest of your body tissues sink. Determining how well you float provides an estimated ratio of fat to body mass.

Electrical measurements

A couple of tests calculate your percentage of body fat by measuring the difference between the electrical characteristics of fat and other tissues in your body.

Blood tests

To rule out other medical conditions that may cause excess body weight, such as a thyroid disorder, doctor may advice for some blood tests. [26].

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