



# Eating Disorders and Obesity

Anita Yarborough

German Isaac

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## Chapter 1

# Introduction to Eating Disorder

### Eating disorder

ICD-10	F50.
ICD-9	307.5
MeSH	D001068

**Eating disorders** are a group of conditions characterized by abnormal eating habits that may involve either insufficient or excessive food intake to the detriment of an individual's physical and emotional health, binge eating disorder, bulimia nervosa, anorexia nervosa being the most common specific forms in the United States, Though primarily thought of as affecting females (an estimated 5–10 million being affected in the U.S.), eating disorders affect males as well (an estimated 1 million U.S. males being affected).

The reason for eating disorders are poorly known, but, it might involve other conditions and situations. One study showed that girls with ADHD has a greater chance of getting an eating disorder than those not affected by ADHD. One study showed that foster girls are more likely to develop bulimia nervosa. Some also think that peer pressure and idealized body-types seen in the media are also a significant factor.

While proper treatment can be highly effective for many of the specific types of eating disorder, the consequences of eating disorders can be severe, including death (whether from direct medical effects of disturbed eating habits or from comorbid conditions such as suicidal thinking).

### ***Specific eating disorders***

- Anorexia nervosa (AN), characterized by refusal to maintain a healthy body weight and an obsessive fear of gaining weight. Anorexia can cause menstruation to stop, it often leads to bone loss, loss of skin integrity etc. The disorder stresses the heart and increases the risk of death.
- Bulimia nervosa (BN), characterized by recurrent binge eating followed by compensatory behaviors such as purging (self-induced vomiting or excessive use of laxatives)

- Binge eating disorder (BED), binge eating without compensatory behavior (Considered to be in the eating disorders not otherwise specified category)
- Purging disorder, characterized by recurrent purging to control weight or shape in the absence of binge eating episodes
- Rumination syndrome, involving the repeated painless regurgitation of food following a meal which is then either re-chewed and re-swallowed, or discarded.
- Diabulimia is the deliberate manipulation of insulin levels by diabetics in an effort to control their weight.
- Food maintenance syndrome is characterized by a set of aberrant eating behaviors of children in foster care.
- Female athlete triad is a syndrome in which disordered eating behavior, amenorrhea and/or oligomenorrhea, and decreased bone mineral density (osteoporosis and osteopenia) are present (though not all patients exhibit all three components).
- Eating disorders not otherwise specified (EDNOS) can refer to a number of disorders. It can refer to a female individual who suffers from anorexia but still has her period; it can refer to someone who may still be an "average healthy weight" but who has anorexic thought patterns and behaviors; it can mean the sufferer equally participates in some anorexic as well as bulimic behaviors (sometimes referred to as purge-type anorexia).
- Pica is defined as a compulsive craving for eating, chewing or licking non-food items or foods containing no nutrition. These can include such things as chalk, plaster, paint chips, baking soda, starch, glue, rust, ice, coffee grounds, and cigarette ashes.
- Night eating syndrome consists of morning anorexia, evening polyphagia (abnormally increased appetite for consumption of food frequently associated with injury to the hypothalamus) and insomnia.
- Nocturnal Sleep Related Eating Disorder
- Orthorexia nervosa is an obsession with a "pure" diet, where it interferes with a person's life. It becomes a way of life filled with chronic concern for the quality of food being consumed. When the person suffering with orthorexia slips up from wavering from their "perfect" diet, they may resort to extreme acts of further self-discipline, including even stricter regimens and fasting.

Several of the above mentioned disorders, such as diabulimia, food maintenance syndrome and orthorexia nervosa, are not recognized as mental disorders in any of the medical manuals, such as the ICD-10 or the DSM-IV.

## **Causes**

It is not known with certainty what causes eating disorders. It can be due to a combination of biological, psychological or environmental causes. It is often said "Genetics loads the gun, environment pulls the trigger." In other words, some people are born with a predisposition to have an ED, and it is brought to the surface pending on their environment and reactions to it. Most people with eating disorders suffer also from body dysmorphic disorder, altering the way a person sees themselves.

## Biological

- Genetic: Numerous studies have been undertaken that show a possible genetic predisposition toward eating disorders as a result of Mendelian inheritance.
- Epigenetics: Epigenetic mechanisms are means by which environmental effects alter gene expression via methods such as DNA methylation; these are independent of and do not alter the underlying DNA sequence. They are heritable, but also may occur throughout the lifespan, and are potentially reversible. Dysregulation of dopaminergic neurotransmission due to epigenetic mechanisms has been implicated in various eating disorders.

*"We conclude that epigenetic mechanisms may contribute to the known alterations of ANP homeostasis in women with eating disorders."*

- Biochemical: Eating behavior is a complex process controlled by the neuroendocrine system of which the Hypothalamus-pituitary-adrenal-axis (HPA axis) is a major component. Dysregulation of the HPA axis has been associated with eating disorders, such as irregularities in the manufacture, amount or transmission of certain neurotransmitters, hormones or neuropeptides and amino acids such as homocysteine, elevated levels of which are found in AN and BN as well as depression.
  - serotonin: a neurotransmitter involved in depression also has an inhibitory effect on eating behavior.
  - norepinephrine is both a neurotransmitter and a hormone; abnormalities in either capacity may affect eating behavior.
  - dopamine: which in addition to being a precursor of norepinephrine and epinephrine is also a neurotransmitter which regulates the rewarding property of food.
- leptin and ghrelin: leptin is a hormone produced primarily by the fat cells in the body; it has an inhibitory effect on appetite by inducing a feeling of satiety. Ghrelin is an appetite inducing hormone produced in the stomach and the upper portion of the small intestine. Circulating levels of both hormones are an important factor in weight control. While often associated with obesity, both hormones and their respective effects have been implicated in the pathophysiology of anorexia nervosa and bulimia nervosa.
- immune system: studies have shown that a majority of patients with anorexia and bulimia nervosa have elevated levels of autoantibodies that affect hormones and neuropeptides that regulate appetite control and the stress response. There may be a direct correlation between autoantibody levels and associated psychological traits.
- infection: PANDAS, is an abbreviation for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections. Children with PANDAS "have obsessive-compulsive disorder (OCD) and/or tic disorders such as Tourette syndrome, and in whom symptoms worsen following infections such as "strep throat" and scarlet fever." (NIMH) There is a possibility that

PANDAS may be a precipitating factor in the development of anorexia nervosa in some cases, (PANDAS AN).

- lesions: studies have shown that lesions to the right frontal lobe or temporal lobe can cause the pathological symptoms of an eating disorder.
- tumors: tumors in various regions of the brain have been implicated in the development of abnormal eating patterns.
- brain calcification: a study highlights a case in which prior calcification of the right thalamus may have contributed to development of anorexia nervosa.
- somatosensory homunculus: is the representation of the body located in the somatosensory cortex, first described by renowned neurosurgeon Wilder Penfield. The illustration was originally termed "Penfield's Homunculus", homunculus meaning little man. "In normal development this representation should adapt as the body goes through its pubertal growth spurt. However, in AN it is hypothesized that there is a lack of plasticity in this area, which may result in impairments of sensory processing and distortion of body image". (Bryan Lask, also proposed by VS Ramachandran)
- Obstetric complications: There have been studies done which show maternal smoking, obstetric and perinatal complications such as maternal anemia, very pre-term birth (32<wks.), being born small for gestational age, neonatal cardiac problems, preeclampsia, placental infarction and sustaining a cephalhematoma at birth increase the risk factor for developing either anorexia nervosa or bulimia nervosa. Some of this developmental risk as in the case of placental infarction, maternal anemia and cardiac problems may cause intrauterine hypoxia, umbilical cord occlusion or cord prolapse may cause ischemia, resulting in cerebral injury, the prefrontal cortex in the fetus and neonate is highly susceptible to damage as a result of oxygen deprivation which has been shown to contribute to executive dysfunction, ADHD, and may affect personality traits associated with both eating disorders and comorbid disorders such as impulsivity, mental rigidity and obsessionality. The problem of perinatal brain injury, in terms of the costs to society and to the affected individuals and their families, is extraordinary. (Yafeng Dong, PhD)

## Psychological

Eating disorders are classified as Axis I disorders in the Diagnostic and Statistical Manual of Mental Health Disorders (DSM-IV) published by the American Psychiatric Association. There are various other psychological issues that may factor into eating disorders, some fulfill the criteria for a separate Axis I diagnosis or a personality disorder which is coded Axis II and thus are considered comorbid to the diagnosed eating disorder. Axis II disorders are subtyped into 3 "clusters", A, B and C. The causality between personality disorders and eating disorders has yet to be fully established. Some people have a previous disorder which may increase their vulnerability to developing an eating disorder. Some develop them afterwards. The severity and type of eating disorder symptoms have been shown to affect comorbidity. The DSM-IV should not be used by laypersons to diagnose themselves, even when used by professionals there has been considerable controversy over the diagnostic criteria used for various diagnoses,

including eating disorders. There has been controversy over various editions of the DSM including the latest edition, DSM-V, due in May 2013.

### Comorbid Disorders

Axis I	Axis II
depression	obsessive compulsive personality disorder
substance abuse, alcoholism	borderline personality disorder
anxiety disorders	narcissistic personality disorder
obsessive compulsive disorder	histrionic personality disorder
Attention-deficit hyperactivity disorder	avoidant personality disorder

### Personality traits

There are various childhood personality traits associated with the development of eating disorders. During adolescence these traits may become intensified due to a variety of physiological and cultural influences such as the hormonal changes associated with puberty, stress related to the approaching demands of maturity and socio-cultural influences and perceived expectations, especially in areas that concern body image. Many personality traits have a genetic component and are highly heritable. Maladaptive levels of certain traits may be acquired as a result of anoxic or traumatic brain injury, neurodegenerative diseases such as Parkinson's disease, neurotoxicity such as lead exposure, bacterial infection such as Lyme disease or viral infection such as *Toxoplasma gondii* as well as hormonal influences. While studies are still continuing via the use of various imaging techniques such as fMRI; these traits have been shown to originate in various regions of the brain such as the amygdala and the prefrontal cortex. Disorders in the prefrontal cortex and the executive functioning system have been shown to affect eating behavior.

### Environmental

#### Child maltreatment

Child abuse which encompasses physical, psychological and sexual abuse, as well as neglect has been shown by innumerable studies to be a precipitating factor in a wide variety of psychiatric disorders, including eating disorders. Children who are subjugated to abuse may develop a disordered eating in an effort to gain some sense of control or for a sense of comfort. Or they may be in an environment where the diet is unhealthy or insufficient. Child abuse and neglect can cause profound changes in both the physiological structure and the neurochemistry of the developing brain. Children who, as wards of the state, were placed in orphanages or foster homes are especially susceptible to developing a disordered eating pattern. In a study done in New Zealand 25% of the study subjects in foster care exhibited an eating disorder (Tarren-Sweeney M. 2006). An unstable home environment is detrimental to the emotional well-being of children, even in the absence of blatant abuse or neglect the stress of an unstable home can contribute to the development of an eating disorder.

### **Social isolation**

Social isolation has been shown to have a deleterious effect on an individuals' physical and emotional well-being. Those that are socially isolated have a higher mortality rate in general as compared to individuals that have established social relationships. This effect on mortality is markedly increased in those with pre-existing medical or psychiatric conditions, and has been especially noted in cases of coronary heart disease. "The magnitude of risk associated with social isolation is comparable with that of cigarette smoking and other major biomedical and psychosocial risk factors." (Brummett et al.)

Social isolation can be inherently stressful, depressing and anxiety provoking. In an attempt to ameliorate these distressful feelings an individual may engage in emotional eating in which food serves as a source of comfort. The loneliness of social isolation and the inherent stressors thus associated have been implicated as triggering factors in binge eating as well.

### **Parental influence**

Parental influence has been shown to be an intrinsic component in developing the eating behaviors of children. This influence is manifested and shaped by a variety of diverse factors such as familial genetic predisposition, dietary choices as dictated by cultural or ethnic preferences, the parents' own body shape and eating patterns, the degree of involvement and expectations of their children's eating behavior as well as the interpersonal relationship of parent and child. This is in addition to the general psychosocial climate of the home and the presence or absence of a nurturing stable environment. It has been shown that maladaptive parental behavior has an important role in the development of eating disorders. As to the more subtle aspects of parental influence it has been shown that eating patterns are established in early childhood and that children should be allowed to decide when their appetite is satisfied as early as the age of two. A direct link has been proven between obesity and parental pressure to eat more.

Coercive tactics in regard to diet have not been proven to be efficacious in controlling a child's eating behavior. Affection and attention have been shown to affect the degree of a child's finickiness and their acceptance of a more varied diet.

### **Peer pressure**

In various studies such as one conducted by The McKnight Investigators, peer pressure was shown to be a significant contributor to body image concerns and attitudes toward eating among subjects in their teens and early twenties.

Eleanor Mackey and co-author, Annette M. La Greca of the University of Miami, studied 236 teen girls from public high schools in southeast Florida. "Teen girls' concerns about their own weight, about how they appear to others and their perceptions that their peers want them to be thin are significantly related to weight-control behavior," says

psychologist Eleanor Mackey of the Children's National Medical Center in Washington and lead author of the study. "Those are really important."

According to one study, 40% of 9- and 10-year-old girls are already trying to lose weight. Such dieting is reported to being influenced by peer behavior, with many of those individuals on a diet reporting that their friends also were dieting. The number of friends dieting and the number of friends who pressured them to diet also played a significant role in their own choices.

### **Cultural pressure**

There is a cultural emphasis on thinness which is especially pervasive in western society. There is an unrealistic stereotype of what constitutes beauty and the ideal body type as portrayed by the media, fashion and entertainment industries. "The cultural pressure on men and women to be "[perfect]" is an important predisposing factor for the development of eating disorders" (Bryan Lask, PhD).

### **In men**

It is estimated that 8 million people in the United States are suffering from an Eating Disorder, and of that number 10% are men. Professionals suggest that the percentage suffering that are men is much higher, but because of the old fashioned idea that this illness strikes only women, few men come forward to find the help they deserve.

To date, the evidence suggests that the gender bias of clinicians means that diagnosing either bulimia or anorexia in men is less likely despite identical behavior. Men are more likely to be diagnosed as suffering depression with associated appetite changes than receive a primary diagnosis of an eating disorder.

In addition, there may often be shrouds of secrecy because of the lack of therapy groups and treatment centers offering groups specifically designed for men. They may feel very alone at the thought of having to sit in a group of women, to be part of a program designed for women, and even at the prospect that a treatment facility will turn them down because of their sex.

Men who participate in low-weight oriented sports such as jockeys, wrestlers and runners are at an increased risk of developing an Eating Disorder such as Anorexia or Bulimia. The pressure to succeed, to be the best, to be competitive and to win at all costs, combined with any non-athletic pressures in their lives (relationship issues, family problems, abuse, etc.) can help to contribute the onset of their disordered eating.

It is not uncommon for men suffering with an Eating Disorder to also suffer with alcohol abuse and/or substance abuse simultaneously (though many women also suffer both disordered eating and substance abuse problems, combined). This may be due to the addictive nature of their psychological health, combined with the strong images put out by society of men's overindulgence in alcohol.

There may also be a link between ADHD, with male sufferers of Anorexia, Bulimia, and self-injury. More research is still needing to be done in this area.

For all those who suffer, men and women alike, there are many possible co-existing psychological illnesses that can be present, including depression, anxiety, PTSD, self-injury behaviors, substance abuse, OCD, borderline personality disorder, and Multiple Personality Disorders.

It is important to remember is that most of the underlying psychological factors that lead to an Eating Disorder are the same for both men and women; low self-esteem, a need to be accepted, depression, anxiety, an inability to cope with emotions & personal issues, and other existing psychological illnesses. All of the physical dangers and complications associated with being the sufferer of an Eating Disorder are the same. A great number of the causes are the same or very similar (family problems, relationship issues, alcoholic/addictive parent, abuse, societal pressure). Most of all, it is important to remember that *all* people with eating disorders deserve to find recovery, happiness, and self-love on the other side.

### ***Symptoms-complications***

Symptoms and complications vary according to the nature and severity of the eating disorder:

#### Possible Symptoms and Complications of Eating Disorders

acne	xerosis	amenorrhoea	tooth loss, cavities
constipation	diarrhea	water retention and/or edema	lanugo
telogen effluvium	cardiac arrest	hypokalemia	death
osteoporosis	electrolyte imbalance	hyponatremia	brain atrophy
pellagra	scurvy	kidney failure	suicide

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder to affect women. Though often associated with obesity it can occur in normal weight individuals. PCOS has been associated with binge eating and bulimic behavior.

### ***Diagnosis***

The initial diagnosis should be made by a competent medical professional. "The medical history is the most powerful tool for diagnosing eating disorders"(American Family Physician). There are many medical disorders that mimic eating disorders and comorbid psychiatric disorders. All organic causes should be ruled out prior to a diagnosis of an eating disorder or any other psychiatric disorder is made.

## Medical

The diagnostic workup typically includes complete medical and psychosocial history and follows a rational and formulaic approach to the diagnosis. Neuroimaging using fMRI, MRI, PET and SPECT scans have been used to detect cases in which a lesion, tumor or other organic condition has been either the sole causative or contributory factor in an eating disorder. "Right frontal intracerebral lesions with their close relationship to the limbic system could be causative for eating disorders, we therefore recommend performing a cranial MRI in all patients with suspected eating disorders" (Trummer M et al. 2002), "intracranial pathology should also be considered however certain is the diagnosis of early-onset anorexia nervosa. Second, neuroimaging plays an important part in diagnosing early-onset anorexia nervosa, both from a clinical and a research prospective".(O'Brien et al. 2001).

## Psychological

### Eating Disorder Specific Psychometric Tests

- Eating Attitudes Test      SCOFF questionnaire
- Body Attitudes Test      Body Attitudes Questionnaire
- Eating Disorder Inventory      Eating Disorder Examination Interview

After ruling out organic causes and the initial diagnosis of an eating disorder being made by a medical professional, a trained mental health professional aids in the assessment and treatment of the underlying psychological components of the eating disorder and any comorbid psychological conditions. The clinician conducts a clinical interview and may employ various psychometric tests. Some are general in nature while others were devised specifically for use in the assessment of eating disorders. Some of the general tests that may be used are the Hamilton Depression Rating Scale and the Beck Depression Inventory.

## Differential diagnoses

There are a variety of medical conditions which may be misdiagnosed as an eating disorder such as Lyme disease which is known as the "great imitator", as it may present as a variety of psychiatric or neurologic disorders including anorexia nervosa.

- Addison's Disease is a disorder of the adrenal cortex which results in decreased hormonal production. Addison's disease, even in subclinical form may mimic many of the symptoms of anorexia nervosa.
- gastric adenocarcinoma is one of the most common forms of cancer in the world. Complications due to this condition have been misdiagnosed as an eating disorder.
- helicobacter pylori is a bacterium which causes stomach ulcers and gastritis and has been shown to be a precipitating factor in the development of gastric carcinomas. It also has an effect on circulating levels of leptin and ghrelin, two hormones which help regulate appetite. Upon successful treatment of helicobacter

pylori associated gastritis in pre-pubertal children they showed "significant increase in BMI, lean and fat mass along with a significant decrease in circulating ghrelin levels and an increase in leptin levels" (Pacifico, L)."SUMMARY: H. pylori has an influence on the release of gastric hormones and therefore plays a role in the regulation of body weight, hunger and satiety,"(Weigt J, Malfertheiner P).

- hypothyroidism, hyperthyroidism, hypoparathyroidism and hyperparathyroidism may mimic some of the symptoms of, can occur concurrently with, be masked by or exacerbate an eating disorder.

There are multiple medical conditions which may be misdiagnosed as a primary psychiatric disorder. These may have a synergistic effect on conditions which mimic an eating disorder or on a properly diagnosed ED. They also may make it more difficult to diagnose and treat an ED.

- Lupus: 19 psychiatric conditions have been associated with systemic lupus erythematosus (SLE), including depression and bipolar disorder.
- Toxoplasma seropositivity: even in the absence of symptomatic toxoplasmosis, toxoplasma gondii exposure has been linked to changes in human behavior and psychiatric disorders including those comorbid with eating disorders such as depression. In reported case studies the response to antidepressant treatment improved only after adequate treatment for toxoplasma.
- neurosyphilis: It is estimated that there may be up to one million cases of untreated syphilis in the US alone. "The disease can present with psychiatric symptoms alone, psychiatric symptoms that can mimic any other psychiatric illness". Many of the manifestations may appear atypical. Up to 1.3% of short term psychiatric admissions may be attributable to neurosyphilis, with a much higher rate in the general psychiatric population. Neurosyphilis like Lyme disease has been given the appellation the "great imitator" for it may present in various ways such as depression and chronic alcoholism. (Ritchie, M Perdigo J.)
- dysautonomia: a term used to describe a wide variety of autonomic nervous system (ANS) disorders may cause a wide variety of psychiatric symptoms including anxiety, panic attacks and depression. Dysautonomia usually involves failure of sympathetic or parasympathetic components of the ANS system but may also include excessive ANS activity. Dysautonomia can occur in conditions such as diabetes and alcoholism.

There are separate psychological disorders which may be misdiagnosed as an eating disorder.

- Emetophobia is an anxiety disorder characterized by an intense fear of vomiting. A person so afflicted may develop rigorous standards of food hygiene, such as not touching food with their hands. They may become socially withdrawn to avoid situations which in their perception may make them vomit. Many who suffer from emetophobia are diagnosed with anorexia or self-starvation. In severe cases of emetophobia they may drastically reduce their food intake.

- phagophobia is an anxiety disorder characterized by a fear of eating, it is usually initiated by an adverse experience while eating such as choking or vomiting. Persons with this disorder may present with complaints of pain while swallowing.
- Body dysmorphic disorder (BDD) is listed as a somatoform disorder that affects up to 2% of the population. BDD is characterized by excessive rumination over an actual or perceived physical flaw. BDD has been diagnosed equally among men and women. While BDD has been misdiagnosed as anorexia nervosa, it also occurs comorbidly in 39% of eating disorder cases. BDD is a chronic and debilitating condition which may lead to social isolation, major depression and suicidal ideation and attempts. Neuroimaging studies to measure response to facial recognition have shown activity predominately in the left hemisphere in the left lateral prefrontal cortex, lateral temporal lobe and left parietal lobe showing hemispheric imbalance in information processing. There is a reported case of the development of BDD in a 21 year old male following an inflammatory brain process. Neuroimaging showed the presence of a new atrophy in the frontotemporal region.

## Chapter-2

# Anorexia Nervosa

### Anorexia Nervosa

"Miss A" - pictured in 1866 and in 1870 after treatment. She was one of the earliest Anorexia nervosa case studies. From the published medical papers of Sir William Gull.

<b>ICD-10</b>	F50.0-F50.1
<b>ICD-9</b>	307.1
<b>OMIM</b>	606788
<b>DiseasesDB</b>	749
<b>eMedicine</b>	emerg/34 med/144
<b>MeSH</b>	D000856

**Anorexia nervosa** is an eating disorder characterized by refusal to maintain a healthy body weight, and an obsessive fear of gaining weight due to a distorted self image which may be maintained by various cognitive biases that alter how the affected individual evaluates and thinks about her or his body, food and eating. It is a serious mental illness with a high incidence of comorbidity and the highest mortality rate of any psychiatric disorder.

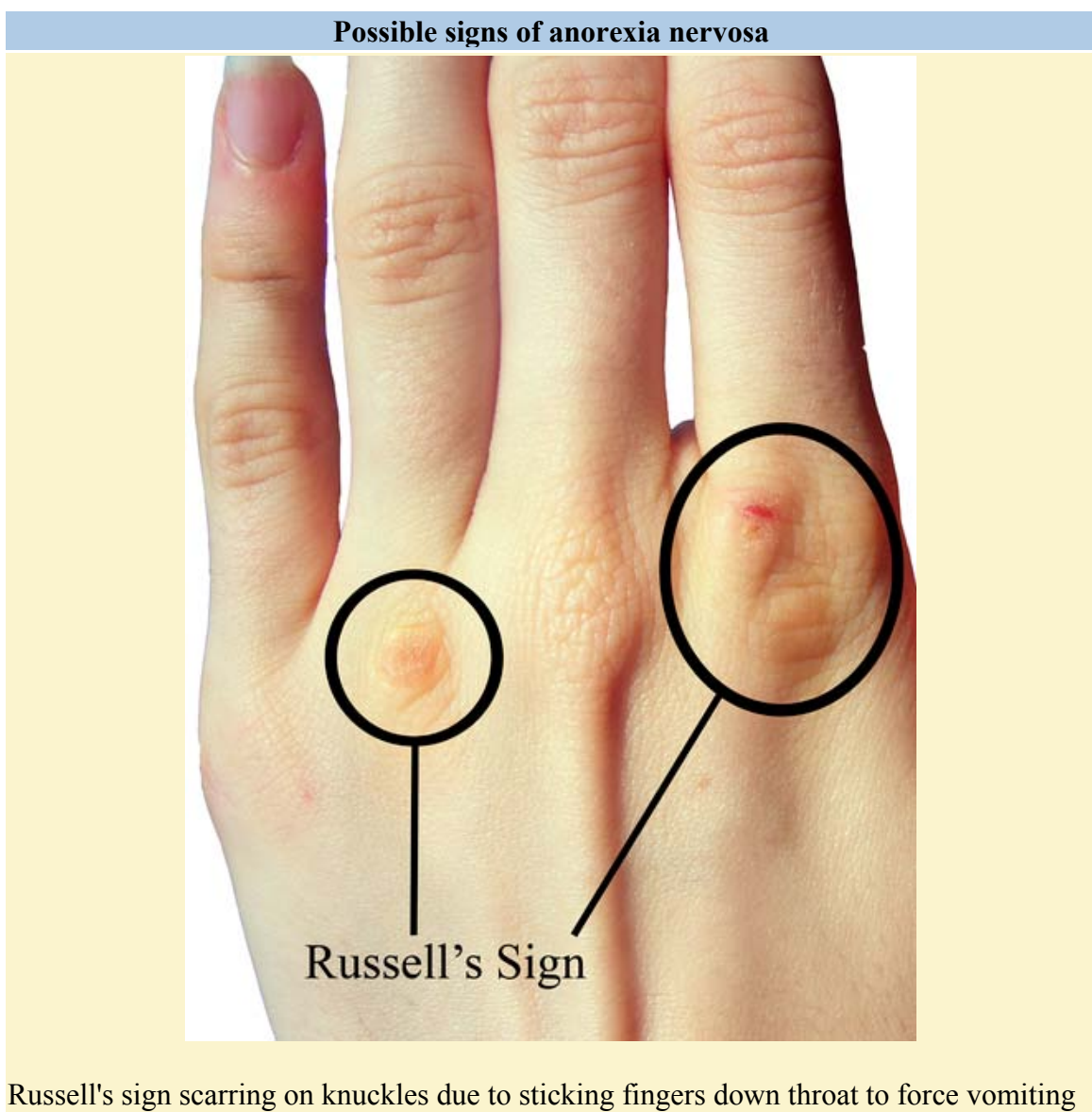
It can affect men and women of all ages, races, socioeconomic and cultural backgrounds. Anorexia nervosa occurs in the ratio of 1:10 in males:females.

The term anorexia nervosa was established in 1873 by Sir William Gull, one of Queen Victoria's personal physicians. The term is of Greek origin: *a* ( $\alpha$ , prefix of negation), *n* ( $\nu$ , link between two vowels) and *orexis* ( $\omicron\rho\epsilon\acute{\xi}\iota\varsigma$ , appetite), thus meaning a lack of desire to eat.

## ***Signs and symptoms***

A person with anorexia nervosa may exhibit a number of signs and symptoms, some of which are listed below. The type and severity vary in each case and may be present but not readily apparent. Anorexia nervosa and the associated malnutrition that results from self-imposed starvation, can cause severe complications in every major organ system in the body.

It should be noted that some of the possible signs listed below (Russell's sign, scarring of knuckles, purging/self-induced vomiting and use/abuse of laxatives, diet pills, i.e., and swollen cheeks/enlargement of the salivary glands) are signs primarily of bulimia, which is a condition that often occurs simultaneously with anorexia.





Chilblains, also known as Perniosis.  
Possible cutaneous complication of anorexia nervosa.

- obvious, rapid, dramatic weight loss
- Russell's sign: scarring of the knuckles from placing fingers down the throat to induce vomiting
- lanugo: soft, fine hair grows on face and body
- obsession with calories and fat content
- preoccupation with food, recipes, or cooking; may cook elaborate dinners for others but not eat themselves
- dieting despite being thin or dangerously underweight
- fear of gaining weight or becoming overweight
- rituals: cuts food into tiny pieces; refuses to eat around others; hides or discards food
- purging: uses laxatives, diet pills, ipecac syrup, or water pills; may engage in self-induced vomiting; may run to the bathroom after eating in order to vomit and quickly get rid of the calories
- may engage in frequent, strenuous exercise
- perception: perceives self to be overweight despite being told by others they are too thin
- becomes intolerant to cold: frequently complains of being cold due to loss of insulating body fat; body temperature lowers (hypothermia) in effort to conserve

calories

- depression: may frequently be in a sad, lethargic state
- solitude: may avoid friends and family; becomes withdrawn and secretive
- clothing: may wear baggy, loose-fitting clothes to cover weight loss if they have been confronted about their health and wish to hide it, while others will wear baggy clothing to hide what they see as an unattractive and overweight body.
- cheeks may become swollen due to enlargement of the salivary glands caused by excessive vomiting
- swollen joints
- abdominal distension

#### Dermatologic signs of anorexia nervosa

xerosis	telogen effluvium	carotenoderma	acne	hyperpigmentation
seborrheic dermatitis	acrocyanosis	perniosis	petechiae	livedo reticularis
interdigital intertrigo	paronychia	generalized pruritus	acquired striae distensae	angular stomatitis
prurigo pigmentosa	edema	linear erythema craquele	acrodermatitis enteropathica	pellagra

#### Possible medical complications of anorexia nervosa

constipation	diarrhea	electrolyte imbalance	cavities	tooth loss
cardiac arrest	amenorrhoea	edema	osteoporosis	osteopenia
hyponatremia	hypokalemia	optic neuropathy	brain atrophy	leukopenia

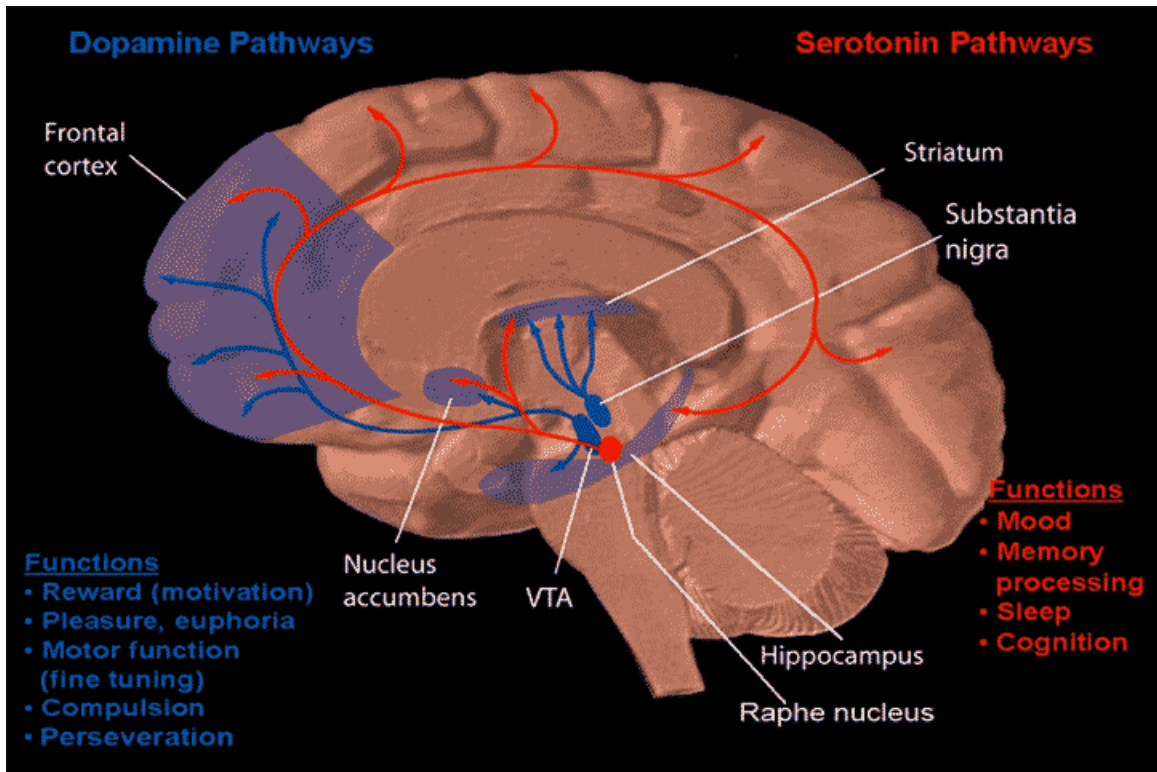
## Causes

Studies have hypothesized that the continuance of disordered eating patterns may be epiphenomena of starvation. The results of the Minnesota Starvation Experiment showed that normal controls exhibit many of the behavioral patterns of anorexia nervosa when subjected to starvation. This may be due to the numerous changes in the neuroendocrine system, which results in a self-perpetuating cycle. Studies have suggested that the initial weight loss such as dieting may be the triggering factor in developing AN in some cases, possibly due to an already inherent predisposition toward AN. One study reports cases of AN resulting from unintended weight loss that resulted from varied causes such as a parasitic infection, medication side effects, and surgery. The weight loss itself was the triggering factor.

## Biological

- Obstetric complications: various prenatal and perinatal complications may factor into the development of AN such as maternal anemia, diabetes mellitus, preeclampsia, placental infarction, and neonatal cardiac abnormalities. Neonatal

- complications may also have an influence on harm avoidance, one of the personality traits associated with the development of AN.
- Genetics: anorexia nervosa is believed to be highly heritable, with estimated inheritance rates ranging from 56% to 84%. Association studies have been performed, studying 128 different polymorphisms related to 43 genes including genes involved in regulation of eating behavior, motivation and reward mechanics, personality traits and emotion. Consistent associations have been identified for polymorphisms associated with agouti related peptide, brain derived neurotrophic factor, catechol-o-methyl transferase, SK3 and opioid receptor delta-1. In one study, variations in the norepinephrine transporter gene promoter were associated with restrictive anorexia nervosa, but not binge-purge anorexia. Recent studies have advanced the theory that the sex difference in incidence and the common onset at the age of puberty may reflect an abnormal response of the brain to anorexic (feeding suppressing) effects of the female sex hormone, estrogen. This viewpoint has been recently supported by a report that abnormal forms of the estrogen receptor are more common in women with anorexia nervosa of the restricting type.
    - epigenetics: Epigenetic mechanisms: are means by which genetic mutations are caused by environmental effects that alter gene expression via methods such as DNA methylation, these are independent of and do not alter the underlying DNA sequence. They are heritable, as was shown in the Överkalix study, but also may occur throughout the lifespan, and are potentially reversible. Dysregulation of dopaminergic neurotransmission and Atrial natriuretic peptide homeostasis due to epigenetic mechanisms, has been implicated in various eating disorders. *"We conclude that epigenetic mechanisms may contribute to the known alterations of ANP homeostasis in women with eating disorders."*



Dysregulation of the dopamine and serotonin pathways has been implicated in the etiology, pathogenesis and pathophysiology of anorexia nervosa.

- serotonin dysregulation; particularly high levels in those areas in the brain with the 5HT<sub>1A</sub> receptor - a system particularly linked to anxiety, mood and impulse control. Starvation has been hypothesized to be a response to these effects, as it is known to lower tryptophan and steroid hormone metabolism, which might reduce serotonin levels at these critical sites and ward off anxiety. Other studies of the 5HT<sub>2A</sub> serotonin receptor (linked to regulation of feeding, mood, and anxiety), suggest that serotonin activity is decreased at these sites. There is evidence that both personality characteristics associated with AN, and disturbances to the serotonin system are still apparent after patients have recovered from anorexia.
- Brain-derived neurotrophic factor (BDNF) is a protein that regulates neuronal development and neuroplasticity, it also plays a role in learning, memory and in the hypothalamic pathway that controls eating behavior and energy homeostasis. BDNF amplifies neurotransmitter responses and promotes synaptic communication in the enteric nervous system. Low levels of BDNF are found in patients with AN and some comorbid disorders such as major depression. Exercise increases levels of BDNF
- leptin and ghrelin; leptin is a hormone produced primarily by the fat cells in white adipose tissue of the body it has an inhibitory (anorexigenic) effect on appetite, by inducing a feeling of satiety. Ghrelin is an appetite inducing (orexigenic) hormone produced in the stomach and the upper portion of the small intestine. Circulating levels of both hormones are an important factor in weight control. While often

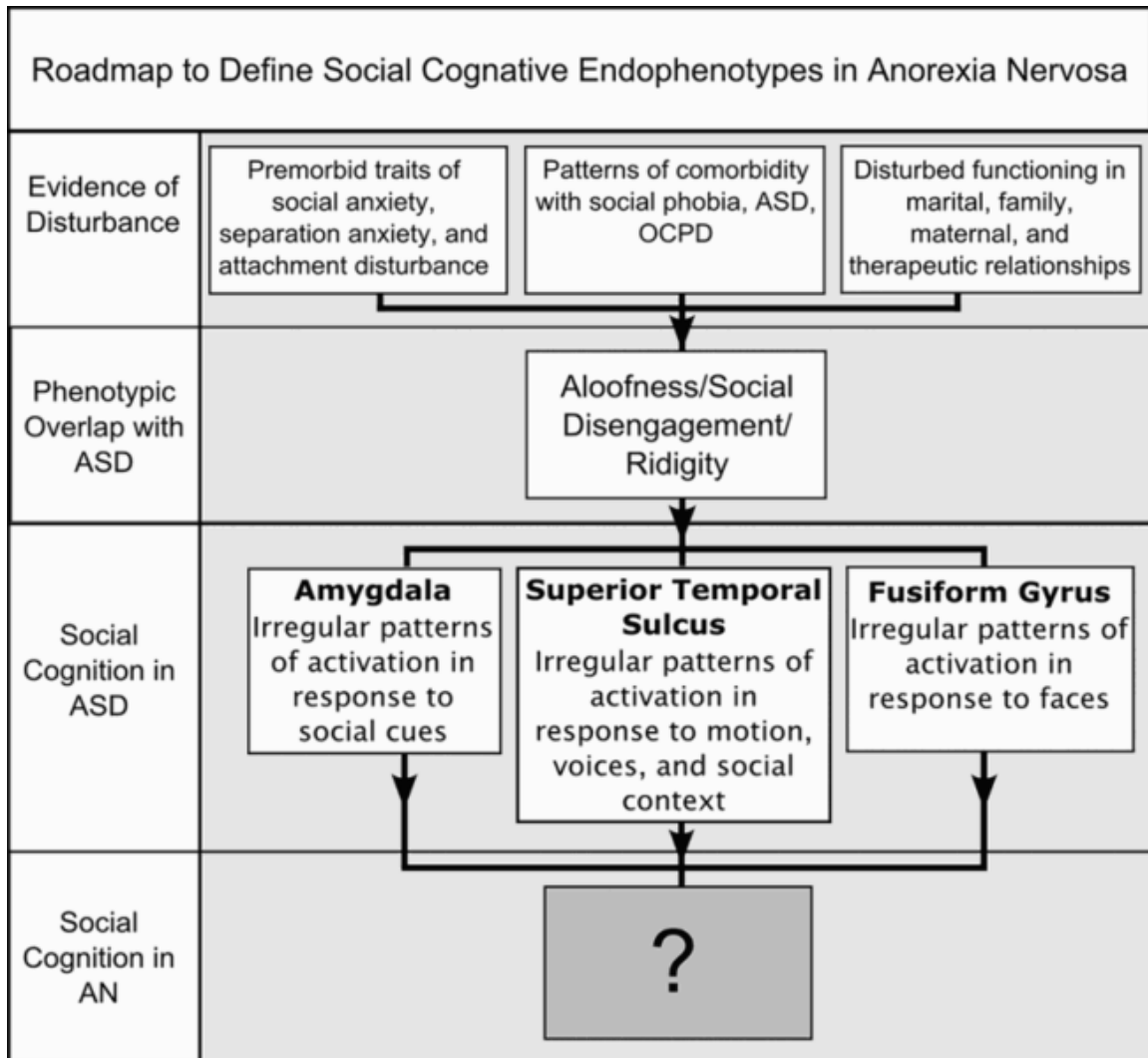
- associated with obesity both have been implicated in the pathophysiology of anorexia nervosa and bulimia nervosa.
- cerebral blood flow (CBF); neuroimaging studies have shown reduced CBF in the temporal lobes of anorectic patients, which may be a predisposing factor in the onset of AN.
  - autoimmune system; Autoantibodies against neuropeptides such as melanocortin have been shown to affect personality traits associated with eating disorders such as those that influence appetite and stress responses.
  - Nutritional deficiencies
    - Zinc deficiency may play a role in Anorexia. It is not thought responsible for causation of the initial illness but there is evidence that it may be an accelerating factor that deepens the pathology of the anorexia. A 1994 randomized, double-blind, placebo-controlled trial showed that zinc (14 mg per day) doubled the rate of body mass increase compared to patients receiving the placebo.

## **Environmental**

Sociocultural studies have highlighted the role of cultural factors, such as the promotion of thinness as the ideal female form in Western industrialized nations, particularly through the media. A recent epidemiological study of 989,871 Swedish residents indicated that gender, ethnicity and socio-economic status were large influences on the chance of developing anorexia, with those with non-European parents among the least likely to be diagnosed with the condition, and those in wealthy, white families being most at risk. People in professions where there is a particular social pressure to be thin (such as models and dancers) were much more likely to develop anorexia during the course of their career, and further research has suggested that those with anorexia have much higher contact with cultural sources that promote weight-loss.

There is a high rate of reported child sexual abuse experiences in clinical groups of who have been diagnosed with anorexia. Although prior sexual abuse is not thought to be a specific risk factor for anorexia, those who have experienced such abuse are more likely to have more serious and chronic symptoms.

## Relationship to autism



A summary of the strategy Zucker *et al.* (2007) used to assess the relationship between anorexia nervosa and the autism spectrum.

Since Gillberg's (1985) and others initial suggestion of relationship between anorexia nervosa and autism, a large scale longitudinal study into teenage onset anorexia nervosa conducted in Sweden confirmed that 23% of people with a long-standing eating disorder are on the autism spectrum. Those on autism spectrum tend to have a worse outcome, but may benefit from the combined use of behavioural and pharmacological therapies tailored to ameliorate autism rather than anorexia nervosa per se. Other studies, most notably research conducted at the Maudsley Hospital UK, furthermore suggest that autistic traits are common in people with anorexia nervosa, shared traits include *e.g.* executive function, autism quotient score, central coherence, theory of mind, cognitive-behavioural flexibility, emotion regulation and understanding facial expressions.

Zucker *et al.* (2007) proposed that conditions on the autism spectrum make up the cognitive endophenotype underlying anorexia nervosa and appealed for increased interdisciplinary collaboration (see figure). A pilot study into the effectiveness Cognitive Behaviour Therapy, which based its treatment protocol on the hypothesised relationship between anorexia nervosa and an underlying autistic like condition, reduced perfectionism and rigidity in 17 out of 19 participants.

## **Diagnosis**

### **Medical**

The initial diagnosis should be made by a competent medical professional. There are multiple medical conditions, such as viral or bacterial infections, hormonal imbalances, neurodegenerative diseases and brain tumors which may mimic psychiatric disorders including anorexia nervosa. According to an in depth study conducted by psychiatrist Richard Hall as published in the Archives of General Psychiatry:

- Medical illness often presents with psychiatric symptoms.
- It is difficult to distinguish physical disorders from functional psychiatric disorders on the basis of psychiatric symptoms alone.
- Detailed physical examination and laboratory screening are indicated as a routine procedure in the initial evaluation of psychiatric patients.
- Most patients are unaware of the medical illness that is causative of their psychiatric symptoms.
- The conditions of patients with medically induced symptoms are often initially misdiagnosed as a functional psychosis.
- There are a variety of tests that may aid in the diagnosis of AN and the assessment of possible secondary effects caused by AN upon the patient.

#### **Medical Tests used in the Diagnosis and Assessment of Anorexia Nervosa**

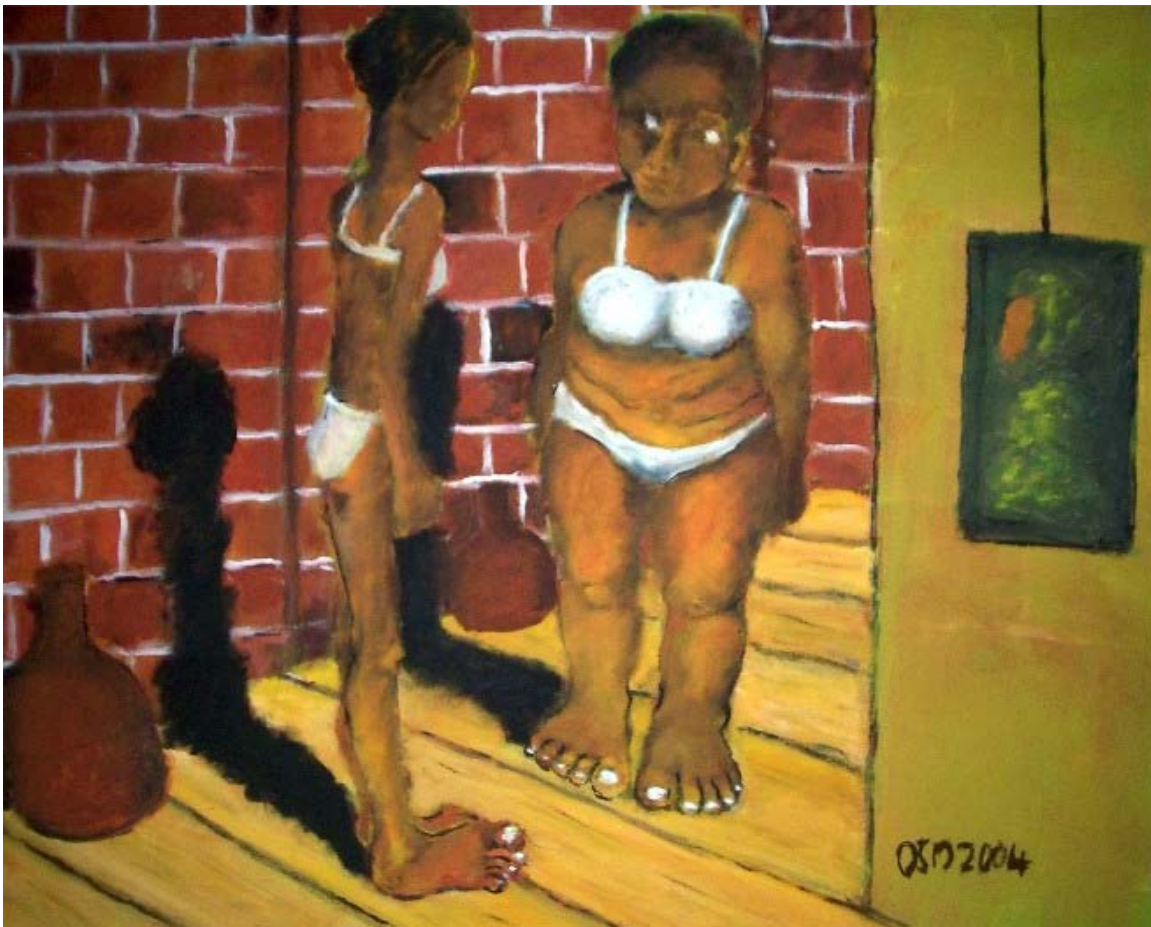
- Complete Blood Count (CBC): a test of the white blood cells, red blood cells and platelets used to assess the presence of various disorders such as leukocytosis, leukopenia, thrombocytosis and anemia which may result from malnutrition.
- urinalysis: a variety of tests performed on the urine used in the diagnosis of medical disorders, to test for substance abuse and as an indicator of overall health
- ELISA: Various subtypes of ELISA used to test for antibodies to various viruses and bacteria such as *Borrelia burgdoferi* (Lyme Disease)
- Western Blot Analysis: Used to confirm the preliminary results of the ELISA
- Chem-20: Chem-20 also known as SMA-20 a group of twenty separate chemical tests performed on blood serum. Tests include cholesterol, protein and electrolytes such as potassium, chlorine and sodium and tests specific to liver and kidney function.
- glucose tolerance test: Oral glucose tolerance test (OGTT) used to assess the body's ability to metabolize glucose. Can be useful in detecting various disorders such as diabetes, an insulinoma, Cushing's Syndrome, hypoglycemia and

- polycystic ovary syndrome
- Secritin-CCK Test: Used to assess function of pancreas and gall bladder
  - Serum cholinesterase test: a test of liver enzymes (acetylcholinesterase and pseudocholinesterase) useful as a test of liver function and to assess the effects of malnutrition
  - Liver Function Test: A series of tests used to assess liver function some of the tests are also used in the assessment of malnutrition, protein deficiency, kidney function, bleeding disorders, Crohn's Disease
  - Lh response to GnRH: Luteinizing hormone (Lh) response to gonadotropin-releasing hormone (GnRH): Tests the pituitary glands' response to GnRh a hormone produced in the hypothalamus. Central hypogonadism is often seen in anorexia nervosa cases.
  - Creatine Kinase Test (CK-Test): measures the circulating blood levels of creatine kinase an enzyme found in the heart (CK-MB), brain (CK-BB) and skeletal muscle (CK-MM).
  - Blood urea nitrogen (BUN) test: urea nitrogen is the byproduct of protein metabolism first formed in the liver then removed from the body by the kidneys. The BUN test is used primarily to test kidney function. A low BUN level may indicate the effects of malnutrition.
  - BUN-to-creatinine ratio: A BUN to creatinine ratio is used to predict various conditions. High BUN/creatinine ratio can occur in severe hydration, acute kidney failure, congestive heart failure, intestinal bleeding. A low BUN/creatinine can indicate a low protein diet, celiac disease rhabdomyolysis, cirrhosis of the liver.
  - echocardiogram: utilizes ultrasound to create a moving picture of the heart to assess function
  - electrocardiogram (EKG or ECG): measures electrical activity of heart can be used to detect various disorders such as hyperkalemia
  - electroencephalogram (EEG): measures the electrical activity of the brain. Can be used to detect abnormalities such as those associated with pituitary tumors
  - Upper GI Series: test used to assess gastrointestinal problems of the middle and upper intestinal tract
  - Thyroid Screen TSH, t4, t3: test used to assess thyroid functioning by checking levels of thyroid-stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3)
  - Parathyroid hormone (PTH) test: tests the functioning of the parathyroid by measuring the amount of (PTH) in the blood. Test is used to diagnose parahypothyroidism. PTH also controls the levels of calcium and phosphorus in the blood (homeostasis).
  - barium enema: an x-ray examination of the lower gastrointestinal tract
- 
- neuroimaging; via the use of various techniques such as PET scan, fMRI, MRI and SPECT imaging should be included in the diagnostic procedure for any eating disorder to detect cases in which a lesion, tumor or other organic condition has been either the sole causative or contributory factor in an eating disorder.

- *"we therefore recommend performing a cranial MRI in all patients with suspected eating disorders"(Trummer M et al.2002)", "intracranial pathology should also be considered however certain is the diagnosis of early-onset anorexia nervosa. Second, neuroimaging plays an important part in diagnosing early-onset anorexia nervosa,..".(O'Brien et al.2001).*

## Psychological

Anorexia nervosa is classified as an Axis I disorder in the Diagnostic and Statistical Manual of Mental Health Disorders (DSM-IV). Published by The American Psychiatric Association. The DSM-IV should not be used by laypersons to diagnose themselves.



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- **DSM-IV-TR:** diagnostic criteria for AN includes intense fear of gaining weight, a refusal to maintain body weight above 85% of the expected weight for a given age and height, and three consecutive missed periods and either refusal to admit the seriousness of the weight loss, or undue influence of shape or weight on one's self image, or a disturbed experience in one's shape or weight. There are two types:

the binge-eating/purging type is characterized by overeating or purging, and the restricting type is not.

- **Criticism of DSM-IV** There has been criticisms over various aspects of the diagnostic criteria utilized for anorexia nervosa in the DSM-IV. Including the requirement of maintaining a body weight below 85% of the expected weight and the requirement of amenorrhea for diagnosis; some women have all the symptoms of AN and continue to menstruate. Those who do not meet these criteria are usually classified as eating disorder not otherwise specified this may affect treatment options and insurance reimbursements. The validity of the AN subtype classification has also been questioned due to the considerable diagnostic overlap between the binge eating/ purging type and the restricting type and the propensity of the patient to switch between the two.
- ICD-10: The criteria are similar, but in addition, specifically mention:
  1. The ways that individuals might induce weight-loss or maintain low body weight (avoiding fattening foods, self-induced vomiting, self-induced purging, excessive exercise, excessive use of appetite suppressants or diuretics).
  2. If onset is before puberty, that development is delayed or arrested.
  3. Certain physiological features, including *"widespread endocrine disorder involving hypothalamic-pituitary-gonadal axis is manifest in women as amenorrhoea and in men as loss of sexual interest and potency. There may also be elevated levels of growth hormones, raised cortisol levels, changes in the peripheral metabolism of thyroid hormone and abnormalities of insulin secretion"*.

### **Differential diagnoses**

There are various medical and psychological conditions that have been misdiagnosed as anorexia nervosa, in some cases the correct diagnosis was not made for more than ten years. In a reported case of achalasia misdiagnosed as AN, the patient spent two months confined to a psychiatric hospital.

There are various other psychological issues that may factor into anorexia nervosa, some fulfill the criteria for a separate Axis I diagnosis or a personality disorder which is coded Axis II and thus are considered comorbid to the diagnosed eating disorder. Axis II disorders are subtyped into 3 "clusters", A, B and C. The causality between personality disorders and eating disorders has yet to be fully established. Some people have a previous disorder which may increase their vulnerability to developing an eating disorder. Some develop them afterwards. The severity and type of eating disorder symptoms have been shown to affect comorbidity.

Comorbid Disorders	
Axis I	Axis II
depression	obsessive compulsive personality disorder
substance abuse, alcoholism	borderline personality disorder
anxiety disorders	narcissistic personality disorder
obsessive compulsive disorder	histrionic personality disorder
Attention-Deficit-Hyperactivity-Disorder	avoidant personality disorder

- Body dysmorphic disorder (BDD) is listed as a somatoform disorder that affects up to 2% of the population. BDD is characterized by excessive rumination over an actual or perceived physical flaw. BDD has been diagnosed equally among men and women. While BDD has been misdiagnosed as anorexia nervosa, it also occurs comorbidly in 25% to 39% of AN cases.

BDD is a chronic and debilitating condition which may lead to social isolation, major depression, suicidal ideation and attempts. Neuroimaging studies to measure response to facial recognition have shown activity predominately in the left hemisphere in the left lateral prefrontal cortex, lateral temporal lobe and left parietal lobe showing hemispheric imbalance in information processing. There is a reported case of the development of BDD in a 21 year old male following an inflammatory brain process. Neuroimaging showed the presence of new atrophy in the frontotemporal region.

The distinction between the diagnoses of anorexia nervosa, bulimia nervosa and eating disorder not otherwise specified (EDNOS) is often difficult to make as there is considerable overlap between patients diagnosed with these conditions. Seemingly minor changes in a patient's overall behavior or attitude can change a diagnosis from "anorexia: binge-eating type" to bulimia nervosa. It is not unusual for a person with an eating disorder to "move through" various diagnoses as his or her behavior and beliefs change over time.

## ***Treatment***

Treatment for anorexia nervosa tries to address three main areas. 1) Restoring the person to a healthy weight; 2) Treating the psychological disorders related to the illness; 3) Reducing or eliminating behaviours or thoughts that originally led to the disordered eating.

- Diet and Nutrition
  - Zinc supplementation has been shown in various studies to be beneficial in the treatment of AN even in patients not suffering from zinc deficiency, by helping to increase weight gain.
  - Essential fatty acids: The omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) have been shown to benefit

various neuropsychiatric disorders. There was reported rapid improvement in a case of severe AN treated with ethyl-eicosapentaenoic acid (E-EPA) and micronutrients. DHA and EPA supplementation has been shown to be a benefit in many of the comorbid disorders of AN including: attention deficit/hyperactivity disorder (ADHD), autism, major depressive disorder (MDD), bipolar disorder, and borderline personality disorder. Accelerated cognitive decline and mild cognitive impairment (MCI) correlate with lowered tissue levels of DHA/EPA, and supplementation has improved cognitive function.

- Nutrition counseling
- Medical Nutrition Therapy;(MNT) also referred to as Nutrition Therapy is the development and provision of a nutritional treatment or therapy based on a detailed assessment of a person's medical history, psychosocial history, physical examination, and dietary history.
- Medication
  - Olanzapine: has been shown to be effective in treating certain aspects of AN including to help raise the body mass index and reduce obsessionality, including obsessional thoughts about food.
- Psychotherapy/Cognitive remediation
  - Cognitive behavioral therapy (CBT) – "The term 'cognitive-behavioral therapy (CBT); is a very general term for a classification of therapies with similarities. There are several approaches to cognitive-behavioral therapy". CBT is an evidence based approach which in studies to date has shown to be useful in adolescents and adults with anorexia nervosa.

Cognitive Behavioral Therapies				
Rational Emotive Behavior Therapy	Dialectical behavior therapy	Rational Living Therapy	Rational Behavior Therapy	Cognitive Therapy

- Acceptance and commitment therapy: A type of CBT, has shown promise in the treatment of AN" *participants experienced clinically significant improvement on at least some measures; no participants worsened or lost weight even at 1-year follow-up.*"
- Cognitive Remediation Therapy (CRT): is a cognitive rehabilitation therapy developed at King's College in London designed to improve neurocognitive abilities such as attention, working memory, cognitive flexibility and planning, and executive functioning which leads to improved social functioning. Neuropsychological studies have shown that patients with AN have difficulties in cognitive flexibility. In studies

conducted at Kings College and in Poland with adolescents CRT was proven to be beneficial in treating anorexia nervosa, in the United States clinical trials are still being conducted by the National Institute of Mental Health on adolescents age 10-17 and Stanford University in subjects over 16 as a conjunctive therapy with Cognitive behavioral therapy.

- Family therapy: various forms of family therapy have been proven to work in the treatment of adolescent AN including "Conjoint family therapy" (CFT), in which the parents and child are seen together by the same therapist, "separated family therapy" (SFT) in which parents and child attend therapy separately with different therapists. *"Eisler's cohort show that, irrespective of the type of FBT, 75% of patients have a good outcome, 15% an intermediate outcome... "*
- Maudsley Family Therapy: A 4 to 5 year follow up study of the Maudsley approach, shows full recovery at rates up to 90%.
- Adjunctive/Alternate Therapies
  - Yoga: In preliminary studies individualized yoga treatment has shown positive results for use as an adjunctive therapy to standard care. The treatment was shown to reduce eating disorder symptoms, including food preoccupation, which decreased immediately after each session. Scores on the Eating Disorder Examination decreased consistently over the course of treatment.
  - Acupuncture/Tui na: According to a study in China positive results were obtained in treating AN with a combination treatment utilizing acupuncture and Tui na, a form of manipulation therapy.
- Experimental therapy
  - Marinol (dronabinol): a synthetic form of delta-9-THC a psychoactive compound extracted from the resin of the cannabis sativa plant is currently the subject of a clinical trial for use in the treatment of AN, the study is slated to end in 2011.
  - Ghrelin treatment: pilot studies have been concluded in the use of ghrelin infusion for the inpatient treatment of patients with AN. The results showed positive effect in the reduction of the associated gastrointestinal symptoms, an increase in appetite and energy intake without adverse effects.

## **Prognosis**

The long term prognosis of anorexia is more on favorable side. The National Comorbidity Replication Survey was conducted among more than 9,282 participants throughout the United States, the results found that the average duration of anorexia

nervosa is 1.7 years. *"Contrary to what people may believe, anorexia is not necessarily a chronic illness; in many cases, it runs its course and people get better..."*

In cases of adolescent anorexia nervosa that utilize Family treatment 75% of patients have a good outcome and an additional 15% show an intermediate yet more positive outcome. In a five year post treatment follow-up of Maudsley Family Therapy the full recovery rate was between 75% and 90%. Even in severe cases of AN, despite a noted 30% relapse rate after hospitalization, and a lengthy time to recovery ranging from 57–79 months, the full recovery rate was still 76%. There were minimal cases of relapse even at the long term follow-up conducted between 10–15 years. The long-term prognosis of anorexia nervosa is changeable: one-fifth of patients stay severely ill. one-fifth of patients recover fully and three-fifth's of patients have a fluctuating and chronic course (Gelder, Mayou and Geddes 2005).

## ***Epidemiology***

Anorexia has an average prevalence of 0.3-1% in women and 0.1% in men for the diagnosis in developed countries. The condition largely affects young adolescent women, with between 15 and 19 years old making up 40% of all cases. Approximately 90% of people with anorexia are female. Anorexia nervosa is more prevalent in the upper social classes and it is declared to be rare in less developed countries (Gelder, Mayou and Geddes 2005).

## ***History***

The history of anorexia nervosa begins with early descriptions dating from the 16th and 17th centuries and the first recognition and description of anorexia nervosa as a disease in the late 19th century.

In the late 19th century, the public attention drawn to "fasting girls" provoked conflict between religion and science. Such cases as Sarah Jacob (the "Welsh Fasting Girl") and Mollie Fancher (the "Brooklyn Enigma") stimulated controversy as experts weighed the claims of complete abstinence from food. Believers referenced the duality of mind and body, while skeptics insisted on the laws of science and material facts of life. Critics accused the fasting girls of hysteria, superstition, and deceit. The progress of secularization and medicalization passed cultural authority from clergy to physicians, transforming anorexia nervosa from revered to reviled.

## Chapter 2

# Bulimia Nervosa

### Bulimia nervosa

ICD-10	F50.2
ICD-9	307.51
DiseasesDB	1770
eMedicine	emerg/810 med/255
MeSH	D052018

**Bulimia nervosa** is an eating disorder characterized by restraining of food intake for a period of time followed by an over intake or bingeing period that results in feelings of guilt and low self-esteem. Sufferers attempt to overcome these feeling through a number of ways. The most common form is defensive vomiting, sometimes called purging; fasting, the use of laxatives, enemas, diuretics, and over exercising are also common. Bulimia nervosa is nine times more likely to occur in women than men (Barker 2003).

The word *bulimia* derives from the Latin (*būlīmia*), which originally comes from the Greek *βουλιμία* (*boulīmīa*; ravenous hunger), a compound of *βους* (*bous*), ox + *λιμός* (*līmos*), hunger. Bulimia nervosa was named and first described by the British psychiatrist Gerald Russell in 1979.

### **The Media**

The media have contributed a lot to the pressure of having the 'ideal' body shape. Television, magazines and all forms of advertisement have left men and women obsessed with how they look and feel about themselves (Barker 2003).

### **Signs and symptoms**

These cycles often involve rapid and out-of-control eating, which may stop when the bulimic is interrupted by another person or the stomach hurts from overextension, followed by self-induced vomiting or other forms of purging. This cycle may be repeated

several times a week or, in more serious cases, several times a day, and may directly cause:

- Chronic gastric reflux after eating
- Dehydration and hypokalemia caused by frequent vomiting
- Electrolyte imbalance, which can lead to cardiac arrhythmia, cardiac arrest, and even death
- Esophagitis, or inflammation of the esophagus
- Oral trauma, in which repetitive insertion of fingers or other objects causes lacerations to the lining of the mouth or throat
- Gastroparesis or delayed emptying
- Constipation
- Infertility
- Enlarged glands in the neck, under the jaw line
- Peptic ulcers
- Calluses or scars on back of hands due to repeated trauma from incisors
- Constant weight fluctuations

The frequent contact between teeth and gastric acid, in particular, may cause:

- Severe dental erosion
- Perimolysis, or the erosion of tooth enamel
- Swollen salivary glands

As with many psychiatric illnesses, delusions can occur with other signs and symptoms leaving the person with a false belief that is not ordinarily accepted by others.

The person may also suffer physical complications such as tetany, epileptic seizures, cardiac arrhythmias and muscle weakness.(ICD-10).

People with bulimia nervosa may also exercise to a point that excludes other activities

## **Related disorders**

Bulimics are much more likely than non-bulimics to have an affective disorder, such as depression or general anxiety disorder: A 1985 Columbia University study on female bulimics at New York State Psychiatric Institute found 70% had suffered depression some time in their lives (as opposed to 25.8% for adult females in a control sample from the general population), rising to 88% for all affective disorders combined. Another study by the Royal Children's Hospital in Melbourne on a cohort of 2000 adolescents similarly found that those meeting at least two of the DSM-IV criteria for bulimia nervosa or anorexia nervosa had a sixfold increase in risk of anxiety and a doubling of risk for substance dependency. Bulimia also has negative effects on the sufferer's dental health due to the acid passed through the mouth from frequent vomiting causing acid erosion, mainly on the posterior dental surface.

## **Diagnosis**

The onset of bulimia nervosa is often during adolescence, between 13 and 20 years of age, and many cases have previously suffered obesity, with many sufferers relapsing in adulthood into episodic bingeing and purging even after initially successful treatment and remission.

According to Barker (2003, p323) Persons with Bulimia are more able to live and interact in everyday chores and tasks such as work and having relationships without the condition overly affecting their abilities.

Bulimia nervosa can be difficult to detect, compared to anorexia nervosa, because bulimics tend to be of average or slightly above or below average weight. Many bulimics may also engage in significantly disordered eating and exercising patterns without meeting the full diagnostic criteria for bulimia nervosa. The diagnostic criteria utilized by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV TR) published by the American Psychiatric Association includes repetitive episodes of binge eating (a discrete episode of overeating during which the individual feels out of control of consumption) compensated for by excessive or inappropriate measures taken to avoid gaining weight. The diagnosis is made only when the behavior is not a part of the symptom complex of Anorexia Nervosa and when the behavior reflects an overemphasis on physical mass or appearance.

There are two sub-types of bulimia nervosa:

- **Purging type** bulimics self-induce vomiting (usually by triggering the gag reflex or ingesting emetics such as syrup of ipecac) to rapidly remove food from the body before it can be digested, or use laxatives, diuretics, or enemas.
- **Non-purging type** bulimics (approximately 6%–8% of cases) exercise or fast excessively after a binge to offset the caloric intake after eating. Purging-type bulimics may also exercise or fast, but as a secondary form of weight control.

## **Management**

People who suffer from bulimia are less likely to end up in hospitalisation and can be treated in outpatients most of the time.

## **Pharmacological**

Some researchers have hypothesized a relationship to mood disorders and clinical trials have been conducted with tricyclic antidepressants, MAO inhibitors, mianserin, fluoxetine, lithium carbonate, nomifensine, trazodone, and bupropion. Research groups who have seen a relationship to seizure disorders have attempted treatment with phenytoin, carbamazepine, and valproic acid. Opiate antagonists naloxone and naltrexone, which block cravings for gambling, have also been used.

There has also been some research characterizing bulimia nervosa as an addiction disorder, and limited clinical use of topiramate, which blocks cravings for opiates, cocaine, alcohol and food. Researchers have also reported positive outcomes when bulimics are treated in an addiction-disorders inpatient unit.

## **Psychotherapy**

There are several empirically-supported psychosocial treatments for bulimia nervosa. Cognitive behavioral therapy (CBT), which involves teaching clients to challenge automatic thoughts and engage in behavioral experiments (e.g., in session eating of "forbidden foods") has demonstrated efficacy both with and without concurrent antidepressant medication. By using CBT patients record how much food they eat and periods of vomiting with the purpose of identifying and avoiding emotional fluctuations that bring on episodes of bulimia on a regular basis (Gelder, Mayou and Geddes 2005). Barker (2003) states that research has found 40-60% of patients using cognitive behaviour therapy to become symptom free. He states in order for the therapy to work, all parties must work together to discuss, record and develop coping strategies. Barker (2003) claims by making people aware of their actions they will think of alternatives. Researchers have also reported some positive outcomes for interpersonal psychotherapy and dialectical behavior therapy.

Maudsley Family Therapy or "Family Based Treatment" (FBT), developed at the Maudsley Hospital in London for the treatment of anorexia nervosa (AN) has been shown to have positive results for the treatment of bulimia nervosa. FBT has been shown through empirical research to be the most efficacious treatment of AN for patients under the age of eighteen and within three years of onset of illness. The studies to date using FBT to treat BN have been promising.

Some researchers have also claimed positive outcomes in hypnotherapy treatment.

## **Epidemiology**

There is little data on the prevalence of bulimia nervosa in-the-large, on general populations. Most studies conducted thus far have been on convenience samples from hospital patients, high school or university students. These have yielded a wide range of results: between 0.1% and 1.4% of males, and between 0.3% and 9.4% of females. Studies on time trends in the prevalence of bulimia nervosa have also yielded inconsistent results. According to Gelder, Mayou and Geddes (2005) bulimia nervosa is prevalent between 1 and 2 per cent of women aged 15–40 years. Bulimia nervosa occurs more frequently in developed countries (Gelder, Mayou and Geddes 2005).

<b>Country</b>	<b>Year</b>	<b>Sample size and type</b>	<b>Incidence</b>
Australia	2008	1,943 adolescents (ages 15–17)	1.0% male 6.4% female
Portugal	2006	2,028 high school students	0.3% female
Brazil	2004	1,807 students (ages 7–19)	0.8% male 1.3% female

Spain	2004	2,509 female adolescents (ages 13–22)	1.4% female
Hungary	2003	580 Budapest residents	0.4% male 3.6% female
Australia	1998	4,200 high school students	0.3% combined
USA	1996	1,152 college students	0.2% male 1.3% female
Norway	1995	19,067 psychiatric patients	0.7% male 7.3% female
Canada	1995	8,116 (random sample)	0.1% male 1.1% female
Japan	1995	2,597 high school students	0.7% male 1.9% female
USA	1992	799 college students	0.4% male 5.1% female

There are higher rates of eating disorders in groups involved in activities which idealize a slim physique, such as dance, gymnastics, modeling, cheerleading, running, acting, rowing and figure skating. Bulimia is more prevalent among Caucasians. Exposure to mass media also appears to have an effect: a survey of 15–18 year-old high schoolgirls in Nadroga, Fiji found the self-reported incidence of purging rose from 0% in 1995 (a few weeks after the introduction of television in the province) to 11.3% in 1998.

## Chapter 3

# Binge Eating Disorder

**Binge eating disorder (BED)** is the most common eating disorder in the United States affecting 3.5% of females and 2% of males and is prevalent in up to 30% of those seeking weight loss treatment. Although it is not yet classified as a separate eating disorder, it was first described in 1959 by psychiatrist and researcher Albert Stunkard as "Night Eating Syndrome" (NES), and the term "Binge Eating Disorder" was coined to describe the same binging-type eating behavior without the exclusive nocturnal component. BED usually leads to obesity although it can occur in normal weight individuals. There may be a genetic inheritance factor involved in BED independent of other obesity risks and there is also a higher incidence of psychiatric comorbidity, with the percentage of individuals with BED and an Axis I comorbid psychiatric disorder being 78.9% and for those with subclinical BED, 63.6%.

### ***Signs***

- Periodically does not exercise control over consumption of food.
- Eats an unusually large amount of food at one time, far more than a normal person would eat in the same amount of time.
- Eats much more quickly during binge episodes than during normal eating episodes.
- Eats until physically uncomfortable and nauseated due to the amount of food just consumed.
- Eats when depressed or bored.
- Eats large amounts of food even when not really hungry.
- Usually eats alone during binge eating episodes, in order to avoid discovery of the disorder.
- Often eats alone during periods of normal eating, owing to feelings of embarrassment about food.
- Feels disgusted, depressed, or guilty after binge eating.
- Rapid weight gain, and/or sudden onset of obesity.

### ***Relationship to other eating disorders***

Binge eating symptoms are also present in bulimia nervosa. The formal diagnosis criteria are similar in that subjects must binge at least twice per week for a minimum period of three months for bulimia nervosa and a minimum of 6 months for BED. Unlike in

bulimia, those with BED do not purge, fast or engage in strenuous exercise after binge eating. Additionally, bulimics are typically of normal weight, are underweight but have been overweight before, or are slightly overweight. Those with binge eating disorder are more likely to be overweight or obese.

Binge eating disorder is similar to, but distinct from, compulsive overeating. Those with BED do not have a compulsion to overeat and do not spend a great deal of time fantasizing about food. On the contrary, some people with binge eating disorder have very negative feelings about food. As with other eating disorders, binge eating is an "expressive disorder"—a disorder that is an expression of deeper psychological problems. Some researchers believe BED is a milder form or subset of bulimia nervosa, while others argue that it is its own distinct disorder. Currently, the DSM-IV categorizes it under Eating disorder not otherwise specified (EDNOS), an indication that more research is needed.

### ***Occurrence and risk factors***

Most people with this problem are either overweight or obese, but people of normal weight can also have the disorder.

About two percent of all adults in the United States (as many as four million Americans) have binge eating disorder. About ten to fifteen percent of people who are mildly obese and who try to lose weight on their own or through commercial weight-loss programs have binge eating disorder. The disorder is even more common in people who are severely obese.

Binge eating disorder is twice as common among women as among men. The disorder is found in all ethno-cultural and racial populations. People who are obese and have binge eating disorder often became overweight at a younger age than those without the disorder. They might also lose and gain back weight more often, or be paranoid about gaining weight.

### ***Causes***

No one knows for sure what causes binge eating disorder. As many as half of all people with binge eating disorder have been depressed in the past. Whether depression causes binge eating disorder, whether binge eating disorder causes depression, or whether the two have a common cause, is not known for sure.

The trigger point can be emotion such as happiness, anger, sadness or boredom. Impulsive behavior and certain other emotional problems can be more common in people with binge eating disorder. However, many people also claim that bingeing occurs regardless of their mood. It is also unclear whether dieting and binge eating are related. Some studies show that about half of all people with binge eating disorder had binge episodes before they started to diet.

Researchers also say that binge eating disorder is more common among competitive athletes such as swimmers or gymnasts whose body form is regularly on public display. Affected athletes in these sports tend to compare their own bodies in a negative way with those of their teammates. There is a research into how brain chemicals and metabolism affect binge eating disorder, but this study is in its early stages.

## ***Complications***

While people tend to overeat from time to time, a consistent habit of frequent consumption of large amounts of food in a short period of time usually leads to weight gain and obesity. The most problematic health consequences of this type of eating disorder is brought on by the weight gain resulting from the bingeing episodes.

People with binge eating disorder may become ill due to a lack of proper nutrition. Bingeing episodes usually include foods that are high in fat, sugar, and/or salt, but low in vitamins and minerals. Individuals are usually very upset about their binge eating and may become depressed. Those who are obese and also have binge eating disorder are at risk for type 2 diabetes, high blood pressure (hypertension), high blood cholesterol levels (hypercholesterolemia), gallbladder disease, heart disease, and certain types of cancer.

Most people with binge eating disorder have tried to control it on their own, but have not been able to control it for very long. Some people miss work, school, or social activities to binge eat. Obese people with binge eating disorder often feel bad about themselves and may avoid social gatherings. Those who binge eat, whether obese or not, feel ashamed, are well aware of their disordered eating patterns, and try to hide their problems. Often they become so good at hiding it that even close friends and family members are unaware that they binge eat. Some of the most common symptoms are:

- Eating large amounts of food, even when not physically hungry. Eating more rapidly than usual.
- Eating until uncomfortably full.
- Eating alone out of embarrassment at the quantity of food being eaten.
- Feelings of disgust, depression, or guilt after eating.

## ***Dieting***

People who are not overweight should avoid dieting because it sometimes makes their binge eating worse. Dieting here means skipping meals, not eating enough calories each day, or avoiding certain kinds of food, such as carbohydrates or fats. Many people with binge eating disorder are obese and have health problems because of their weight. People with binge eating disorder who are obese may find it harder to stay in a weight-loss program. They also may lose less weight than other people, and may regain weight more quickly due to a slowing of the metabolism. (This can be worse when they also have problems like depression, trouble controlling their behavior, and problems dealing with other people.) These people may need treatment for binge eating disorder before they try to lose weight. Dieting is usually not successful for those with BED, as they will usually

gain back all of the weight lost, and sometimes more. Those with BED have more difficulty adhering to traditional weight-loss treatment.



Measuring body weight on a scale

**Dieting** is the practice of ingesting food in a regulated fashion to achieve or maintain a controlled weight. In most cases dieting is used in combination with physical exercise to lose weight in those who are overweight or obese. Some athletes, however, follow a diet to gain weight (usually in the form of muscle). Diets can also be used to maintain a stable body weight.

Diets to promote weight loss are generally divided into four categories: low-fat, low-carbohydrate, low-calorie, and very low calorie. A meta-analysis of six randomized controlled trials found no difference between the main diet types (low calorie, low carbohydrate, and low fat), with a 2–4 kilogram weight loss in all studies. At two years, all calorie-reduced diet types cause equal weight loss irrespective of the macronutrients emphasized.

The first popular diet was "Banting", named after William Banting. In his 1863 pamphlet, *Letter on Corpulence, Addressed to the Public*, he outlined the details of a particular low-carbohydrate, low-calorie diet that had led to his own dramatic weight loss.

## ***Types of diets***

### **Low-fat diets**

Low-fat diets involve the reduction of the percentage of fat in one's diet. Calorie consumption is reduced because less fat is consumed. Diets of this type include NCEP Step I and II. A meta-analysis of 16 trials of 2–12 months' duration found that low-fat diets (without intentional restriction of caloric intake) resulted in average weight loss of 3.2 kg (7.1 lb) over habitual eating.

### **Low-carbohydrate diets**

Low carbohydrate diets such as Atkins and Protein Power are relatively high in protein. Low-carbohydrate diets are sometimes *ketogenic* (i.e. they restrict carbohydrate intake sufficiently to cause ketosis).

### **Low-calorie diets**

Low-calorie diets usually produce an energy deficit of 500–1,000 calories per day, which can result in a 0.5 kilogram (1.1 lb) to 1 kilogram (2.2 lb) weight loss per week. Amongst some of the most commonly used low-calorie diets include DASH diet, Diet to Go, and Weight Watchers. The National Institutes of Health reviewed 34 randomized controlled trials to determine the effectiveness of low-calorie diets. They found that these diets lowered total body mass by 8% over 3–12 months.

### **Detox diets**

Detox diets claim to eliminate toxins from the human body, increasing the amount of urine produced, thus not giving the body time enough to absorb fats and toxins contained in everyday meals. Detox diets often have side effects, caused by the absence of these toxins, during the first two or three days, that may include, but are not limited to headaches, diarrhea and feeling sleepy. A detox diet should never be embraced without first seeking medical advice on the subject.

### **Very low-calorie diets**

Very low calorie diets provide 200–800 calories per day, maintaining protein intake but limiting calories from both fat and carbohydrates. They subject the body to starvation and produce an average weekly weight loss of 1.5–2.5 kilograms (3.3–5.5 lb). "2-4-6-8", a popular diet of this variety, follows a four-day cycle in which only 200 calories are consumed the first day, 400 the second day, 600 the third day, 800 the fourth day, and then the cycle repeats. These diets are not recommended for general use as they are associated with adverse side effects such as loss of lean muscle mass, increased risks of gout, and electrolyte imbalances. People attempting these diets must be monitored closely by a physician to prevent complications.

## ***Fat loss versus muscle loss***

Weight loss typically involves the loss of fat, water and muscle. Overweight people, or people suffering from obesity, typically aim to reduce the percentage of body fat. Additionally, as muscle tissue is denser than fat, fat loss results in increased loss of body volume compared with muscle loss. Reducing even 10% body fat can therefore have a dramatic effect on a person's body shape. To determine the proportion of weight loss that is due to decreased fat tissue, various methods of measuring body fat percentage have been developed.

Muscle loss during weight loss can be restricted by regularly lifting weights (or doing push-ups and other strength-oriented calisthenics) and by maintaining sufficient protein intake. Those on low-carbohydrate diets, and those doing particularly strenuous exercise, may wish to increase their protein intake. According to the National Academy of Sciences, the Dietary Reference Intake for protein is "0.8 grams per kilogram of body weight for adults."

Excessive protein intake, though not connected to declined kidney functioning in healthy individuals, may be harmful to those with certain kidney diseases. There is no conclusive evidence that moderately high protein diets in healthy individuals are dangerous, it has only been shown that these diets are dangerous in individuals already suffering from kidney and liver problems.

The Basal Metabolic Rate, which is the amount of calories the body expends at rest, meaning without performing any physical activity, is influenced by the person's total weight and total amount of muscle. The more muscle, the more calories a person can burn naturally. When the amount of muscle is increased, then more calories can be ingested without gaining weight. On the contrary, if the amount of fat is increased, increasing the number of calories ingested will only add weight.

Normally, when people lose weight, they lose a combination of fat and muscle. If the diet plan includes a daily caloric intake greater than the BMR, the person will most likely lose fat. On the contrary, if the person follows a diet that includes a lower caloric intake than the BMR, this person will lose fat but also a higher percentage of muscle. Severe diets may make people lose 50% fat and 50% muscle weight thus affecting their metabolism because by losing muscle the BMR gets affected. For instance, when a person goes on a low carb diet, the initial weight loss results from the glycogen depletion. Glycogen is a mixture of glucose and water mainly stored in the muscles. Therefore, much of the initial weight loss comes from muscle loss which affects the possibility to maintain a sustainable weight control. A study performed at the University of Connecticut also showed that athletes under a low carb diet not only experience a decrease in their performance but also a drop both in muscle power and cardiovascular performance.

Maintaining muscle mass while losing fat is therefore a key factor to reach both the ideal weight and body composition. To achieve this goal, experts advise not to reduce carbohydrates aggressively. Fat can be lost by reducing the calorie intake by 20% of daily

needs for two days. This reduced calorie intake, even in the presence of 100% carbohydrate consumption, allows for reduction of fat without muscle loss because the glycogen in the muscle is properly replenished.

Exercising on days when the highest amount of carbohydrates is consumed, 1.5 to 2 hours after eating, is also helpful to achieve a balanced fat reduction in the absence of muscle loss. Within this window of time, sugar and insulin levels are undergoing a slow decline. When insulin levels start dropping, the pancreas then produces the hormone glucagon while releasing nutrients stored in the fat cells to the blood to be turned into energy. On the contrary, if blood sugar levels suffer a high increase, insulin feeds the muscle cells and deposits excess into fat cells. Furthermore, if insulin levels decrease too much, the muscle cells do not receive the appropriate amount of food they require. There should always be a meal left during the day after exercising to allow the muscles to recover from exercise.

### ***Energy obtained from food***

The energy intake from food is limited by the efficiency of digestion and the efficiency of utilization. The efficiency of digestion is largely dependent on the type of food being eaten, while efficiency of utilization is affected by a variety of factors, including age, gender, body weight, hormone levels, and many more.

Chewing, especially in the elderly, has been shown to increase the intake of micronutrients. However, the effect of chewing on the intake of macronutrients, such as sugars, fats, and proteins has not been observed.

### ***Proper nutrition***

“ I notice that the  
mongoose gets  
lean on a diet of  
cockroaches.  
This would be  
invaluable to fat  
young ladies at  
home. ”

—David Livingstone, *Open Letter*

Food provides nutrients from six broad classes: proteins, fats, carbohydrates, vitamins, dietary minerals, and water. Carbohydrates are metabolized to provide energy. Proteins provide amino acids, which are required for cell construction, especially for the construction of muscle cells. Essential fatty acids are required for brain and cell membrane construction. Vitamins and trace minerals help to keep good electrolyte balance and are used for metabolic processes. Dietary fiber also affects one's health, although it's not digested into the body.

The National Academy of Sciences and the World Health Organization publish guidelines for dietary intakes of all known essential nutrients.

Sometimes dieters will ingest excessive amounts of vitamin and mineral supplements. While this is usually harmless, some nutrients are dangerous. Men (and women who don't menstruate) need to be wary of iron poisoning. Retinol (oil-soluble vitamin A) is toxic in large doses. Vitamin E supplements have been found in some studies to increase mortality, congenital heart defects in offspring and an increased risk of stroke. Most people can obtain their nutritional needs from their diet. In any event, a multivitamin taken once a day will suffice for the majority of the population.

Weight loss diets that manipulate the proportion of macronutrients (low-fat, low-carbohydrate, etc.) have not been shown to be any more effective than diets that maintain a typical mix of foods with smaller portions and perhaps some substitutions (e.g. low-fat milk, or less salad dressing). Extreme diets may, in some cases, lead to malnutrition.

Besides the importance of eating a balanced diet that includes all the necessary nutrients, other factors also contribute to healthy nutrition. Eating 5 or 6 small to medium sized meals throughout the day (instead of three big meals) has been shown to improve the metabolism. As well, drinking sufficient amounts of water can help eliminate toxins and fat. Processed, cooked, fried foods as well as sweets, junk foods, and alcohol should also be avoided in a healthy diet.

Nutritionists also agree on the importance of avoiding fats, especially saturated fats, to reduce weight and to be healthier. They also agree on the importance of reducing salt intake because commercial foods such as snacks, biscuits, and bread, among others, already contain salt, thus contributing to an excess of salt daily intake.

MyPyramid Food Guidance System is the result of extensive research performed by the United States Department of Agriculture to revise the original Food Guide Pyramid. It offers a wide array of personalized options to help individuals make healthy food choices. It also provides advice on physical activity.

### ***How the body eliminates fat***

All body processes require energy in order to function properly. When the body is expending more energy than it is consuming (e.g. when exercising), the body's cells rely on internally stored energy sources, such as complex carbohydrates and fats, for energy. The first source to which the body turns is glycogen (by glycogenolysis). Glycogen is a complex carbohydrate, 65% of which is stored in skeletal muscles and the remainder, in the liver (totaling about 2000 kcal in the whole body). It is created from the excess of ingested macronutrients, mainly carbohydrates. When those sources are nearly depleted, the body begins lipolysis, the mobilization and catabolism of fat stores for energy. In this process, fats, obtained from adipose tissue, or fat cells, are broken down into glycerol and fatty acids, which can be used to generate energy. The primary by-products of

metabolism are carbon dioxide and water; carbon dioxide is expelled through the respiratory system.

Fats are also secreted by the sebaceous glands (in the skin).

### ***Psychological aspects of weight loss***

Diets affect the "energy in" component of the energy balance by limiting or altering the distribution of foods. Techniques that affect the appetite can limit energy intake by affecting the desire to overeat.

Cognitive Behavior Therapy has been effective in producing long term weight loss. Judith S. Beck has been one of the most prominent practitioners and writers to bring this method to a popular audience.

Successful weight management, keeping it off for two years or more, demands a psychological shift as much as eating and activity changes. Key ingredients to this internal shift are developing better coping strategies, gaining support from others and learning to manage stress that triggers emotional eating. Dieting leads people to be very self critical which inevitable leads to helplessness and giving up. Learning to manage self attack is central to dieting success. All of these changes lead people to finally feel a core sense of self-efficacy or autonomy in making healthier choices each day. Some experts, for example Barry Simon MD, endorse this psychological component of successful dieting.

Consumption of low-energy, fiber-rich foods, such as non-starchy vegetables, is effective in obtaining satiation (the feeling of "fullness"). Exercise is also useful in controlling appetite as is drinking water and sleeping.

The use of drugs to control appetite is also common. Stimulants are often taken as a means to suppress hunger in people who are dieting. Ephedrine (through facilitating the release of adrenaline and noradrenaline) stimulates the alpha(1)-adrenoreceptor subtype, which is known to act as an anorectic. L-Phenylalanine, an amino acid found in whey protein powders also has the ability to suppress appetite by increasing the hormone cholecystokinin (CCK) which sends a satiety signal to the brain.

### ***Weight loss groups***

Some weight loss group's goal is to make money, some for plain charity. The former include Weight Watchers and Peertrainer. The latter include, Overeaters Anonymous, also several groups run by local churches, hospitals, and like-minded individuals.

These organizations' customs and practices differ widely. Some groups are modelled on twelve-step programs, while others are quite informal. Some groups advocate certain prepared foods or special menus, while others train dieters to make healthy choices from restaurant menus and while grocery-shopping and cooking.

## ***Food diary***

A 2008 study published in the American Journal of Preventive Medicine showed that dieters who kept a daily food diary (or diet journal), lost twice as much weight as those who did not keep a food log, suggesting that if you write your food down, you wouldn't eat as much calories. Accordingly, diet journal software and websites have gained significant popularity, and help people track calorie consumption, calorie burning, weight loss goals, and nutritional balance.

## ***Medications***

Certain medications can be prescribed to assist in weight loss. The most recent prescription weight loss medication released is Acomplia (generic name Rimonabant), manufactured by Sanofi Aventis. Used to treat obesity in persons with a BMI (body mass index) of 30 or above, as well as for smoking cessation treatments, Acomplia is still pending FDA approval for use in the United States. Other weight loss medications, like amphetamines, are dangerous and are now banned for casual weight loss. Some supplements, including those containing vitamins and minerals, may not be effective for weight loss.

## ***Diuretics***

Diuretics induce weight loss through the excretion of water. Diuretics, which can be used in the forms of medications, supplements, or herbs, reduce overall body weight, but have no effect on an individual's total body fat content. Diuretics can thicken the blood, cause cramping, kidney and liver damage. In a single report, the death of Jacqueline Henson was found to be related to swelling in her brain, which was associated with excessive water consumption over a short period of time, while she was on a special water diet.

## ***Stimulants***

Stimulants such as ephedrine, green tea, caffeine or synephrine work to increase the basal metabolic rate.

## ***Dangers of fasting***

Lengthy fasting can be dangerous due to the risk of malnutrition and should be carried out under medical supervision. During prolonged fasting or very low calorie diets, the reduction of blood glucose, the preferred energy source of the brain, causes the body to deplete its glycogen stores. Once glycogen is depleted the body begins to fuel the brain using ketones, while also metabolizing body protein (including but not limited to skeletal muscle) to be used to synthesize sugars for use as energy by the rest of the body. Most experts believe that a prolonged fast can lead to muscle wasting although some dispute this. The use of short-term fasting, or various forms of intermittent fasting have been used as a form of dieting to circumvent this issue.

## ***Side effects***

Dieting, especially extreme food-intake reduction and rapid weight loss, can have the following side effects and consequences:

- Prolonged hunger
- Depression
- Reduced sex drive
- Fatigue
- Irritability
- Fainting
- Sinus problems (especially post-nasal drip)
- Muscle atrophy
- Rashes
- Acidosis
- Bloodshot eyes
- Gallbladder disease
- Seizures
- Malnutrition, possibly leading to death
- Constipation, due to lack of food-intake
- Dehydration, due to lack of fluid-intake
- Lowered metabolism, if food intake is inadequate to the level of exercise, causing future attempts at weight loss to become more difficult
- Risk of developing Eating Disorders, especially Anorexia Nervosa or Bulimia Nervosa, even if initial intentions of dieting were health-wise
- Subsequent weight re-gain

## ***Low carbohydrate versus low fat***

Many studies have focused on diets that reduce calories via a low-carbohydrate (Atkins diet, Scarsdale diet, Zone diet) diet versus a low-fat diet (LEARN diet, Ornish diet). The Nurses' Health Study, an observational cohort study, found that low carbohydrate diets based on vegetable sources of fat and protein are associated with less coronary heart disease. The same study also found no correlation (with multivariate adjustment) between animal fat intake and coronary heart disease (table 4).

A meta-analysis of randomized controlled trials by the international Cochrane Collaboration in 2002 concluded that fat-restricted diets are no better than calorie restricted diets in achieving long term weight loss in overweight or obese people. A more recent meta-analysis that included randomized controlled trials published after the Cochrane review found that "low-carbohydrate, non-energy-restricted diets appear to be at least as effective as low-fat, energy-restricted diets in inducing weight loss for up to 1 year. However, potential favorable changes in triglyceride and high-density lipoprotein cholesterol values should be weighed against potential unfavorable changes in low-density lipoprotein cholesterol values when low-carbohydrate diets to induce weight loss are considered."

The Women's Health Initiative Randomized Controlled Dietary Modification Trial found that a diet of total fat to 20% of energy and increasing consumption of vegetables and fruit to at least 5 servings daily and grains to at least 6 servings daily resulted in:

- no reduction in cardiovascular disease
- no statistically significant reduction in invasive breast cancer
- no reductions in colorectal cancer

Additional recent randomized controlled trials have found that:

- A comparison of Atkins, Zone diet, Ornish diet, and LEARN diet in *premenopausal women* found the greatest benefit from the Atkins diet.
- The choice of diet for a specific person may be influenced by measuring the individual's insulin secretion:

In young adults "Reducing glycemic [carbohydrate] load may be especially important to achieve weight loss among individuals with high insulin secretion." This is consistent with prior studies of diabetic patients in which low carbohydrate diets were more beneficial.

The American Diabetes Association released for the first time a recommendation (in its January 2008 Clinical Practice Recommendations) for a low carbohydrate diet to reduce weight for those with or at risk of Type 2 diabetes.

### ***Low glycemic index***

"The glycemic index (GI) factor is a ranking of foods based on their overall effect on blood sugar levels. The diet based around this research is called the Low GI diet. Low glycemic index foods, such as lentils, provide a slower, more consistent source of glucose to the bloodstream, thereby stimulating less insulin release than high glycemic index foods, such as white bread."

The glycemic load is "the mathematical product of the glycemic index and the carbohydrate amount".

In a randomized controlled trial that compared four diets that varied in carbohydrate amount and glycemic index found complicated results:

- Diet 1 and 2 were high carbohydrate (55% of total energy intake)
  - Diet 1 was high-glycemic index
  - Diet 2 was low-glycemic index
- Diet 3 and 4 were high protein (25% of total energy intake)
  - Diet 3 was high-glycemic index
  - Diet 4 was low-glycemic index

Diets 2 and 3 lost the most weight and fat mass; however, low density lipoprotein fell in Diet 2 and rose in Diet 3. Thus the authors concluded that the high-carbohydrate, low-glycemic index diet was the most favorable.

A meta-analysis by the Cochrane Collaboration concluded that low glycemic index or low glycemic load diets led to more weight loss and better lipid profiles. *However*, the Cochrane Collaboration grouped low glycemic index and low glycemic load diets together and did not try to separate the effects of the load versus the index.

## ***Treatment***

People with binge eating disorder, whether or not they want to lose weight, should seek help from health professionals including physicians, nutritionists, psychiatrists, psychologists, clinical social workers or by attending 12-step Overeaters Anonymous meetings. Even those who are not overweight are usually upset by their binge eating, and treatment can help them.

Although mental health professionals may be attuned to the signs of binge eating disorders, most physicians do not raise the question, either because they are uninformed about the condition or too embarrassed to ask about it. Because it is not a recognized psychiatric disorder in the Diagnostic and Statistical Manual of Mental Disorders, it is difficult to obtain insurance reimbursement for treatments.

There are several different ways to treat binge eating disorder. Cognitive-behavioral therapy teaches people how to keep track of their eating and change their unhealthy eating habits. It also teaches them how to change the way they act in tough situations. Interpersonal psychotherapy helps people look at their relationships with friends and family and make changes in problem areas. Drug therapy, such as antidepressants, may be helpful for some people.

Researchers are still trying to find the treatment that is the most helpful in controlling binge eating disorder. The methods mentioned here seem to be equally helpful. For people who are overweight, a weight-loss program to improve health and to build self-esteem, as well as counselling to pinpoint the root of the psychological problems triggering their binge episodes, might be the best choice.

A clinical trial in Helsinki is investigating the use of intra-nasal naloxone for binge eating disorder, using the same approach as the highly successful Sinclair Method for alcohol addiction. Results of this trial are expected 2011.

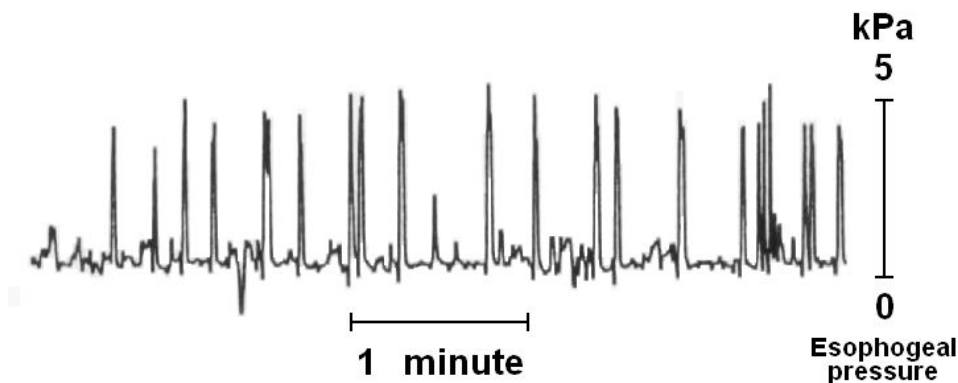
## Chapter 4

# Rumination Syndrome and Diabulimia

## Rumination Syndrome

### Rumination syndrome

#### Antral Manometry in Rumination syndrome



A postprandial manometry of a patient with rumination syndrome showing intra-abdominal pressure. The "spikes" are characteristic of the abdominal wall contractions responsible for the regurgitation in rumination.

**ICD-10** P92.1, F98.2

**ICD-9** 307.53

**DiseasesDB** 34255

**MedlinePlus** 001539

**eMedicine** article/916297

**MeSH** D019959

**Rumination syndrome**, or **Merycism** is an under-diagnosed chronic eating disorder, characterized by effortless regurgitation of most meals following consumption. There is no retching, nausea, heartburn, odours, or abdominal pains associated with the

regurgitation, as there is with typical vomiting. The disorder has been historically documented as affecting only infants, young children, and people with cognitive disabilities (where the prevalence is as high as 10% in institutionalized patients with various mental disabilities). Today it is being diagnosed in increasing numbers of otherwise healthy adolescents and adults, though there is a lack of awareness of the condition by doctors, patients and the general public.

Rumination syndrome presents itself in a variety of ways, especially when comparing an adult without a mental disability to an infant or to a mentally impaired individual. Like most eating disorders, rumination can adversely affect normal functioning and the social lives of individuals. It has been linked with depression.

There is little comprehensive data regarding rumination syndrome in otherwise healthy individuals. Most people with the disorder are private about their illness, and are often misdiagnosed due to the number of symptoms, and the clinical similarities between rumination syndrome and other disorders of the stomach and esophagus, such as gastroparesis and bulimia nervosa. These include the acid-induced erosion of the esophagus and enamel, halitosis, malnutrition, severe weight loss and an unquenchable appetite. Individuals may begin regurgitating within a minute following ingestion, and the full cycle of ingestion and regurgitation can mimic the bingeing and purging of bulimia.

Diagnosis of rumination syndrome is non-invasive, and based on a history of the individual. Treatment is promising, with upwards of 85% of individuals responding positively to treatment, including infants and the mentally handicapped.

## ***Classification***

Rumination syndrome is an eating disorder which affects the functioning of the stomach and esophagus, also known as a *functional gastroduodenal disorder*. It is grouped alongside other eating disorders such as bulimia and pica, which are themselves grouped under non-psychotic mental disorder.

## ***Signs and symptoms***

While the number and severity of symptoms varies among individuals, repetitive regurgitation of undigested food (known as rumination) after the start of a meal is always present. In some individuals, the regurgitation is small, occurring over a long period of time following ingestion, and can be rechewed and swallowed. In others, the amount can be bilious and short lasting, and must be expelled. While some only experience symptoms following some meals, most experience episodes following any ingestion, from a single bite to a massive feast. However, some long-term patients will find a select couple of food or drink items that do not trigger a response.

Unlike typical vomiting, the regurgitation is typically described as effortless and unforced. There is seldom nausea preceding the expulsion, and the undigested food lacks the bitter taste and odour of stomach acid and bile.

Symptoms can begin to manifest at any point from the ingestion of the meal to 120 minutes thereafter. However, the more common range is between 30 seconds to 1 hour after the completion of a meal. Symptoms tend to cease when the ruminated contents become acidic.

Abdominal pain (38.1%), lack of fecal production or constipation (21.1%), nausea (17.0%), diarrhea (8.2%), bloating (4.1%), and dental decay (3.4%) are also described as common symptoms in day-to-day life. These symptoms are not necessarily prevalent during regurgitation episodes, and can happen at any time. Weight loss is often observed (42.2%) at an average loss of 9.6 kilograms, and is more common in cases where the disorder has gone undiagnosed for a longer period of time, though this may be expected of the nutrition deficiencies that often accompany the disorder as a consequence of its symptoms. Depression has also been linked with rumination syndrome, though the effects of it on rumination syndrome are unknown.

## ***Causes***

The cause of rumination syndrome is unknown. However, studies have drawn a correlation between hypothesized causes and the history of patients with the disorder. In infants and the cognitively impaired, the disease has normally been attributed to over-stimulation and under-stimulation from parents and caregivers, causing the individual to seek self-gratification and self-stimulus due to the lack or abundance of external stimuli. The disorder has also commonly been attributed to a bout of illness, a period of stress in the individual's recent past, and to changes in medication.

In adults and adolescents, hypothesized causes generally fall into one of either category: habit-induced, and trauma-induced. Habit-induced individuals generally have a past history of bulimia nervosa or of intentional regurgitation (magicians and professional regurgitators, for example), which though initially self-induced, forms a subconscious habit that can continue to manifest itself outside the control of the affected individual. Trauma-induced individuals describe an emotional or physical injury (such as recent surgery, psychological distress, concussions, deaths in the family, etc.), which preceded the onset of rumination, often by several months.

## ***Diagnosis***

Rumination syndrome is diagnosed based on a complete history of the individual. Costly and invasive studies such as gastroduodenal manometry and esophageal PH testing are unnecessary and will often aid in misdiagnosis. Based on typical observed features, several criteria have been suggested for diagnosing rumination syndrome. The primary symptom, the regurgitation of recently ingested food, must be consistent, occurring for at least six weeks of the past twelve months. The regurgitation must begin within

30 minutes of the completion of a meal. Patients may either chew the regurgitated matter or expel it. The symptoms must stop within 90 minutes, or when the regurgitated matter becomes acidic. The symptoms must not be the result of a mechanical obstruction, and should not respond to the standard treatment for gastroesophageal reflux disease.

In adults, the diagnosis is supported by the absence of classical or structural diseases of the gastrointestinal system. Supportive criteria include regurgitant that is not sour or acidic tasting, is generally odourless, is effortless, or at most preceded by a belching sensation, that there is no retching preceding the regurgitation, and that the act is not associated with nausea or heartburn.

Patients visit an average of five physicians over 2.75 years before being correctly diagnosed with rumination syndrome.

### **Differential diagnosis**

Rumination syndrome in adults is a complicated disorder whose symptoms can mimic those of several other gastroesophageal disorders and diseases. Bulimia nervosa and gastroparesis are especially prevalent among the misdiagnoses of rumination.

Bulimia nervosa, among adults and especially adolescents, is by far the most common misdiagnosis patients will hear during their experiences with rumination syndrome. This is due to the similarities in symptoms to an outside observer - "vomiting" following food intake - which, in long-term patients, may include ingesting copious amounts to offset malnutrition, and a lack of willingness to expose their condition and its symptoms. While it has been suggested that there is a connection between rumination and bulimia, unlike bulimia, rumination is not self-inflicted. Adults and adolescents with rumination syndrome are generally well aware of their gradually increasing malnutrition, but are unable to control the reflex. In contrast, those with bulimia intentionally induce vomiting, and seldom re-swallow food.

Gastroparesis is another common misdiagnosis. Like rumination syndrome, patients with gastroparesis often bring up food following the ingestion of a meal. Unlike rumination, gastroparesis causes vomiting (in contrast to regurgitation) of food, which is not being digested further, from the stomach. This vomiting occurs several hours after a meal is ingested, is preceded by nausea and retching, and has the bitter or sour taste typical of vomit.

### ***Pathophysiology***

Rumination syndrome is a poorly understood disorder, and a number of theories have speculated the mechanisms that cause the regurgitation, which is a unique symptom to this disorder. While no theory has gained a consensus, some are more notable and widely published than others.

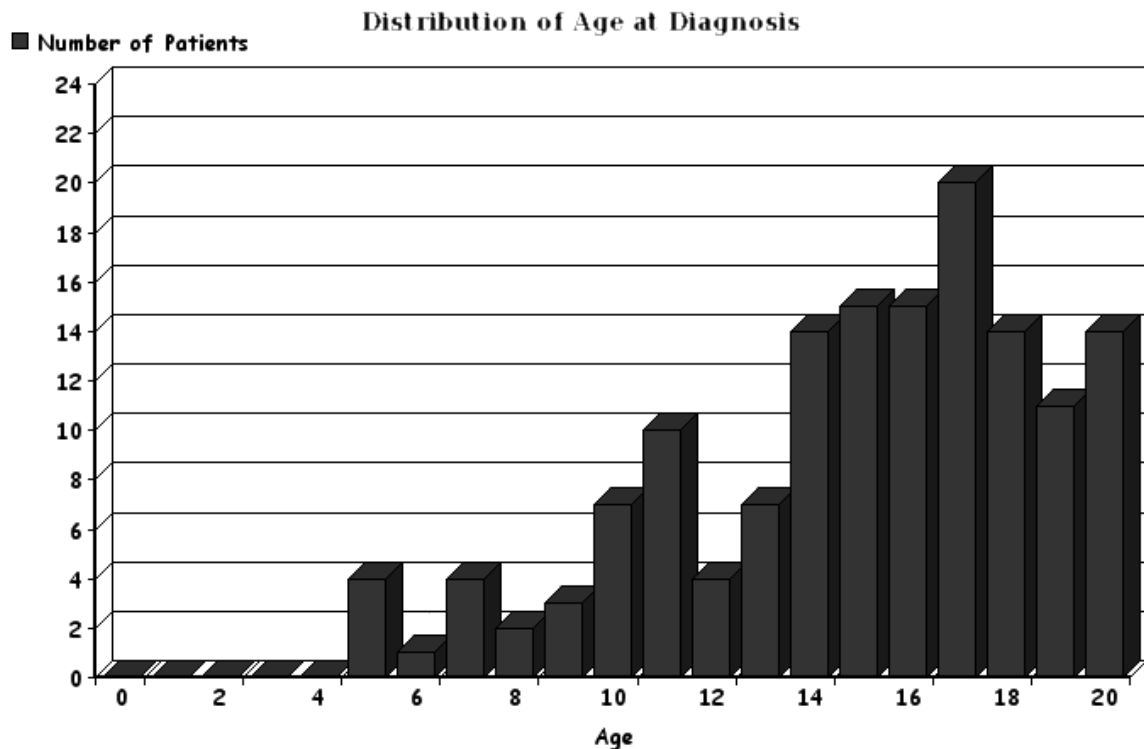
The most widely documented mechanism is that the ingestion of food causes gastric distention, which is followed by abdominal compression and the simultaneous relaxation of the lower esophageal sphincter (LES). This creates a common cavity between the stomach and the oropharynx that allows the partially digested material to return to the mouth. There are several offered explanations for the sudden relaxation of the LES. Among these explanations is that it is a learned voluntary relaxation, which is common in those with or having had bulimia. While this relaxation may be voluntary, the overall process of rumination is still generally involuntary. Relaxation due to intra-abdominal pressure is another proposed explanation, which would make abdominal compression the primary mechanism. The third is an adaptation of the belch reflex, which is the most commonly described mechanism. The swallowing of air immediately prior to regurgitation causes the activation of the belching reflex that triggers the relaxation of the LES. Patients often describe a feeling similar to the onset of a belch preceding rumination.

### ***Treatment and prognosis***

There is presently no known cure for rumination. Proton pump inhibitors and other medications have been used to little or no effect. Treatment is different for infants and the mentally handicapped than for adults and adolescents of normal intelligence. Among the former two, behavioral and mild aversive training has shown to cause improvement in most cases. Aversive training involves associating the ruminating behavior with negative results, and rewarding good behavior and eating. Placing a sour or bitter taste on the tongue when the individual begins the movements or breathing patterns typical of his or her ruminating behavior is the generally accepted method for aversive training, although some older studies advocate the use of pinching. In patients of normal intelligence, rumination is not an intentional behavior and is habitually reversed using diaphragmatic breathing to counter the urge to regurgitate. Alongside reassurance, explanation and habit reversal, patients are shown how to breathe using their diaphragms prior to and during the normal rumination period. A similar breathing pattern can be used to prevent normal vomiting. Breathing in this method works by physically preventing the abdominal contractions required to expel stomach contents.

Supportive therapy and diaphragmatic breathing has shown to cause improvement in 56% of cases, and total cessation of symptoms in an additional 30% in one study of 54 adolescent patients who were followed up 10 months after initial treatments. Patients who successfully use the technique often notice an immediate change in health for the better. Individuals who have had bulimia or who intentionally induced vomiting in the past have a reduced chance for improvement due to the reinforced behavior. The technique is not used with infants or young children due to the complex timing and concentration required for it to be successful. Most infants grow out of the disorder within a year or with aversive training.

## Epidemiology



Chial, Camilleri, Williams, Litzinger, Perrault. *Pediatrics* 2003;111:159

### Age distribution at diagnosis

Rumination disorder was initially documented as affecting newborns, infants, children and individuals with mental and functional disabilities (the cognitively handicapped). It has since been recognized to occur in both males and females of all ages and cognitive abilities.

Among the latter, it is described with almost equal prevalence among infants (6–10% of the population) and institutionalized adults (8–10%). In infants, it typically occurs within the first 3–12 months of age.

The occurrence of rumination syndrome within the general population has not been defined. Rumination is sometimes described as rare, but has also been described as not rare, but rather rarely recognized. The disorder has a female predominance. The typical age of adolescent onset is 12.9, give or take 0.4 years ( $\pm$ ), with males affected sooner than females ( $11.0 \pm 0.8$  for males versus  $13.8 \pm 0.5$  for females).

There is little evidence concerning the impact of hereditary influence in rumination syndrome. However, case reports involving entire families with rumination exist.

## ***History***

The term *rumination* is derived from the Latin word *ruminare*, which means *to chew the cud*. First described in ancient times, and mentioned in the writings of Aristotle, rumination syndrome was clinically documented in 1618 by Italian anatomist Fabricus ab Aquapendente, who wrote of the symptoms in a patient of his.

Among the earliest cases of rumination was that of a physician in the nineteenth century, Charles-Édouard Brown-Séquard, who acquired the condition as the result of experiments upon himself. As a way of evaluating and testing the acid response of the stomach to various foods, the doctor would swallow sponges tied to a string, then intentionally regurgitate them to analyze the contents. As a result of these experiments, the doctor eventually regurgitated his meals habitually by reflex.

Numerous case reports exist from before the twentieth century, but were influenced greatly by the methods and thinking used in that time. By the early twentieth century, it was becoming increasingly evident that rumination presented itself in a variety of ways in response to a variety of conditions. Although still considered a disorder of infancy and cognitive disability at that time, the difference in presentation between infants and adults was well established.

Studies of rumination in otherwise healthy adults became decreasingly rare starting in the 1900s, and the majority of published reports analyzing the syndrome in mentally healthy patients appeared thereafter. At first, adult rumination was described and treated as a benign condition. It is now described as otherwise. While the base of patients to examine has gradually increased as more and more people come forward with their symptoms, awareness of the condition by the medical community and the general public is still limited.

## ***In other animals***

The chewing of cud by animals such as cows, goats, and giraffes is considered normal behavior. These animals are known as ruminants. Such behavior, though termed rumination, is not related to human rumination syndrome, but is ordinary. Involuntary rumination, similar to what is seen in humans, has been described in gorillas and other primates.

# Diabulimia

**Diabulimia** (a portmanteau of *diabetes* and *bulimia*) refers to an eating disorder in which people with Type 1 diabetes deliberately give themselves less insulin than they need, for the purpose of weight loss. Diabulimia is not currently recognized as a formal diagnosis by the medical or psychiatric communities. However, the phrases “disturbed eating behavior” or “disordered eating behavior” (DEB in both cases), or disordered eating (DE) are quite common in medical and psychiatric literature which addresses the condition of patients who have Type 1 diabetes and who also intentionally manipulate insulin doses to control weight.

Failure to administer insulin places the body in a starvation state, resulting in breakdown of muscle and fat into ketone bodies and subsequently ketoacids, while at the same time making the body unable to process sugars that have been consumed, so the sugars are excreted in the urine rather than being used by the body for energy or stored as fat. This typically results in significant weight loss but also places the patient at risk of a life-threatening condition known as diabetic ketoacidosis. Prolonged failure to administer insulin results in long-term complications such as diabetic neuropathy. Insulin restriction is associated not only with increased rates of diabetes complications but increased mortality risk as well. Diabetics who restrict insulin die at earlier ages on average than those diabetics who use insulin properly.

Following a diagnosis of Type 1 diabetes, a patient is prescribed insulin injections, given a controlled diet, and must check blood sugar several times a day. This lifestyle may result in weight gain, which some (particularly teen girls) may be unhappy about. This may lead them to neglect their insulin treatment for the purpose of losing weight.

Often, people with Type 1 diabetes who omit insulin injections will have already been diagnosed with an eating disorder such as anorexia nervosa, bulimia nervosa and/or compulsive eating. In cases where a person with Type 1 diabetes has another eating disorder, there is a tendency to discuss the other eating disorder more openly than they discuss diabulimia, as many people with diabetes are embarrassed or don't want to deal with the reality that they have lost control of their diabetes. These individuals are often not aware that diabulimia is more common than they think and is also very difficult to overcome. Unlike anorexia and bulimia, diabulimia sometimes requires the afflicted individual to stop caring for a medical condition. Unlike vomiting or starving, there is sometimes no clear action or willpower involved. Diabulimia may be more appealing to individuals who want to lose weight and do not want to feel hungry, or do not want to engage in purging via vomiting. Often there is an obsessive compulsive urge to engage in this activity for the purpose of emotional disassociation or a need to satisfy feelings of control.

This condition can be triggered or exacerbated by the need for diabetics to exercise constant vigilance in regard to food, weight and glycemic control. In adolescents the need for parental control over the young diabetic's life, and the increased weight gain that insulin treatment can cause, may play roles in the increased risk for onset of anorexia

and/or bulimia. The frustration of managing blood sugars and their subsequent effects on weight and self perception (altered by dealing with a chronic illness) can also be damaging to self esteem and body image.

A person with diabulimia, especially if not caught and treated early, is likely to suffer the negative effects on the body of diabetes earlier than a person with diabetes who is managing their diabetes in a faithful manner. Long-term potential repercussions of diabetes include renal failure, blindness and diabetic neuropathy. With diabulimia there is an increased chance of death. Diabetic ketoacidosis (DKA) is very common in persons with Type 1 diabetes who have diabulimia. This is due to the body's need for a constant supply of energy, which lack of insulin prevents. DKA is a very serious condition that occurs when one doesn't have enough insulin; without treatment it results in death within a very short span of time.

Diabulimia tends to start in adolescence and is more likely to occur in women than men. One can identify a patient as having diabulimia if there are many unexplainable spikes in their Hemoglobin A1c, weight loss, lack of marks from fingerpricks, lack of prescription refills for diabetes medications, and records that do not match the HbA1c.

## **Symptoms**

### **Short term**

These are the short term symptoms of patients with diabulimia

- Constant urination
- Constant thirst
- Excessive appetite
- High blood glucose levels (often over 600)
- Weakness
- Fatigue
- Large amounts of glucose in the urine
- Inability to concentrate
- Electrolyte disturbance
- Severe ketonuria, and, in DKA, severe ketonemia
- Low sodium levels

### **Medium term**

These are the medium term symptoms of patients with diabulimia. They are prevalent when diabulimia has not been treated and hence also includes the short term symptoms

- Muscle atrophy
- GERD
- Indigestion
- Severe weight loss

- Proteinuria
- Moderate to severe dehydration
- Edema with fluid replacement
- High cholesterol
- Death

## **Long term**

If a person with Type 1 diabetes who has diabulimia suffers from the disease for more than a short time—usually due to alternating phases during which insulin is injected properly, and relapses, during which they have diabulimia—then the following longer-term symptoms can be expected:

- Severe kidney damage
- Blindness
- Severe neuropathy (nerve damage to hands and feet)
- Extreme fatigue
- Edema (during blood sugars controlled phases)
- Heart problems
- High cholesterol
- Osteoporosis
- Death

## **Causes**

Many authoritative articles have been published which show that preteen and teenage girls with Type 1 diabetes have significantly higher rates of eating disorders of all types than do girls without diabetes.

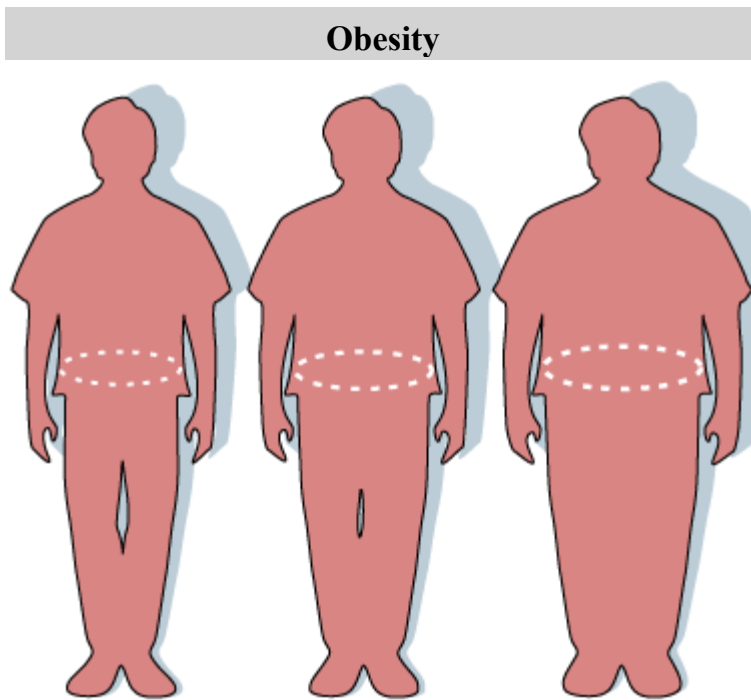
Many articles and studies further conclude that diabetic females have, on average, higher body mass index (BMI) than do their nondiabetic counterparts. Girls and young adult woman with higher BMIs are also shown to be more likely to have disordered eating behavior (DEB).

Of diabetics who have DEB, a significant number intentionally misuse insulin as a means to control weight.

Suspension of insulin, combined with overeating and resulting in ketoacidosis, may be a call for psychological help or attempts to escape unpleasant or undesirable environments. Less frequently, they may be manifestations of suicidal intent. Multiple hospitalizations for ketoacidosis or hypoglycemia are cues to screen for an underlying emotional conflict. Dealing with the feelings brought on by the restrictive regime of diabetes 1 treatment can be overwhelming. In addition, patients may experience anxiety over the possibility of complications developing from diabetes and possible decreased life span.

## Chapter 5

# Obesity



Silhouettes and waist circumferences representing normal,  
overweight, and obese

<b>ICD-10</b>	E66.
<b>ICD-9</b>	278
<b>OMIM</b>	601665
<b>DiseasesDB</b>	9099
<b>MedlinePlus</b>	003101
<b>eMedicine</b>	med/1653
<b>MeSH</b>	<i>C23.888.144.699.500</i>

**Obesity** is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems. Body mass index (BMI), a measurement which compares weight and height, defines people as overweight (pre-obese) if their BMI is between  $25 \text{ kg/m}^2$  and  $30 \text{ kg/m}^2$ , and obese when it is greater than  $30 \text{ kg/m}^2$ .

Obesity increases the likelihood of various diseases, particularly heart disease, type 2 diabetes, breathing difficulties during sleep, certain types of cancer, and osteoarthritis. Obesity is most commonly caused by a combination of excessive dietary calories, lack of physical activity, and genetic susceptibility, although a few cases are caused primarily by genes, endocrine disorders, medications or psychiatric illness. Evidence to support the view that some obese people eat little yet gain weight due to a slow metabolism is limited; on average obese people have a greater energy expenditure than their thin counterparts due to the energy required to maintain an increased body mass.

Dieting and physical exercise are the mainstays of treatment for obesity. Moreover, it is important to improve diet quality by reducing the consumption of energy-dense foods such as those high in fat and sugars, and by increasing the intake of dietary fiber. To supplement this, or in case of failure, anti-obesity drugs may be taken to reduce appetite or inhibit fat absorption. In severe cases, surgery is performed or an intragastric balloon is placed to reduce stomach volume and/or bowel length, leading to earlier satiation and reduced ability to absorb nutrients from food.

Obesity is a leading preventable cause of death worldwide, with increasing prevalence in adults and children, and authorities view it as one of the most serious public health problems of the 21st century. Obesity is stigmatized in much of the modern world (particularly in the Western world), though it was widely perceived as a symbol of wealth and fertility at other times in history, and still is in some parts of the world.

### ***Classification***

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health. It is defined by body mass index (BMI) and further evaluated in terms of fat distribution via the waist–hip ratio and total cardiovascular risk factors. BMI is closely related to both percentage body fat and total body fat.



A "super obese" male with a BMI of  $47 \text{ kg/m}^2$ : weight 146 kg (322 lb), height 177 cm (5 ft 10 in)

In children, a healthy weight varies with age and sex. Obesity in children and adolescents is defined not as an absolute number, but in relation to a historical normal group, such that obesity is a BMI greater than the 95th percentile. The reference data on which these percentiles are based are from 1963 to 1994, and thus have not been affected by the recent increases in weight.

<b>BMI</b>	<b>Classification</b>
< 18.5	underweight
18.5–24.9	normal weight
25.0–29.9	overweight
30.0–34.9	class I obesity
35.0–39.9	class II obesity
$\geq 40.0$	class III obesity

BMI is calculated by dividing the subject's mass by the square of his or her height, typically expressed either in metric or US "customary" units:

$$\text{Metric: } BMI = \text{kilograms} / \text{meters}^2$$

$$\text{US customary and imperial: } BMI = lb * 703 / in^2$$

where *lb* is the subject's weight in pounds and *in* is the subject's height in inches.

The most commonly used definitions, established by the World Health Organization (WHO) in 1997 and published in 2000, provide the values listed in the table at right.

Some modifications to the WHO definitions have been made by particular bodies. The surgical literature breaks down "class III" obesity into further categories whose exact values are still disputed.

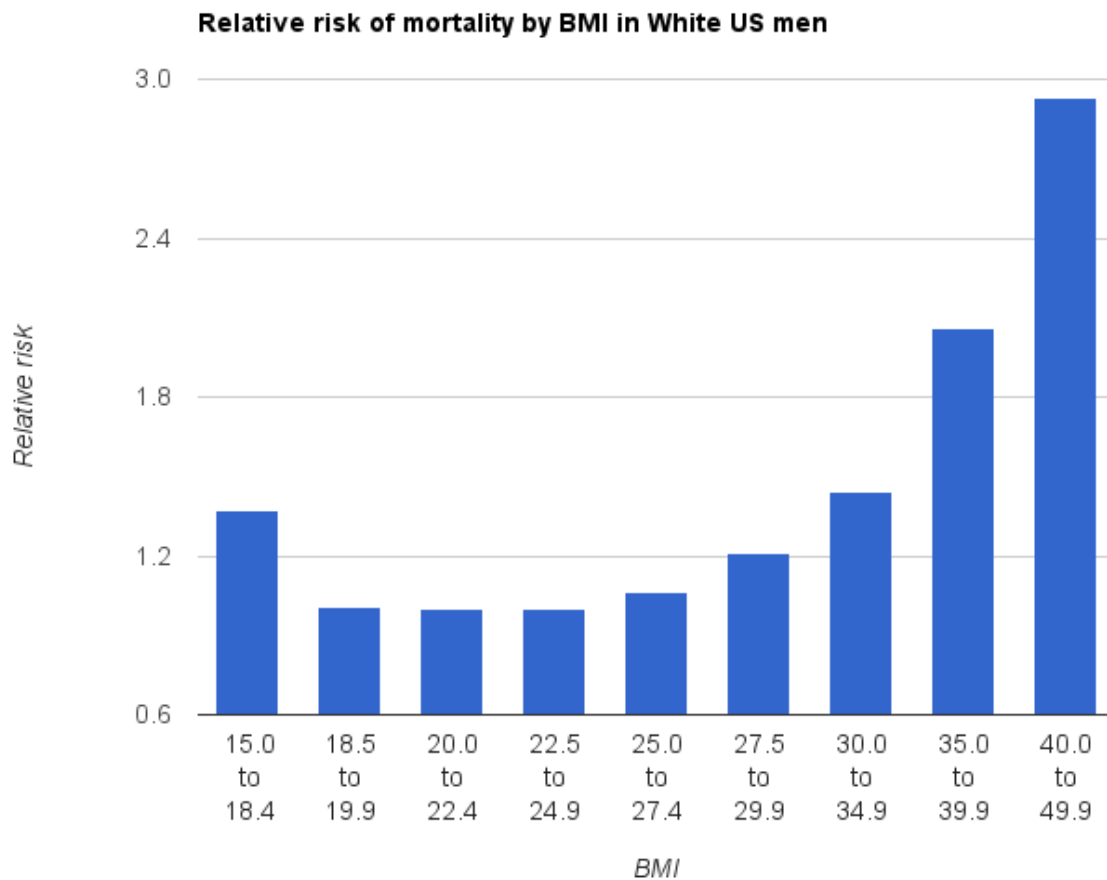
- Any BMI  $\geq 35$  or 40 is *severe obesity*
- A BMI of  $\geq 35$  or 40–44.9 or 49.9 is *morbid obesity*
- A BMI of  $\geq 45$  or 50 is *super obesity*

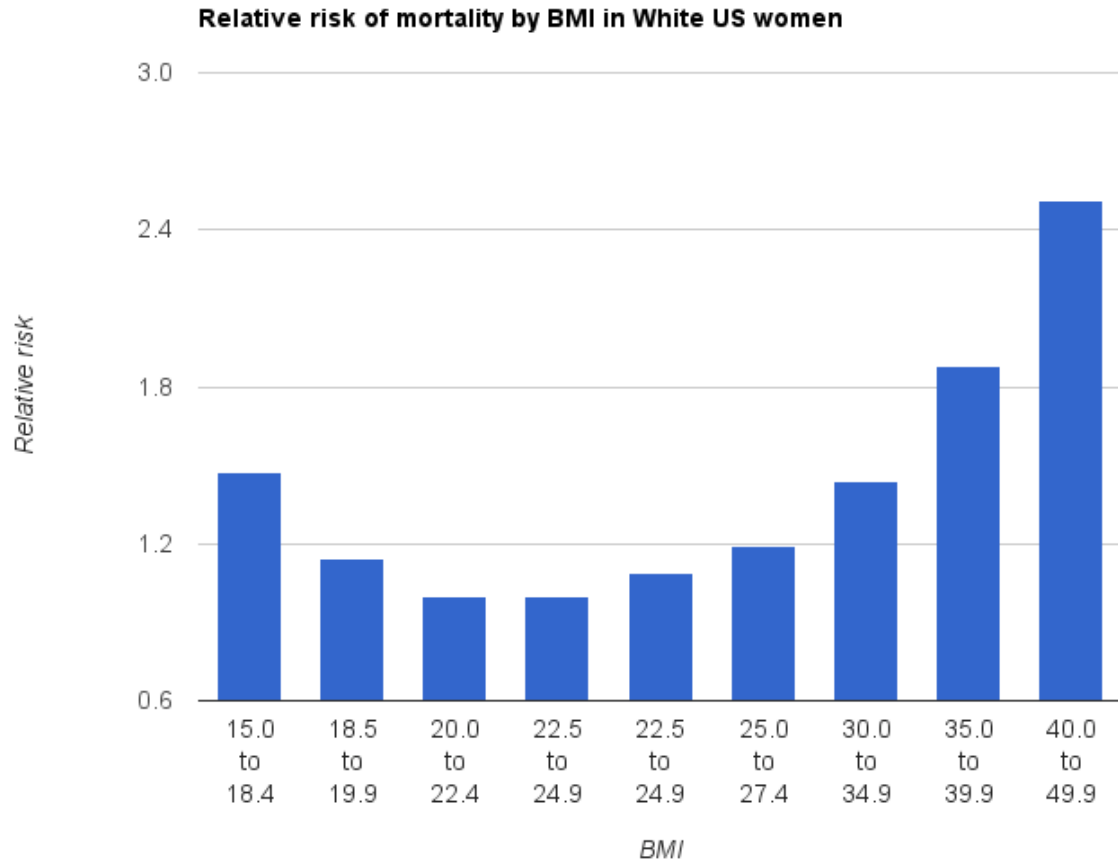
As Asian populations develop negative health consequences at a lower BMI than Caucasians, some nations have redefined obesity; the Japanese have defined obesity as any BMI greater than 25 while China uses a BMI of greater than 28.

### Effects on health

Excessive body weight is associated with various diseases, particularly cardiovascular diseases, diabetes mellitus type 2, obstructive sleep apnea, certain types of cancer, and osteoarthritis. As a result, obesity has been found to reduce life expectancy.

### Mortality





Relative risk of death for White men (top) and women (bottom) who have never smoked in the United States by BMI.

Obesity is one of the leading preventable causes of death worldwide. Large-scale American and European studies have found that mortality risk is lowest at a BMI of 20–25 kg/m<sup>2</sup> in non-smokers and at 24–27 kg/m<sup>2</sup> in current smokers, with risk increasing along with changes in either direction. A BMI above 32 has been associated with a doubled mortality rate among women over a 16-year period. In the United States obesity is estimated to cause an excess 111,909 to 365,000 deaths per year, while 1 million (7.7%) of deaths in the European Union are attributed to excess weight. On average, obesity reduces life expectancy by six to seven years: a BMI of 30–35 reduces life expectancy by two to four years, while severe obesity (BMI > 40) reduces life expectancy by 10 years.

### **Morbidity**

Obesity increases the risk of many physical and mental conditions. These comorbidities are most commonly shown in metabolic syndrome, a combination of medical disorders which includes: diabetes mellitus type 2, high blood pressure, high blood cholesterol, and high triglyceride levels.

Complications are either directly caused by obesity or indirectly related through mechanisms sharing a common cause such as a poor diet or a sedentary lifestyle. The strength of the link between obesity and specific conditions varies. One of the strongest is the link with type 2 diabetes. Excess body fat underlies 64% of cases of diabetes in men and 77% of cases in women.

Health consequences fall into two broad categories: those attributable to the effects of increased fat mass (such as osteoarthritis, obstructive sleep apnea, social stigmatization) and those due to the increased number of fat cells (diabetes, cancer, cardiovascular disease, non-alcoholic fatty liver disease). Increases in body fat alter the body's response to insulin, potentially leading to insulin resistance. Increased fat also creates a proinflammatory state, and a prothrombotic state.

Medical field	Condition	Medical field	Condition				
Cardiology	<ul style="list-style-type: none"> <li>ischemic heart disease: angina and myocardial infarction</li> <li>congestive heart failure</li> <li>high blood pressure</li> <li>abnormal cholesterol levels</li> <li>deep vein thrombosis and pulmonary embolism</li> </ul>	Dermatology	<ul style="list-style-type: none"> <li>stretch marks</li> <li>acanthosis nigricans</li> <li>lymphedema</li> <li>cellulitis</li> <li>hirsutism</li> <li>intertrigo</li> </ul>				
	Endocrinology and Reproductive medicine		<ul style="list-style-type: none"> <li>diabetes mellitus</li> <li>polycystic ovarian syndrome</li> <li>menstrual disorders</li> <li>infertility</li> <li>complications during pregnancy</li> <li>birth defects</li> <li>intrauterine fetal death</li> </ul>	Gastrointestinal	<ul style="list-style-type: none"> <li>gastroesophageal reflux disease</li> <li>fatty liver disease</li> <li>cholelithiasis (gallstones)</li> </ul>		
			Neurology		<ul style="list-style-type: none"> <li>stroke</li> <li>meralgia paresthetica</li> <li>migraines</li> <li>carpal tunnel syndrome</li> <li>dementia</li> <li>idiopathic</li> </ul>	Oncology	<ul style="list-style-type: none"> <li>breast, ovarian</li> <li>esophageal, colorectal</li> <li>liver, pancreatic</li> <li>gallbladder, stomach</li> <li>endometrial, cervical</li> </ul>

	intracranial hypertension		<ul style="list-style-type: none"> <li>• prostate, kidney</li> <li>• non-Hodgkin's lymphoma, multiple myeloma</li> </ul>
	<ul style="list-style-type: none"> <li>• multiple sclerosis</li> </ul>		<ul style="list-style-type: none"> <li>• obstructive sleep apnea</li> <li>• obesity hypoventilation syndrome</li> </ul>
Psychiatry	<ul style="list-style-type: none"> <li>• depression in women</li> <li>• social stigmatization</li> </ul>	Respirology	<ul style="list-style-type: none"> <li>• asthma</li> <li>• increased complications during general anaesthesia</li> </ul>
Rheumatology and Orthopedics	<ul style="list-style-type: none"> <li>• gout</li> <li>• poor mobility</li> <li>• osteoarthritis</li> <li>• low back pain</li> </ul>	Urology and Nephrology	<ul style="list-style-type: none"> <li>• erectile dysfunction</li> <li>• urinary incontinence</li> <li>• chronic renal failure</li> <li>• hypogonadism</li> </ul>

### **Obesity survival paradox**

Although the negative health consequences of obesity in the general population are well supported by the available evidence, health outcomes in certain subgroups seem to be improved at an increased BMI, a phenomenon known as the obesity survival paradox. The paradox was first described in 1999 in overweight and obese people undergoing hemodialysis, and has subsequently been found in those with heart failure and peripheral artery disease (PAD).

In people with heart failure, those with a BMI between 30.0–34.9 had lower mortality than those with a normal weight. This has been attributed to the fact that people often lose weight as they become progressively more ill. Similar findings have been made in other types of heart disease. People with class I obesity and heart disease do not have greater rates of further heart problems than people of normal weight who also have heart disease. In people with greater degrees of obesity, however, risk of further events is increased. Even after cardiac bypass surgery, no increase in mortality is seen in the overweight and obese. One study found that the improved survival could be explained by the more aggressive treatment obese people receive after a cardiac event. Another found that if one takes into account chronic obstructive pulmonary disease (COPD) in those with PAD the benefit of obesity no longer exists.

## Causes

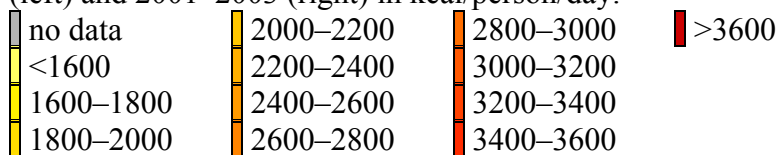
At an individual level, a combination of excessive caloric intake and a lack of physical activity is thought to explain most cases of obesity. A limited number of cases are due primarily to genetics, medical reasons, or psychiatric illness. In contrast, increasing rates of obesity at a societal level are felt to be due to an easily accessible and palatable diet, increased reliance on cars, and mechanized manufacturing.

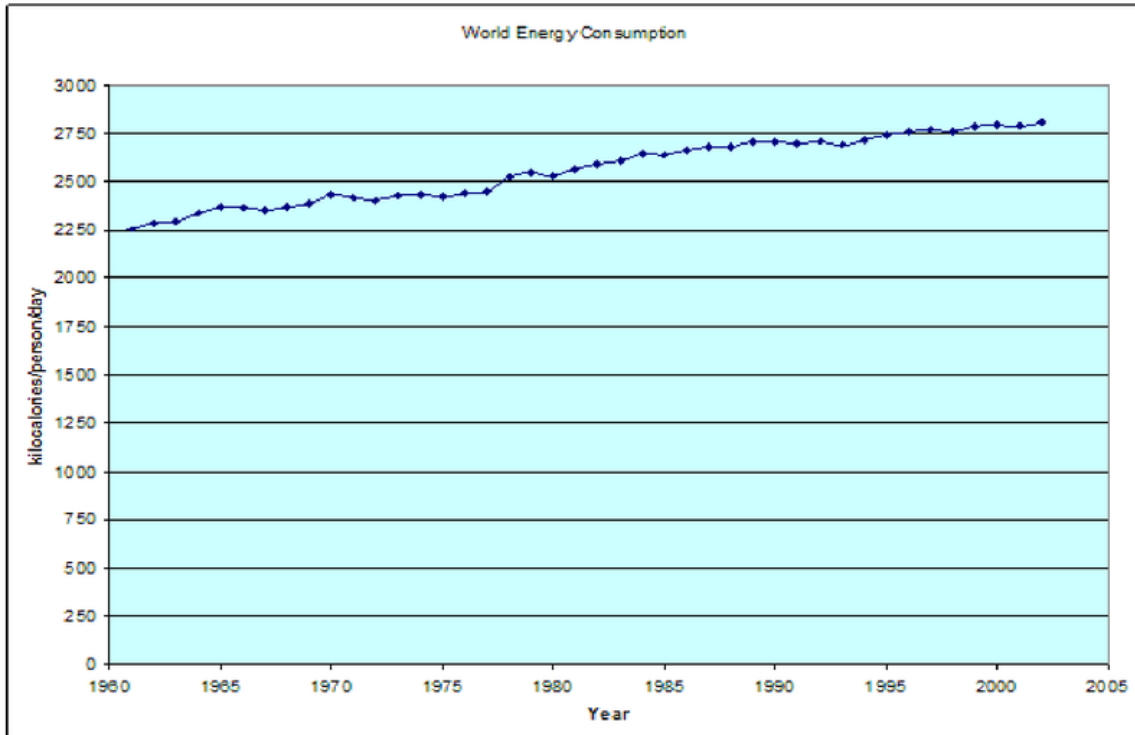
A 2006 review identified ten other possible contributors to the recent increase of obesity: (1) insufficient sleep, (2) endocrine disruptors (environmental pollutants that interfere with lipid metabolism), (3) decreased variability in ambient temperature, (4) decreased rates of smoking, because smoking suppresses appetite, (5) increased use of medications that can cause weight gain (e.g., atypical antipsychotics), (6) proportional increases in ethnic and age groups that tend to be heavier, (7) pregnancy at a later age (which may cause susceptibility to obesity in children), (8) epigenetic risk factors passed on generationally, (9) natural selection for higher BMI, and (10) assortative mating leading to increased concentration of obesity risk factors (this would not necessarily increase the number of obese people, but would increase the average population weight). While there is substantial evidence supporting the influence of these mechanisms on the increased prevalence of obesity, the evidence is still inconclusive, and the authors state that these are probably less influential than the ones discussed in the previous paragraph.

## Diet



Map of dietary energy availability per person per day in 1961 (left) and 2001–2003 (right) in kcal/person/day.





Average per capita energy consumption of the world from 1961 to 2002

The per capita dietary energy supply varies markedly between different regions and countries. It has also changed significantly over time. From the early 1970s to the late 1990s the average calories available per person per day (the amount of food bought) has increased in all parts of the world except Eastern Europe. The United States had the highest availability with 3,654 calories per person in 1996. This increased further in 2003 to 3,754. During the late 1990s Europeans had 3,394 calories per person, in the developing areas of Asia there were 2,648 calories per person, and in sub-Saharan Africa people had 2,176 calories per person. Total calorie consumption has been found to be related to obesity.

The widespread availability of nutritional guidelines has done little to address the problems of overeating and poor dietary choice. From 1971 to 2000, obesity rates in the United States increased from 14.5% to 30.9%. During the same period, an increase occurred in the average amount of calories consumed. For women, the average increase was 335 calories per day (1,542 calories in 1971 and 1,877 calories in 2004), while for men the average increase was 168 calories per day (2,450 calories in 1971 and 2,618 calories in 2004). Most of these extra calories came from an increase in carbohydrate consumption rather than fat consumption. The primary sources of these extra carbohydrates are sweetened beverages, which now account for almost 25 percent of daily calories in young adults in America. Consumption of sweetened drinks is believed to be contributing to the rising rates of obesity.

As societies become increasingly reliant on energy-dense, big-portion, fast-food meals, the association between fast-food consumption and obesity becomes more concerning. In the United States consumption of fast-food meals tripled and calorie intake from these meals quadrupled between 1977 and 1995.

Agricultural policy and techniques in the United States and Europe have led to lower food prices. In the United States, subsidization of corn, soy, wheat, and rice through the U.S. farm bill has made the main sources of processed food cheap compared to fruits and vegetables.

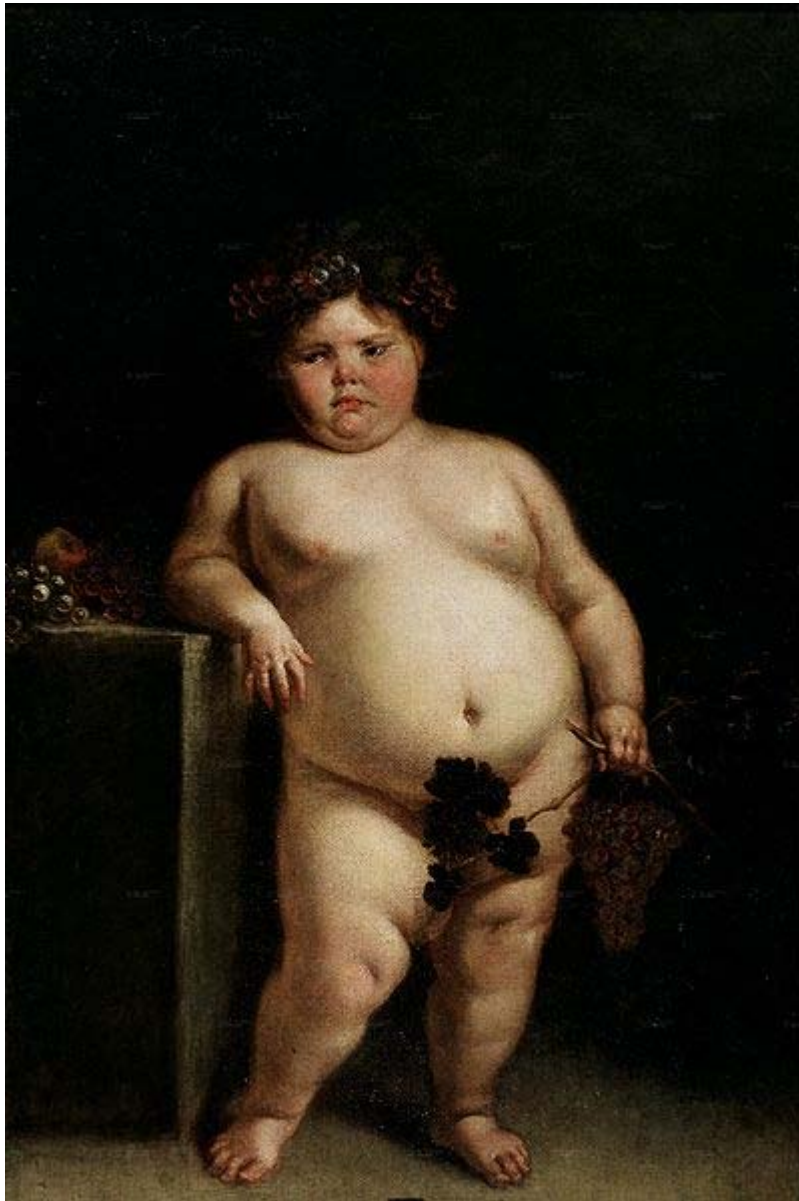
Obese people consistently under-report their food consumption as compared to people of normal weight. This is supported both by tests of people carried out in a calorimeter room and by direct observation.

### **Sedentary lifestyle**

A sedentary lifestyle plays a significant role in obesity. Worldwide there has been a large shift towards less physically demanding work, and currently at least 60% of the world's population gets insufficient exercise. This is primarily due to increasing use of mechanized transportation and a greater prevalence of labor-saving technology in the home. In children, there appear to be declines in levels of physical activity due to less walking and physical education. World trends in active leisure time physical activity are less clear. The World Health Organization indicates people worldwide are taking up less active recreational pursuits, while a study from Finland found an increase and a study from the United States found leisure-time physical activity has not changed significantly.

In both children and adults, there is an association between television viewing time and the risk of obesity. A 2008 meta-analysis found 63 of 73 studies (86%) showed an increased rate of childhood obesity with increased media exposure, with rates increasing proportionally to time spent watching television.

## Genetics



A 1680 painting by Juan Carreno de Miranda of a girl presumed to have Prader-Willi syndrome

Like many other medical conditions, obesity is the result of an interplay between genetic and environmental factors. Polymorphisms in various genes controlling appetite and metabolism predispose to obesity when sufficient calories are present. As of 2006 more than 41 of these sites have been linked to the development of obesity when a favorable environment is present. People with two copies of the FTO gene (fat mass and obesity associated gene) has been found on average to weigh 3–4 kg more and have a 1.67-fold greater risk of obesity compared to those without the risk allele. The percentage of obesity that can be attributed to genetics varies, depending on the population examined, from 6% to 85%.

Obesity is a major feature in several syndromes, such as Prader-Willi syndrome, Bardet-Biedl syndrome, Cohen syndrome, and MOMO syndrome. (The term "non-syndromic obesity" is sometimes used to exclude these conditions.) In people with early-onset severe obesity (defined by an onset before 10 years of age and body mass index over three standard deviations above normal), 7% harbor a single point DNA mutation.

Studies that have focused upon inheritance patterns rather than upon specific genes have found that 80% of the offspring of two obese parents were obese, in contrast to less than 10% of the offspring of two parents who were of normal weight.

The thrifty gene hypothesis postulates that certain ethnic groups may be more prone to obesity in an equivalent environment. Their ability to take advantage of rare periods of abundance by storing energy as fat would be advantageous during times of varying food availability, and individuals with greater adipose reserves would be more likely survive famine. This tendency to store fat, however, would be maladaptive in societies with stable food supplies. This is the presumed reason that Pima Indians, who evolved in a desert ecosystem, developed some of the highest rates of obesity when exposed to a Western lifestyle.

## **Medical and psychiatric illness**

Certain physical and mental illnesses and the pharmaceutical substances used to treat them can increase risk of obesity. Medical illnesses that increase obesity risk include several rare genetic syndromes (listed above) as well as some congenital or acquired conditions: hypothyroidism, Cushing's syndrome, growth hormone deficiency, and the eating disorders: binge eating disorder and night eating syndrome. However, obesity is not regarded as a psychiatric disorder, and therefore is not listed in the DSM-IVR as a psychiatric illness. The risk of overweight and obesity is higher in patients with psychiatric disorders than in persons without psychiatric disorders.

Certain medications may cause weight gain or changes in body composition; these include insulin, sulfonylureas, thiazolidinediones, atypical antipsychotics, antidepressants, steroids, certain anticonvulsants (phenytoin and valproate), pizotifen, and some forms of hormonal contraception.

## **Social determinants**

While genetic influences are important to understanding obesity, they cannot explain the current dramatic increase seen within specific countries or globally. Though it is accepted that calorie consumption in excess of calorie expenditure leads to obesity on an individual basis, the cause of the shifts in these two factors on the societal scale is much debated. There are a number of theories as to the cause but most believe it is a combination of various factors.

The correlation between social class and BMI varies globally. A review in 1989 found that in developed countries women of a high social class were less likely to be obese. No

significant differences were seen among men of different social classes. In the developing world, women, men, and children from high social classes had greater rates of obesity. An update of this review carried out in 2007 found the same relationships, but they were weaker. The decrease in strength of correlation was felt to be due to the effects of globalization. Among developed countries, levels of adult obesity, and percentage of teenage children who are overweight, are correlated with income inequality. A similar relationship is seen between US states: more adults, even in higher social classes, are obese in more unequal states.

Many explanations have been put forth for associations between BMI and social class. It is thought that in developed countries, the wealthy are able to afford more nutritious food, they are under greater social pressure to remain slim, and have more opportunities along with greater expectations for physical fitness. In undeveloped countries the ability to afford food, high energy expenditure with physical labor, and cultural values favoring a larger body size are believed to contribute to the observed patterns. Attitudes toward body mass held by people in one's life may also play a role in obesity. A correlation in BMI changes over time has been found between friends, siblings, and spouses. Stress and perceived low social status appear to increase risk of obesity.

Smoking has a significant effect on an individual's weight. Those who quit smoking gain an average of 4.4 kilograms (9.7 lb) for men and 5.0 kilograms (11.0 lb) for women over ten years. However, changing rates of smoking have had little effect on the overall rates of obesity.

In the United States the number of children a person has is related to their risk of obesity. A woman's risk increases by 7% per child, while a man's risk increases by 4% per child. This could be partly explained by the fact that having dependent children decreases physical activity in Western parents.

In the developing world urbanization is playing a role in increasing rate of obesity. In China overall rates of obesity are below 5%; however, in some cities rates of obesity are greater than 20%.

Malnutrition in early life is believed to play a role in the rising rates of obesity in the developing world. Endocrine changes that occur during periods of malnutrition may promote the storage of fat once more calories become available.

## **Infectious agents**

The study of the effect of infectious agents on metabolism is still in its early stages. Gut flora has been shown to differ between lean and obese humans. There is an indication that gut flora in obese and lean individuals can affect the metabolic potential. This apparent alteration of the metabolic potential is believed to confer a greater capacity to harvest energy contributing to obesity. Whether these differences are the direct cause or the result of obesity has yet to be determined unequivocally.

An association between viruses and obesity has been found in humans and several different animal species. The amount that these associations may have contributed to the rising rate of obesity is yet to be determined.

### ***Pathophysiology***

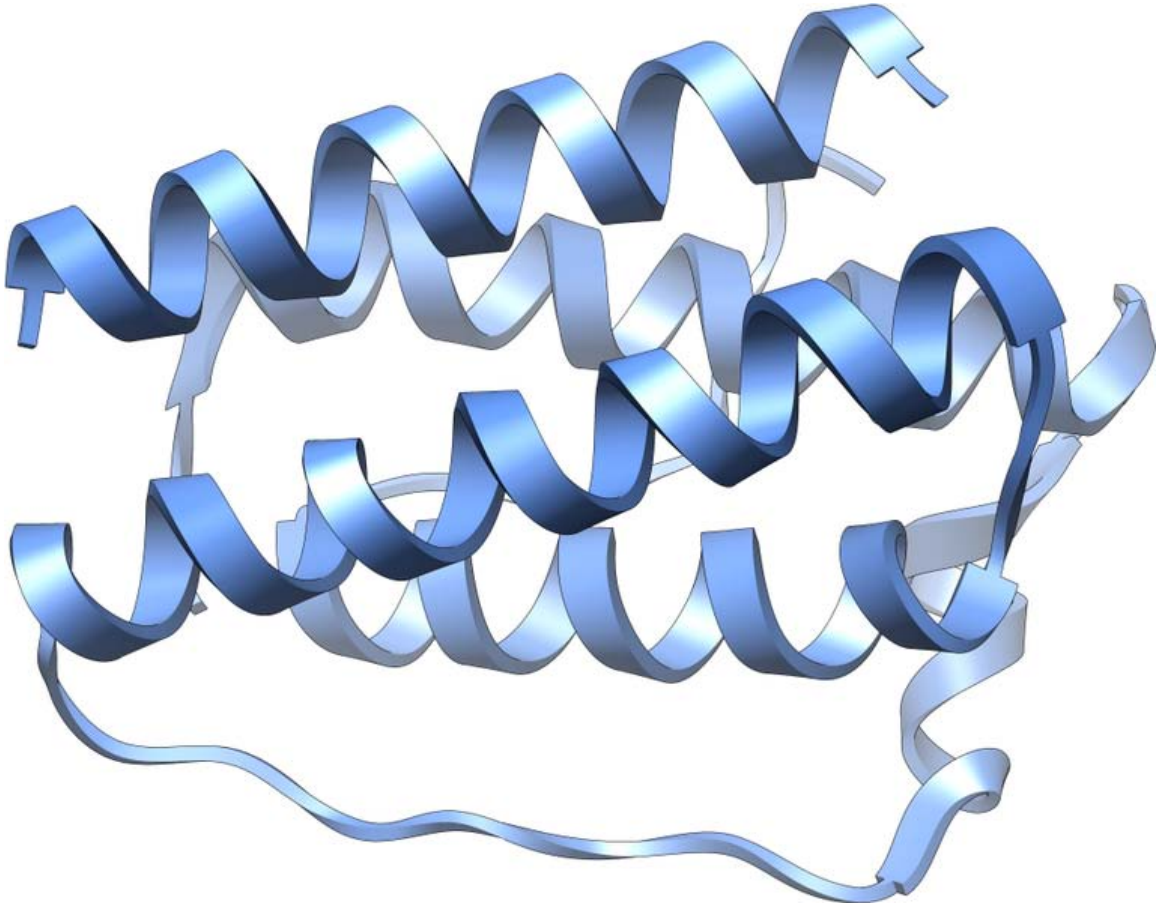


A comparison of a mouse unable to produce leptin thus resulting in obesity (left) and a normal mouse (right)

Flier summarizes the many possible pathophysiological mechanisms involved in the development and maintenance of obesity. This field of research had been almost unapproached until leptin was discovered in 1994. Since this discovery, many other hormonal mechanisms have been elucidated that participate in the regulation of appetite and food intake, storage patterns of adipose tissue, and development of insulin resistance. Since leptin's discovery, ghrelin, insulin, orexin, PYY 3-36, cholecystokinin, adiponectin, as well as many other mediators have been studied. The adipokines are mediators produced by adipose tissue; their action is thought to modify many obesity-related diseases.

Leptin and ghrelin are considered to be complementary in their influence on appetite, with ghrelin produced by the stomach modulating short-term appetitive control (i.e. to eat when the stomach is empty and to stop when the stomach is stretched). Leptin is produced by adipose tissue to signal fat storage reserves in the body, and mediates long-term appetitive controls (i.e. to eat more when fat storages are low and less when fat storages are high). Although administration of leptin may be effective in a small subset of

obese individuals who are leptin deficient, most obese individuals are thought to be leptin resistant and have been found to have high levels of leptin. This resistance is thought to explain in part why administration of leptin has not been shown to be effective in suppressing appetite in most obese people.



A graphic depiction of a leptin molecule

While leptin and ghrelin are produced peripherally, they control appetite through their actions on the central nervous system. In particular, they and other appetite-related hormones act on the hypothalamus, a region of the brain central to the regulation of food intake and energy expenditure. There are several circuits within the hypothalamus that contribute to its role in integrating appetite, the melanocortin pathway being the most well understood. The circuit begins with an area of the hypothalamus, the arcuate nucleus, that has outputs to the lateral hypothalamus (LH) and ventromedial hypothalamus (VMH), the brain's feeding and satiety centers, respectively.

The arcuate nucleus contains two distinct groups of neurons. The first group coexpresses neuropeptide Y (NPY) and agouti-related peptide (AgRP) and has stimulatory inputs to the LH and inhibitory inputs to the VMH. The second group coexpresses pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) and has stimulatory inputs to the VMH and inhibitory inputs to the LH. Consequently,

NPY/AgRP neurons stimulate feeding and inhibit satiety, while POMC/CART neurons stimulate satiety and inhibit feeding. Both groups of arcuate nucleus neurons are regulated in part by leptin. Leptin inhibits the NPY/AgRP group while stimulating the POMC/CART group. Thus a deficiency in leptin signaling, either via leptin deficiency or leptin resistance, leads to overfeeding and may account for some genetic and acquired forms of obesity.

## Management



Orlistat (Xenical) the most commonly used medication to treat obesity and sibutramine (Meridia) a recently withdrawn medication due to cardiovascular side effects

The main treatment for obesity consists of dieting and physical exercise. Diet programs may produce weight loss over the short term, but maintaining this weight loss is frequently difficult and often requires making exercise and a lower calorie diet a permanent part of a person's lifestyle. Success rates of long-term weight loss maintenance with lifestyle changes are low ranging from 2–20%.

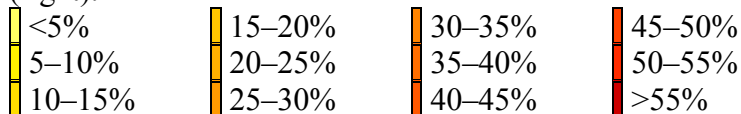
One medication, orlistat (Xenical), is current widely available and approved for long term use. Weight loss however is modest with an average of 2.9 kg (6.4 lb) at 1 to 4 years and there is little information on how these drugs affect longer-term complications of obesity. Its use is associated with high rates of gastrointestinal side effects.

The most effective treatment for obesity is bariatric surgery. Surgery for severe obesity is associated with long-term weight loss and decreased overall mortality. One study found a weight loss of between 14% and 25% (depending on the type of procedure performed) at 10 years, and a 29% reduction in all cause mortality when compared to standard weight loss measures. However, due to its cost and the risk of complications, researchers are searching for other effective yet less invasive treatments.

## **Epidemiology**



World obesity prevalence among males (left) and females (right).



Before the 20th century, obesity was rare; in 1997 the WHO formally recognized obesity as a global epidemic. As of 2005 the WHO estimates that at least 400 million adults (9.8%) are obese, with higher rates among women than men. The rate of obesity also increases with age at least up to 50 or 60 years old and severe obesity in the United States, Australia, and Canada is increasing faster than the overall rate of obesity.

Once considered a problem only of high-income countries, obesity rates are rising worldwide and affecting both the developed and developing world. These increases have been felt most dramatically in urban settings. The only remaining region of the world where obesity is not common is sub-Saharan Africa.

## **Public health**

The World Health Organization (WHO) predicts that overweight and obesity may soon replace more traditional public health concerns such as undernutrition and infectious diseases as the most significant cause of poor health. Obesity is a public health and policy problem because of its prevalence, costs, and health effects. Public health efforts seek to understand and correct the environmental factors responsible for the increasing prevalence of obesity in the population. Solutions look at changing the factors that cause excess calorie consumption and inhibit physical activity. Efforts include federally reimbursed meal programs in schools, limiting direct junk food marketing to children, and decreasing access to sugar-sweetened beverages in schools. When constructing urban environments, efforts have been made to increase access to parks and to develop pedestrian routes.

Many countries and groups have published reports pertaining to obesity. In 1998 the first US Federal guidelines were published, titled "Clinical Guidelines on the Identification,

Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report". In 2006 the Canadian Obesity Network published the "Canadian Clinical Practice Guidelines (CPG) on the Management and Prevention of Obesity in Adults and Children". This is a comprehensive evidence-based guideline to address the management and prevention of overweight and obesity in adults and children.

In 2004, the United Kingdom Royal College of Physicians, the Faculty of Public Health and the Royal College of Paediatrics and Child Health released the report "Storing up Problems", which highlighted the growing problem of obesity in the UK. The same year, the House of Commons Health Select Committee published its "most comprehensive inquiry [...] ever undertaken" into the impact of obesity on health and society in the UK and possible approaches to the problem. In 2006, the National Institute for Health and Clinical Excellence (NICE) issued a guideline on the diagnosis and management of obesity, as well as policy implications for non-healthcare organizations such as local councils.

A 2007 report produced by Sir Derek Wanless for the King's Fund warned that unless further action was taken, obesity had the capacity to cripple the National Health Service financially. In the United States organizations such as the Bill Clinton Foundation's Alliance for a Healthier Generation and Action for Healthy Kids are working to combat childhood obesity. Additionally, the Centers for Disease Control and Prevention co-hosted the first-ever Weight of the Nation Conference in 2009 with the goal of focusing national attention on the obesity epidemic.

Comprehensive approaches are being looked at to address the rising rates of obesity. The Obesity Policy Action (OPA) framework divides measure into 'upstream' policies, 'midstream' policies, 'downstream' policies. 'Upstream' policies look at changing society, 'midstream' policies try to alter individuals' behavior to prevent obesity, and 'downstream' policies try to treat currently afflicted people.

## ***Economic impact***



Services must accommodate obese people with specialist equipment such as much wider chairs.

In addition to its health impacts, obesity leads to many problems including disadvantages in employment and increased business costs. These effects are felt by all levels of society from individuals, to corporations, to governments.

The estimate range for annual expenditures on diet products is \$40 billion to \$100 billion in the US alone. In 1998, the medical costs attributable to obesity in the US were \$78.5 billion or 9.1% of all medical expenditures, while the cost of obesity in Canada was estimated at CA\$2 billion in 1997 (2.4% of total health costs).

Obesity prevention programs have been found to reduce the cost of treating obesity-related disease. However, the longer people live, the more medical costs they incur. Researchers therefore conclude that reducing obesity may improve the public's health, but it is unlikely to reduce overall health spending.

Obesity can lead to social stigmatization and disadvantages in employment. When compared to their normal weight counterparts, obese workers on average have higher

rates of absenteeism from work and take more disability leave, thus increasing costs for employers and decreasing productivity. A study examining Duke University employees found that people with a BMI over 40 filed twice as many workers' compensation claims as those whose BMI was 18.5–24.9. They also had more than 12 times as many lost work days. The most common injuries in this group were due to falls and lifting, thus affecting the lower extremities, wrists or hands, and backs. The US state of Alabama Employees' Insurance Board approved a controversial plan to charge obese workers \$25 per month if they do not take measures to reduce their weight and improve their health. These measures started in January 2010 and apply to those with a BMI of greater than 35 kg/m<sup>2</sup> who fail to make improvements in their health after one year.

Some research shows that obese people are less likely to be hired for a job and are less likely to be promoted. Obese people are also paid less than their non-obese counterparts for an equivalent job. Obese women on average make 6% less and obese men make 3% less.

Specific industries, such as the airline and food industries, have special concerns. Due to rising rates of obesity, airlines face higher fuel costs and pressures to increase seating width. In 2000, the extra weight of obese passengers cost airlines US\$275 million. Costs for restaurants are increased by litigation accusing them of causing obesity. In 2005 the US Congress discussed legislation to prevent civil law suits against the food industry in relation to obesity; however, it did not become law.

## ***History and culture***

### **Etymology**

*Obesity* is from the Latin *obesitas*, which means "stout, fat, or plump." *Ēsus* is the past participle of *edere* (to eat), with *ob* (over) added to it. *The Oxford English Dictionary* documents its first usage in 1611 by Randle Cotgrave.

## Historical trends



During the Middle Ages and the Renaissance obesity was often seen as a sign of wealth, and was relatively common among the elite: *The Tuscan General Alessandro del Borro*, attributed to Charles Mellin, 1645

The Greeks were the first to recognize obesity as a medical disorder. Hippocrates wrote that "Corpulence is not only a disease itself, but the harbinger of others". The Indian surgeon Sushruta (6th century BCE) related obesity to diabetes and heart disorders. He recommended physical work to help cure it and its side effects. For most of human history mankind struggled with food scarcity. Obesity has thus historically been viewed as a sign of wealth and prosperity. It was common among high officials in Europe in the Middle Ages and the Renaissance as well as in Ancient East Asian civilizations.

With the onset of the industrial revolution it was realized that the military and economic might of nations were dependent on both the body size and strength of their soldiers and workers. Increasing the average body mass index from what is now considered underweight to what is now the normal range played a significant role in the development of industrialized societies. Height and weight thus both increased through the

19th century in the developed world. During the 20th century, as populations reached their genetic potential for height, weight began increasing much more than height, resulting in obesity. In the 1950s increasing wealth in the developed world decreased child mortality, but as body weight increased heart and kidney disease became more common. During this time period insurance companies realized the connection between weight and life expectancy and increased premiums for the obese.

Many cultures throughout history have viewed obesity as the result of a character flaw. The *obesus* or fat character in Greek comedy was a glutton and figure of mockery. During Christian times food was viewed as a gateway to the sins of sloth and lust. In modern Western culture, excess weight is often regarded as unattractive, and obesity is commonly associated with various negative stereotypes. People of all ages can face social stigmatization, and may be targeted by bullies or shunned by their peers. Obesity is once again a reason for discrimination.



*Venus of Willendorf* created 24,000–22,000 BC

Public perceptions in Western society regarding healthy body weight differ from those regarding the weight that is considered ideal – and both have changed since the beginning of the 20th century. The weight that is viewed as an ideal has become lower since the 1920s. This is illustrated by the fact that the average height of Miss America pageant winners increased by 2% from 1922 to 1999, while their average weight decreased by 12%. On the other hand, people's views concerning healthy weight have changed in the opposite direction. In Britain the weight at which people considered themselves to be overweight was significantly higher in 2007 than in 1999. These changes are believed to be due to increasing rates of adiposity leading to increased acceptance of extra body fat as being normal.

Obesity is still seen as a sign of wealth and well-being in many parts of Africa. This has become particularly common since the HIV epidemic began.

## **The arts**

The first sculptural representations of the human body 20,000–35,000 years ago depict obese females. Some attribute the Venus figurines to the tendency to emphasize fertility while others feel they represent "fatness" in the people of the time. Corpulence is, however, absent in both Greek and Roman art, probably in keeping with their ideals regarding moderation. This continued through much of Christian European history, with only those of low socioeconomic status being depicted as obese.

During the Renaissance some of the upper class began flaunting their large size, as can be seen in portraits of Henry the VIII and Alessandro del Borro. Rubens (1577–1640) regularly depicted full-bodied women in his pictures, from which derives the term Rubenesque. These women, however, still maintained the "hourglass" shape with its relationship to fertility. During the 19th century, views on obesity changed in the Western world. After centuries of obesity being synonymous with wealth and social status, slimness began to be seen as the desirable standard.

## Size acceptance



Overweight people, such as U.S. President William Howard Taft, have been ridiculed at various times.

The principal goal of the fat acceptance movement is to decrease discrimination against people who are overweight and obese. However, some in the movement are also attempting to challenge the established relationship between obesity and negative health outcomes.

A number of organizations exist that promote the acceptance of obesity. They have increased in prominence in the latter half of the 20th century. The US-based National Association to Advance Fat Acceptance (NAAFA) was formed in 1969 and describes itself as a civil rights organization dedicated to ending size discrimination.

The International Size Acceptance Association (ISAA) is a non-governmental organization (NGO) which was founded in 1997. It has more of a global orientation and describes its mission as promoting size acceptance and helping to end weight-based

discrimination. These groups often argue for the recognition of obesity as a disability under the US Americans With Disabilities Act (ADA). The American legal system, however, has decided that the potential public health costs exceed the benefits of extending this anti-discrimination law to cover obesity.

Multiple books such as *The Diet Myth* by Paul Campos argue that the health risks of obesity are mostly unproven and the real problem is the social stigma facing the obese. Similarly, *The Obesity Epidemic* by Michael Gard argues that obesity is a moral and ideological construct, rather than a health problem. Other groups are also trying to challenge obesity's connection to poor health. The Center for Consumer Freedom, an organization partly supported by the restaurant and food industry, has run ads saying that obesity is not an epidemic but "hype".

People are known to select potential partners based on a similar body mass. The rising rates of obesity have therefore provided greater opportunities for overweight people to find partners. Certain subcultures also label themselves as particularly attracted to the obese. Chubby culture and fat admirers are examples.

### ***Childhood obesity***

The healthy BMI range varies with the age and sex of the child. Obesity in children and adolescents is defined as a BMI greater than the 95th percentile. The reference data that these percentiles are based on is from 1963 to 1994 and thus has not been affected by the recent increases in rates of obesity. Childhood obesity has reached epidemic proportions in 21st century, with rising rates in both the developed and developing world. Rates of obesity in Canadian boys have increased from 11% in 1980s to over 30% in 1990s, while during this same time period rates increased from 4 to 14% in Brazilian children.

As with obesity in adults, many different factors contribute to the rising rates of childhood obesity. Changing diet and decreasing physical activity are believed to be the two most important in causing the recent increase in the rates. Because childhood obesity often persists into adulthood and is associated with numerous chronic illnesses, children who are obese are often tested for hypertension, diabetes, hyperlipidemia, and fatty liver. Treatments used in children are primarily lifestyle interventions and behavioral techniques. Medications are not FDA approved for use in this age group.

### ***In other animals***

Obesity in pets is common in many countries. Rates of overweight and obesity in dogs in the United States range from 23% to 41% with about 5.1% obese. Rates of obesity in cats was slightly higher at 6.4%. In Australia the rate of obesity among dogs in a veterinary setting has been found to be 7.6%. The risk of obesity in dogs is related to whether or not their owners are obese; however, there is no similar correlation between cats and their owners.

## Chapter 6

# Classification of Obesity



An obese male with a body mass index of  $46 \text{ kg/m}^2$ : weight 146 kg (322 lb), height 177 cm (5 ft 10 in)

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse affect on health. Relative weight and body mass index (BMI) are nearly identical and are reasonable estimates of body fatness as measured by percentage body fat. However, BMI does not account for the wide variation in body fat distribution, and may not correspond to the same degree of fatness or associated health risk in different individuals and populations. Other measurements of fat distribution include the waist–hip ratio and body fat percentage. Normal weight obesity is a condition of having normal body weight, but high body fat percentages with the same health risks of obesity.

### ***BMI***

Body mass index or BMI is a simple and widely used method for estimating body fat mass. BMI was developed in the 19th century by the Belgian statistician and anthropometrist Adolphe Quetelet. BMI is an accurate reflection of body fat percentage

in the majority of the adult population. It however is less accurate in people such as body builders and pregnant women. A formula combining BMI, age and gender can be used to estimate a person's body fat percentage to an accuracy of 4%. An alternative method, body volume index (BVI), is being developed in an effort to better take into account different body shapes.

<b>BMI</b>	<b>Classification</b>
< 18.5	underweight
18.5–24.9	normal weight
25.0–29.9	overweight
30.0–34.9	class I obesity
35.0–39.9	class II obesity
≥ 40.0	class III obesity

BMI is calculated by dividing the subject's mass by the square of his or her height, typically expressed either in metric or US "Customary" units:

$$\text{Metric: } BMI = \text{kilograms} / \text{meters}^2$$
$$\text{US/Customary and imperial: } BMI = \text{lb} \times 703 / \text{in}^2$$

where *lb* is the subject's weight in pounds and *in* is the subject's height in inches.

The most commonly used definitions, established by the World Health Organization (WHO) in 1997 and published in 2000, provide the values listed in the table at right.

Some modifications to the WHO definitions have been made by particular bodies. The surgical literature breaks down "class III" obesity into further categories who's exact values are still disputed.

- Any BMI ≥ 35 or 40 is *severe obesity*
- A BMI of ≥ 35 or 40–44.9 or 49.9 is *morbid obesity*
- A BMI of ≥ 45 or 50 is *super obese*

As Asian populations develop negative health consequences at a lower BMI than Caucasians, some nations have redefined obesity. The Japanese have defined obesity as any BMI greater than 25 while China uses a BMI of greater than 28.

### ***Waist circumference and waist–hip ratio***

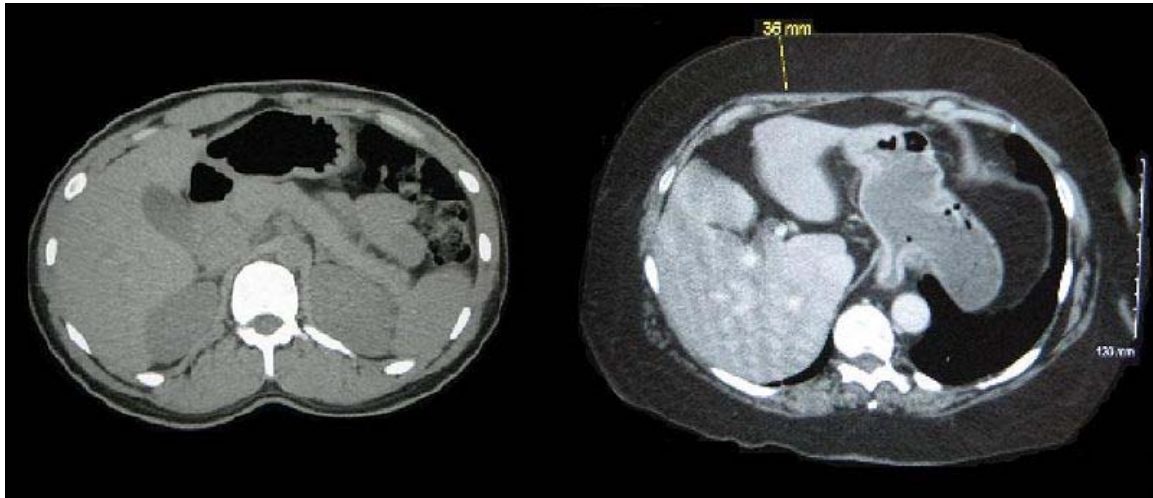
In the United States a waist circumference of >102 cm in men and >88 cm in women or the waist–hip ratio (the circumference of the waist divided by that of the hips of >0.9 for men and >0.85 for women) are used to define central obesity.

In the European Union waist circumference of ≥ 94 cm in men and ≥ 80 cm in non pregnant women are used as cut offs for central obesity.

A lower cut off of 90 cm has been recommended for South Asian and Chinese men, while a cut off of 85 cm has been recommended for Japanese men.

In those with a BMI under 35, intra-abdominal body fat is related to negative health outcomes independent of total body fat. Intra-abdominal or visceral fat has a particularly strong correlation with cardiovascular disease. In a study of 15,000 people, waist circumference also correlated better with metabolic syndrome than BMI. Women with abdominal obesity have a cardiovascular risk similar to that of men. In people with a BMI over 35, measurement of waist circumference however adds little to the predictive power of BMI as most individuals with this BMI have an abnormal waist circumferences.

### **Body fat percentage**



Cross-sections of the torso of a person of normal weight (left) and an obese person (right), taken by CT scan. Note the 3.6 cm (1.4 inches) of subcutaneous fat on the obese person.

Body fat percentage is total body fat expressed as a percentage of total body weight. There is no generally accepted definition of obesity based on total body fat. Most researchers have used >25% in men, and >30% in women, as cut-points to define obesity. However, the finding that metabolic disturbance increases with increasing body fat percentage suggests that focusing exclusively on cut-points of body fat percent may be of limited value.

Body fat percentage can be estimated from a person's BMI by the following formula:

$$\text{Bodyfat}\% = (1.2 * \text{BMI}) + (0.23 * \text{age}) - 5.4 - (10.8 * \text{gender})$$

where gender is 0 if female and 1 if male

This formula takes into account the fact that body fat percentage tends to be 10 percentage points greater in women than in men for a given BMI. It recognizes that a person's percentage body fat tends to increase as they age, even if their weight and BMI

remain constant. The results of this formula have been shown to have an accuracy of 4% in one group of individuals.

There are many other methods used to determine body fat percentage. Hydrostatic weighing, one of the most accurate methods of body fat calculation, involves weighting a person underwater. Two other simpler and less accurate methods have been used historically but are now not recommended. The first is the skinfold test, in which a pinch of skin is precisely measured to determine the thickness of the subcutaneous fat layer. The other is bioelectrical impedance analysis which uses electrical resistance. Bioelectrical impedance has not been shown to provide an advantage over BMI.

Body fat percentage measurement techniques used mainly for research include computed tomography (CT scan), magnetic resonance imaging (MRI), and dual energy X-ray absorptiometry (DEXA). These techniques provide very accurate measurements, but it can be difficult to obtain in the severely obese due to weight limits of most equipment and insufficient diameter of many CT or MRI scanners.

### ***Childhood obesity***



Variations in apparent body fat among children

The healthy BMI range varies with the age and sex of the child. Obesity in children and adolescents is defined as a BMI greater than the 95th percentile. The reference data that these percentiles are based on is from 1963 to 1994 and thus has not been affected by the recent increases in rates of obesity.

Childhood obesity has reached epidemic proportions in 21st century with rising rates in both the developed and developing world. Rates of obesity in Canadian boys have increased from 11% in 1980s to over 30% in 1990s, while during this same time period rates increased from 4 to 14% in Brazilian children.

As with obesity in adults many different factors contribute to the rising rates of childhood obesity. Changing diet and decreasing physical activity are believed to be the two most important in causing the recent increase in the rate of obesity. Activities from self propelled transport, to school physical education, and organized sports has been declining in many countries.

Because childhood obesity often persists into adulthood, and is associated with numerous chronic illnesses, it is important that children who are obese be tested for hypertension, diabetes, hyperlipidemia, and fatty liver.

Treatments used in children are primarily lifestyle interventions and behavioral techniques. Medications are not FDA approved for use in this age group.

## Chapter 7

# Abdominal Obesity

**Abdominal obesity**, colloquially known as **belly fat** or clinically as **central obesity**, is the accumulation of abdominal fat resulting in an increase in waist size. There is a strong correlation between central obesity and cardiovascular disease.

Visceral fat, also known as organ fat or *intra-abdominal fat*, is located inside the peritoneal cavity, packed in between internal organs and torso, as opposed to subcutaneous fat which is found underneath the skin, and intramuscular fat which is found interspersed in skeletal muscle. Visceral fat is composed of several adipose depots including mesenteric, epididymal white adipose tissue (EWAT) and perirenal fat. An excess of visceral fat is known as central obesity, the "pot belly" or "beer belly" effect, in which the abdomen protrudes excessively. This body type is also known as "apple shaped", as opposed to "pear shaped", in which fat is deposited on the hips and buttocks.

### **Causes**

The immediate cause of obesity is net energy imbalance — the organism consumes more usable calories than it expends, wastes, or discards via elimination. The fundamental cause of obesity is not well understood, but is presumably a combination of the organism's genes and environment. The specific cause of central fat is also not well understood.

In humans, central obesity is correlated with overeating and a sedentary lifestyle. Hypercortisolism, such as in Cushing's syndrome also leads to central obesity. Many prescription drugs can also have side effects resulting in obesity.

Because fat in the midsection contains the greatest amount of cortisol receptors, fat is created and stored in the midsection, specifically in fat cell deposits deep in the abdomen.

### **Diagnosis**

While central obesity can be obvious just by looking at the naked body, the severity of central obesity is determined by taking waist and hip measurements. The absolute waist circumference (>102 centimetres (40 in) in men and >88 centimetres (35 in) in women) and the waist-hip ratio (>0.9 for men and >0.85 for women) are both used as measures of

central obesity. A differential diagnosis includes distinguishing central obesity from ascites and intestinal bloating. In the cohort of 15,000 people participating in the National Health and Nutrition Examination Survey (NHANES III), waist circumference explained obesity-related health risk better than the body mass index (or BMI) when metabolic syndrome was taken as an outcome measure and this difference was statistically significant. In other words, excessive waist circumference appears to be more of a risk factor for metabolic syndrome than BMI.

An increasing acceptance of the importance of central obesity within the medical profession as an indicator of health risk has led to new developments in obesity diagnosis such as the Body Volume Index, which measures central obesity by measuring a person's body shape and their weight distribution.

BVI is based upon the principle that excess abdominal weight, measured by part volume as a percentage of total volume, constitutes a greater health risk. Recent validation has concluded that total and regional body volume estimates correlate positively and significantly with biomarkers of cardio-vascular risk and BVI calculations correlate significantly with all biomarkers of cardio-vascular risk.

## **Health risks**



Excess adipose tissue on a male

Central obesity is associated with a statistically higher risk of heart disease, hypertension, insulin resistance, and Diabetes Mellitus Type 2. Belly fat is a symptom of metabolic syndrome, and is an indicator used in the diagnosis of that disorder.

Central obesity can be a feature of lipodystrophies, a group of diseases which is either inherited, or due to secondary causes (often protease inhibitors, a group of medications against AIDS). Central obesity is a symptom of Cushing's syndrome and is also common in patients with polycystic ovary syndrome (PCOS). Central obesity is associated with glucose intolerance and dyslipidemia.

### **Relationship with diabetes**

There are numerous theories as to the exact cause and mechanism in Type 2 Diabetes. Central obesity is known to predispose individuals for insulin resistance. Abdominal fat

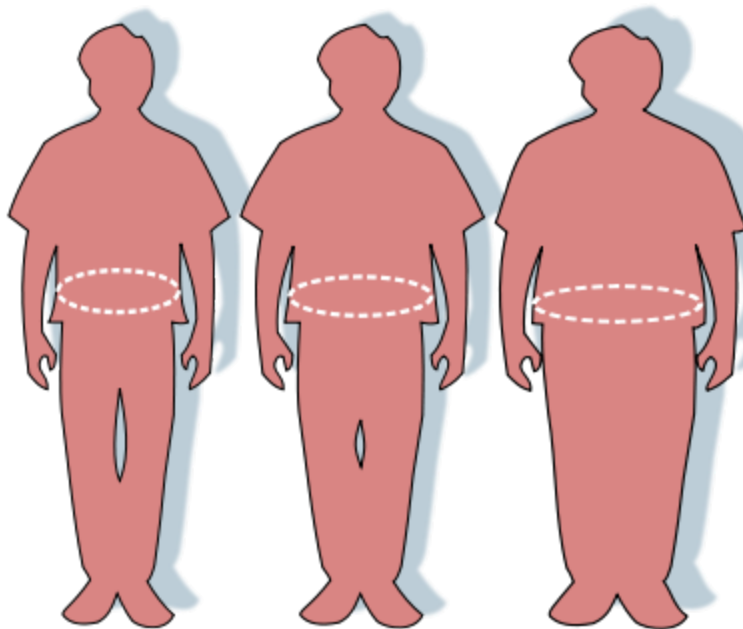
is especially active hormonally, secreting a group of hormones called adipokines that may possibly impair glucose tolerance.

Insulin resistance is a major feature of Diabetes Mellitus Type 2 (T2DM), and central obesity is correlated with both insulin resistance and T2DM itself. Increased adiposity (obesity) raises serum resistin levels, which in turn directly correlate to insulin resistance. Studies have also confirmed a direct correlation between resistin levels and T2DM. And it is waistline adipose tissue (central obesity) which seems to be the foremost type of fat deposits contributing to rising levels of serum resistin. Conversely, serum resistin levels have been found to *decline* with decreased adiposity following medical treatment.

### **Relationship with Alzheimer's Disease**

A US study reported in May 2010 *Annals of Neurology* examining over 700 adults found evidence to suggest higher volumes of visceral fat, regardless of overall weight, were associated with smaller brain volumes and increased risk of dementia.

### ***Waist-hip ratio***



Silhouettes and waist circumferences representing normal, overweight, and obese

The absolute waist circumference (>102 cm in men and >88 cm in women) and the waist-hip ratio (the circumference of the waist divided by that of the hips of >0.9 for men and >0.85 for women) are both used as measures of central obesity.

In those with a BMI under 35, intra-abdominal body fat is related to negative health outcomes independent of total body fat. Intra-abdominal or visceral fat has a particularly strong correlation with cardiovascular disease.

## **Sex differences**

Female sex hormone causes fat to be stored in the buttocks, thighs, and hips in women. Men are more likely to have fat stored in the belly due to sex hormone differences. When women reach menopause and the estrogen produced by ovaries declines, fat migrates from their buttocks, hips and thighs to their waists; later fat is stored in the belly.

## ***Prevention and treatments***

Performing adequate aerobic exercise and eating a healthy diet can prevent central obesity, and losing weight via these methods is the main way to reverse the condition.

Adjunctive therapies which may be prescribed by a physician are orlistat or sibutramine, although the latter has been associated with increased cardiovascular events and strokes and has been withdrawn from the market in the United States, the UK, the EU, Australia, Canada, Hong Kong, Thailand and Mexico.

In the presence of diabetes mellitus type 2, the physician might instead prescribe metformin and thiazolidinediones (rosiglitazone or pioglitazone) as anti-diabetic drugs rather than sulfonylurea derivatives. Thiazolidinediones may cause slight weight gain but decrease "pathologic" abdominal fat, and therefore may be prescribed for diabetics with central obesity.

## **Sit-ups myth**

There is a common misconception that spot exercise (that is, exercising a specific muscle or location of the body) most effectively burns fat at the desired location, but this is not the case. Spot exercise is beneficial for building specific muscles, but it has little effect, if any, on fat in that area of the body, or on the body's distribution of body fat. The same logic applies to sit-ups and belly fat. Sit-ups, crunches and other abdominal exercises are useful in building the abdominal muscles, but they have little effect, if any, on the adipose tissue located there.

## ***Slang terms***



Love handles are made up of excess fat around hips

Several colloquial terms used to refer to central obesity, and to people who have it, refer to beer drinking. However, there is little scientific evidence that beer drinkers are more prone to abdominal obesity, despite it being known colloquially as "beer belly", "beer gut", or "beer pot". One of the few studies conducted on the subject did not find that beer drinkers are more prone to abdominal obesity than nondrinkers or drinkers of wine or spirits. Chronic alcoholism can lead to cirrhosis, symptoms of which include gynecomastia (enlarged breasts) and ascites (abdominal fluid). These symptoms can suggest the appearance of central obesity.

"Love handles" and "spare tire" are colloquial terms for a layer of fat that is deposited around a person's midsection, especially visible on the sides over the abdominal external oblique muscle.

"Muffin top" is a pejorative term used for a person whose midsection spills over the waistline of his or her trousers in a manner that resembles the top of a muffin spilling over its baking pan.

"Pot belly" is another colloquial term used to describe a person who has an excessive amount of abdominal fat. This is especially pronounced and visible over clothing and may be indicative of other health related problems.

## Chapter 8

# Childhood Obesity

### Childhood obesity



Children with varying degrees of body fat.

**ICD-10**            E66.

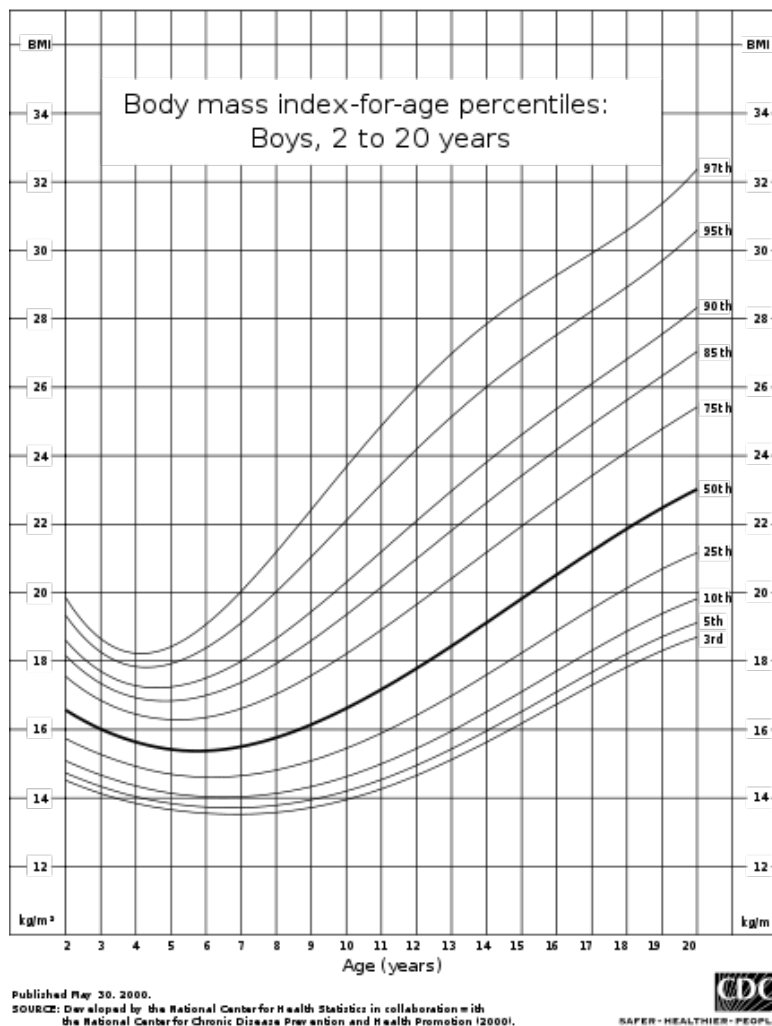
**ICD-9**            278

<b>DiseasesDB</b>	9099
<b>MedlinePlus</b>	003101
<b>eMedicine</b>	med/1653
<b>MeSH</b>	C23.888.144.699.500

**Childhood obesity** is a condition where excess body fat negatively affects a child's health or wellbeing. As methods to determine body fat directly are difficult, the diagnosis of obesity is often based on BMI. Due to the rising prevalence of obesity in children and its many adverse health effects it is being recognized as a serious public health concern. The term overweight rather than obese is often used in children as it is less stigmatizing.

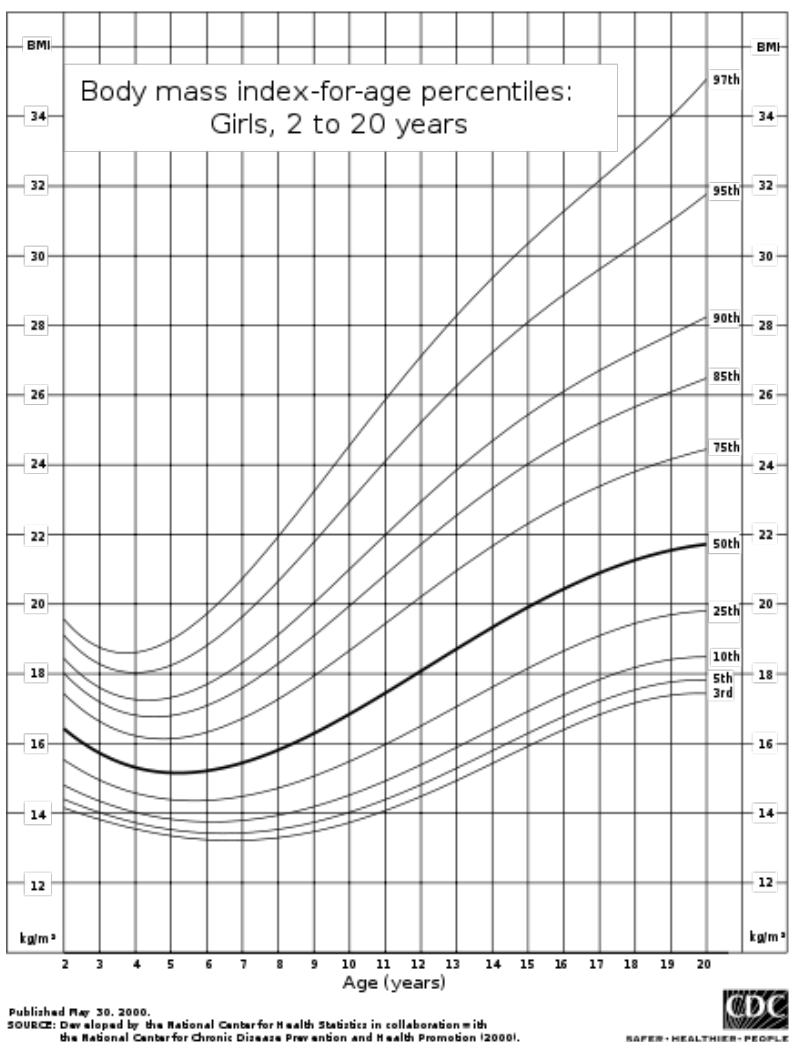
### Classification

CDC Growth Charts United States



BMI for age percentiles for boys 2 to 20 years of age

## CDC Growth Charts United States



BMI for age percentiles for girls 2 to 20 years of age.

Body mass index (BMI) is acceptable for determining obesity for children two years of age and older. The normal range for BMI in children vary with age and sex. The Center for Disease Control defines obesity as a BMI greater than the 95th percentile. It has published tables for determining this in children.

### ***Effects on health***

The first problems to occur in obese children are usually emotional or psychological. Childhood obesity however can also lead to life-threatening conditions including diabetes, high blood pressure, heart disease, sleep problems, cancer, and other disorders. Some of the other disorders would include liver disease, early puberty or menarche, eating disorders such as anorexia and bulimia, skin infections, and asthma and other respiratory problems. Studies have shown that overweight children are more likely to

grow up to be overweight adults. Obesity during adolescence has been found to increase mortality rates during adulthood.

Obese children often suffer from teasing by their peers. Some are harassed or discriminated against by their own family. Stereotypes abound and may lead to low self esteem and depression.

A 2008 study has found that children who are obese have carotid arteries which have prematurely aged by as much as thirty years as well as abnormal levels of cholesterol.

<b>System</b>	<b>Condition</b>	<b>System</b>	<b>Condition</b>
Endocrine	<ul style="list-style-type: none"> <li>• Impaired glucose tolerance</li> <li>• Diabetes mellitus</li> <li>• Metabolic syndrome</li> <li>• Hyperandrogenism</li> <li>• Effects on growth and puberty</li> <li>• Nulliparity and nulligravidity</li> </ul>	Cardiovascular	<ul style="list-style-type: none"> <li>• Hypertension</li> <li>• Hyperlipidemia</li> <li>• Increased risk of coronary heart disease as an adult</li> </ul>
Gastrointestinal	<ul style="list-style-type: none"> <li>• Nonalcoholic fatty liver disease</li> <li>• Cholelithiasis</li> </ul>	Respiratory	<ul style="list-style-type: none"> <li>• Obstructive sleep apnea</li> <li>• Obesity hypoventilation syndrome</li> </ul>
Musculoskeletal	<ul style="list-style-type: none"> <li>• Slipped capital femoral epiphysis (SCFE)</li> <li>• Tibia vara (Blount disease)</li> </ul>	Neurological	<ul style="list-style-type: none"> <li>• Idiopathic intracranial hypertension</li> </ul>
Psychosocial	<ul style="list-style-type: none"> <li>• Distorted peer relationships</li> <li>• Poor self esteem</li> <li>• Anxiety</li> <li>• Depression</li> </ul>	Skin	<ul style="list-style-type: none"> <li>• Furunculosis</li> <li>• Intertrigo</li> </ul>

## **Causes**

As with many conditions, childhood obesity can be brought on by a range of factors which often act in combination.

## Dietary

The effects of eating habits on childhood obesity are difficult to determine. A three year randomized controlled study of 1,704 3rd grade children which provided two healthy meals a day in combination with an exercise program and dietary counsellings failed to show a significant reduction in percentage body fat when compared to a control group. This was partly due to the fact that even though the children believed they were eating less their actual calorie consumption did not decrease with the intervention. At the same time observed energy expenditure remained similar between the groups. This occurred even though dietary fat intake decreased from 34% to 27%. A second study of 5,106 children showed similar results. Even though the children ate an improved diet there was no effect found on BMI. Why these studies did not bring about the desired effect of curbing childhood obesity has been attributed to the interventions not being sufficient enough. Changes were made primarily in the school environment while it is felt that they must occur in the home, the community, and the school simultaneously to have a significant effect.

Calorie-rich drinks and foods are readily available to children. Consumption of sugar-laden soft drinks may contribute to childhood obesity. In a study of 548 children over a 19 month period the likelihood of obesity increased by 1.6 for every additional soft drink consumed per day.

Calorie-dense, prepared snacks are available in many locations frequented by children. As childhood obesity has become more prevalent, snack vending machines in school settings have been reduced by law in a small number of localities. Eating at fast food restaurants is very common among young people with 75% of 7th to 12th grade students consuming fast food in a given week. The fast food industry is also at fault for the rise in childhood obesity. This industry spends about \$42 billion on advertisements aimed at young children. McDonald's alone has thirteen websites that are viewed by 365,000 children and 294,000 teenagers each month. In addition, fast food restaurants give out toys in children's meals, which helps to entice children. Forty percent of children ask their parents to take them to fast food restaurants on a daily basis. To make matters worse, out of 3000 combinations created from popular items on children's menus at fast food restaurants, only 13 meet the recommended nutritional guidelines for young children. Some literature has found a relationship between fast food consumption and obesity. Including a study which found that fast food restaurants near schools increases the risk of obesity among the student population.

Whole milk consumption verses 2% milk consumption in children of one to two years of age had no effect on weight, height, or body fat percentage. Therefore, whole milk continues to be recommended for this age group. However the trend of substituting sweetened drink for milk has been found to lead to excess weight gain.

## **Sedentary lifestyle**

Physical inactivity of children has also shown to be a serious cause, and children who fail to engage in regular physical activity are at greater risk of obesity. Researchers studied the physical activity of 133 children over a three week period using an accelerometer to measure each child's level of physical activity. They discovered the obese children were 35% less active on school days and 65% less active on weekends compared to non-obese children.

Physical inactivity as a child could result in physical inactivity as an adult. In a fitness survey of 6,000 adults, researchers discovered that 25% of those who were considered active at ages 14 to 19 were also active adults, compared to 2% of those who were inactive at ages 14 to 19, who were now said to be active adults. Staying physically inactive leaves unused energy in the body, most of which is stored as fat. Researchers studied 16 men over a 14 day period and fed them 50% more of their energy required every day through fats and carbohydrates. They discovered that carbohydrate overfeeding produced 75–85% excess energy being stored as body fat and fat overfeeding produced 90–95% storage of excess energy as body fat.

Many children fail to exercise because they are spending time doing stationary activities such as computer usage, playing video games or watching television. TV and other technology may be large factors of physically inactive children. Researchers provided a technology questionnaire to 4,561 children, ages 14, 16, and 18. They discovered children were 21.5% more likely to be overweight when watching 4+ hours of TV per day, 4.5% more likely to be overweight when using a computer one or more hours per day, and unaffected by potential weight gain from playing video games. A randomized trial showed that reducing TV viewing and computer use can decrease age-adjusted BMI; reduced calorie intake was thought to be the greatest contributor to the BMI decrease.

Technological activities are not the only household influences of childhood obesity. Low-income households can affect a child's tendency to gain weight. Over a three week period researchers studied the relationship of socioeconomic status (SES) to body composition in 194 children, ages 11–12. They measured weight, waist girth, stretch stature, skinfolds, physical activity, TV viewing, and SES; researchers discovered clear SES inclines to upper class children compared to the lower class children.

Childhood inactivity is linked to obesity in the United States with more children being overweight at younger ages. In a 2009 preschool study 89% of a preschoolers' day was found to be sedentary while the same study also found that even when outside, 56 percent of activities were still sedentary. One factor believed to contribute to the lack of activity found was little teacher motivation, but when toys, such as balls were made available, the children were more likely to play.

## Genetics

Childhood obesity is often the result of an interplay between many genetic and environmental factors. Polymorphisms in various genes controlling appetite and metabolism predispose individuals to obesity when sufficient calories are present. As such obesity is a major feature of a number of rare genetic conditions that often present in childhood.

- Prader-Willi syndrome with an incidence between 1 in 12,000 and 1 in 15,000 live births is characterized by hyperphagia and food preoccupations which leads to rapid weight gain in those affected.
- Bardet-Biedl syndrome
- MOMO syndrome
- Leptin receptor mutations
- Congenital leptin deficiency
- Melanocortin receptor mutations

In children with early-onset severe obesity (defined by an onset before ten years of age and body mass index over three standard deviations above normal), 7% harbor a single locus mutation. One study found that 80% of the offspring of two obese parents were obese in contrast to less than 10% of the offspring of two parents who were of normal weight. The percentage of obesity that can be attributed to genetics varies from 6% to 85% depending on the population examined. Compare: secondhand obesity.

## Home environment

Children's food choices are also influenced by family meals. Researchers provided a household eating questionnaire to 18,177 children, ranging in ages 11–21, and discovered that four out of five parents let their children make their own food decisions. They also discovered that compared to adolescents who ate three or fewer meals per week, those who ate four to five family meals per week were 19% less likely to report poor consumption of vegetables, 22% less likely to report poor consumption of fruits, and 19% less likely to report poor consumption of dairy foods. Adolescents who ate six to seven family meals per week, compared to those who ate three or fewer family meals per week, were 38% less likely to report poor consumption of vegetables, 31% less likely to report poor consumption of fruits, and 27% less likely to report poor consumption of dairy foods. The results of a survey in the UK published in 2010 imply that children raised by their grandparents are more likely to be obese as adults than those raised by their parents. An American study released in 2011 found the more mothers work the more children are more likely to be overweight or obese.

## Developmental factors

Various developmental factors may affect rates of obesity. Breast-feeding for example may protect against obesity in later life with the duration of breast-feeding inversely associated with the risk of being overweight later on. A child's body growth pattern may

influence the tendency to gain weight. Researchers measured the standard deviation (SD [weight and length]) scores in a cohort study of 848 babies. They found that infants who had an SD score above 0.67 had catch up growth (they were less likely to be overweight) compared to infants who had less than a 0.67 SD score (they were more likely to gain weight).

A child's weight may be influenced when he/she is only an infant. Researchers did a cohort study on 19,397 babies, from their birth until age seven and discovered that fat babies at four months were 1.38 times more likely to be overweight at seven years old compared to normal weight babies. Fat babies at the age of one were 1.17 times more likely to be overweight at age seven compared to normal weight babies.

## **Medical illness**

Cushing's syndrome (a condition in which the body contains excess amounts of cortisol) may also influence childhood obesity. Researchers analyzed two isoforms (proteins that have the same purpose as other proteins, but are programmed by different genes) in the cells of 16 adults undergoing abdominal surgery. They discovered that one type of isoform created oxo-reductase activity (the alteration of cortisone to cortisol) and this activity increased 127.5 pmol mg sup when the other type of isoform was treated with cortisol and insulin. The activity of the cortisol and insulin can possibly activate Cushing's syndrome.

Hypothyroidism is a hormonal cause of obesity, but it does not significantly affect obese people who have it more than obese people who do not have it. In a comparison of 108 obese patients with hypothyroidism to 131 obese patients without hypothyroidism, researchers discovered that those with hypothyroidism had only 0.077 points more on the caloric intake scale than did those without hypothyroidism.

## **Psychological factors**

Researchers surveyed 1,520 children, ages 9–10, with a four year follow up and discovered a positive correlation between obesity and low self esteem in the four year follow up. They also discovered that decreased self esteem led to 19% of obese children feeling sad, 48% of them feeling bored, and 21% of them feeling nervous. In comparison, 8% of normal weight children felt sad, 42% of them felt bored, and 12% of them felt nervous. Stress can influence a child's eating habits. Researchers tested the stress inventory of 28 college females and discovered that those who were binge eating had a mean of 29.65 points on the perceived stress scale, compared to the control group who had a mean of 15.19 points. This evidence may demonstrate a link between eating and stress.

Feelings of depression can cause a child to overeat. Researchers provided an in-home interview to 9,374 adolescents, in grades seven through 12 and discovered that there was not a direct correlation with children eating in response to depression. Of all the obese adolescents, 8.2% had said to be depressed, compared to 8.9% of the non-obese

adolescents who said they were depressed. Antidepressants, however, seem to have very little influence on childhood obesity. Researchers provided a depression questionnaire to 487 overweight/obese subjects and found that 7% of those with low depression symptoms were using antidepressants and had an average BMI score of 44.3, 27% of those with moderate depression symptoms were using antidepressants and had an average BMI score of 44.7, and 31% of those with major depression symptoms were using antidepressants and had an average BMI score of 44.2.

## Management

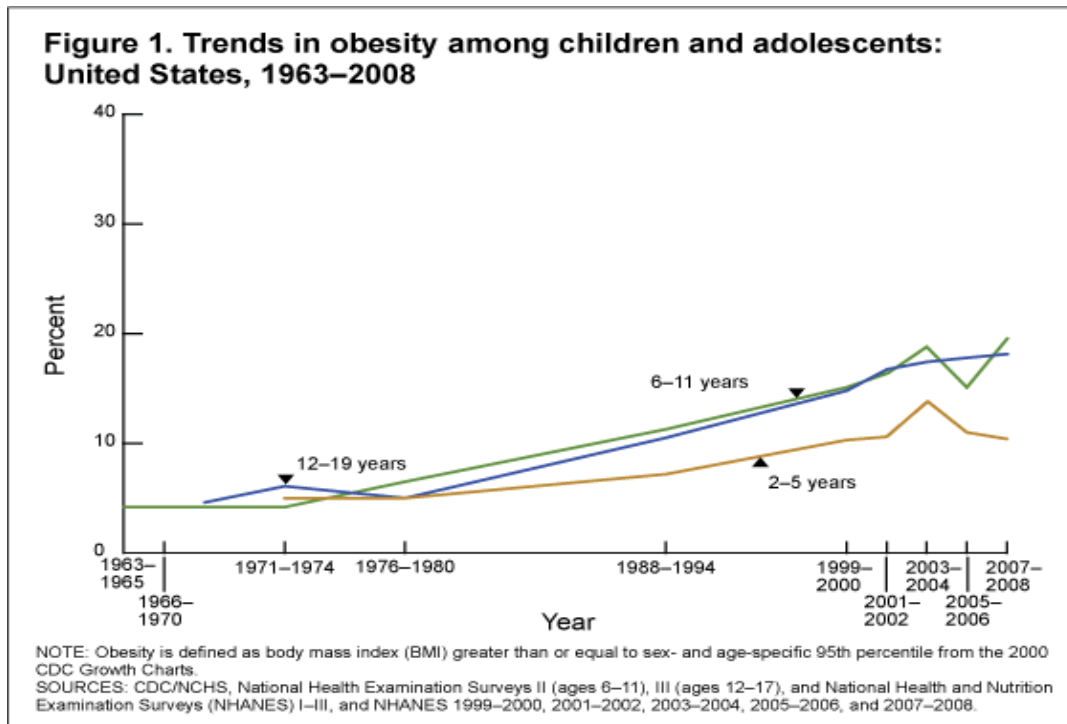
### Lifestyle

Exclusive breast-feeding is recommended in all newborn infants for its nutritional and other beneficial effects. It may also protect against obesity in later life.

### Medications

There are no medications currently approved for the treatment of obesity in children. Orlistat and sibutramine may however be helpful in managing moderate obesity in adolescence. Sibutramine is approved for adolescents older than 16. It works by altering the brain's chemistry and decreasing appetite. Orlistat is approved for adolescents older than 12. It works by preventing the absorption of fat in the intestines.

## Epidemiology



Prevalence of overweight among children 2 to 19 years in the USA

Rates of childhood obesity have increased greatly between 1980 and 2010. Currently 10% of children worldwide are either overweight or obese.

## **Canada**

The rate of overweight and obesity among Canadian children has decreased dramatically in recent years. In boys, the rate decreased from 11% in 1980s to 3% in 1990s.

## **Brazil**

The rate of overweight and obesity in Brazilian children increased from 4% in the 1980s to 14% in the 1990s.

## **United States**

The rate of obesity among children and adolescents in the United States has nearly tripled between the early 1980s and 2000. It has however not changed significantly between 2000 and 2006 with the most recent statistics showing a level just over 17 percent. In 2008, the rate of overweight and obese children in the United States was 32%, and had stopped climbing.

## **Australia**

Since the onset of the 21st Century, Australia has found that childhood obesity has followed trend with the United States. Information garnered has concluded that the increase has occurred in the lower socioeconomic areas where poor nutritional education has been blamed.

## **India**

Childhood Obesity is a Silent epidemic shaping in India, which has characteristically been seen in the upper socio economic strata of the society.

## **Research**

A study of 1800 children aged 2 to 12 in Colac, Australia tested a program of restricted diet (no carbonated drinks or sweets) and increased exercise. Interim results included a 68% increase in after school activity programs, 21% reduction in television viewing, and an average of 1 kg weight reduction compared to a control group.

A survey carried out by the American Obesity Association into parental attitudes towards their children's weight showed the majority of parents think that recess should not be reduced or replaced. Almost 30% said that they were concerned with their child's weight. 35% of parents thought that their child's school was not teaching them enough about childhood obesity, and over 5% thought that childhood obesity was the greatest risk to their child's long term health.

A Northwestern University study indicates that inadequate sleep has a negative impact on a child's performance in school, their emotional and social welfare, and increases their risk of being overweight. This study was the first nationally represented, longitudinal investigation of the correlation between sleep, Body Mass Index (BMI) and overweight status in children between the ages of 3 and 18. The study found that an extra hour of sleep lowered the children's risk of being overweight from 36% to 30%, while it lessened older children's risk from 34% to 30%.

## Chapter 9

# Obesity-Associated Morbidity



Gynecomastia as seen in an obese male

Whether obesity should be considered a disease on its own, it is also an important risk factor for many chronic physical and mental illnesses.

### ***Cardiology***

#### **Ischemic heart disease**

Obesity is associated with cardiovascular diseases including angina and myocardial infarction. A 2002 report concluded that 21% of ischemic heart disease is due to obesity while a 2008 European consensus puts the number at 35%.

## **Congestive heart failure**

Having a BMI of greater than 30 increases ones risk of heart failure by two.

## **High blood pressure**

More than 85% of hypertension occurs in people with a BMI of greater than 25. The risk of hypertension is 5 times higher in the obese as compared to those of normal weight. A definitive link between obesity and hypertension has been found using animal and clinical studies, from these it has been realized that many mechanisms are potential causes of obesity induced hypertension. These mechanisms include the activation of the sympathetic nervous system as well as the activation of the renin–angiotensin-aldosterone system.

## **Abnormal cholesterol levels**

Obesity is associated with an increased LDL cholesterol and a lowered HDL cholesterol.

## **Deep vein thrombosis and Pulmonary embolism**

Obesity increases one's risk of venous thromboembolism by 2.3 fold.

## ***Dermatology***



Stretch marks on the abdomen

- stretch marks
- acanthosis nigricans
- lymphedema
- cellulitis
- hirsutism
- intertrigo

## ***Endocrinology and reproductive medicine***

### **Diabetes mellitus**

One of the strongest links between obesity and disease is that with type 2 diabetes. These two conditions are so strongly linked that researchers in the 1970s started calling it “diabesity”. Excess weight is behind 64% of cases of diabetes in men and 77% of cases in women.

### **Polycystic ovarian syndrome (PCOS)**

Due to its association with insulin resistance, the risk of PCOS increases with adiposity. In the US approximately 60% of patients with PCOS have a BMI of greater than 30.

### **Menstrual disorders**

#### **Infertility**

Obesity leads to infertility in both men and women. This is primarily due to excess estrogen interfering with normal ovulation in women and altering spermatogenesis in men. It is believed to cause 6% of primary infertility.

### **Complications of pregnancy**

Obesity is related to many complications in pregnancy including: haemorrhage, infection, increased hospital stays for the mother, and increased NICU requirements for the infant. Obese women have more than twice the rate of C-sections compared to women of normal weight. Obese women also have increased risk of preterm births and low birth weight infants.

### **Birth defects**

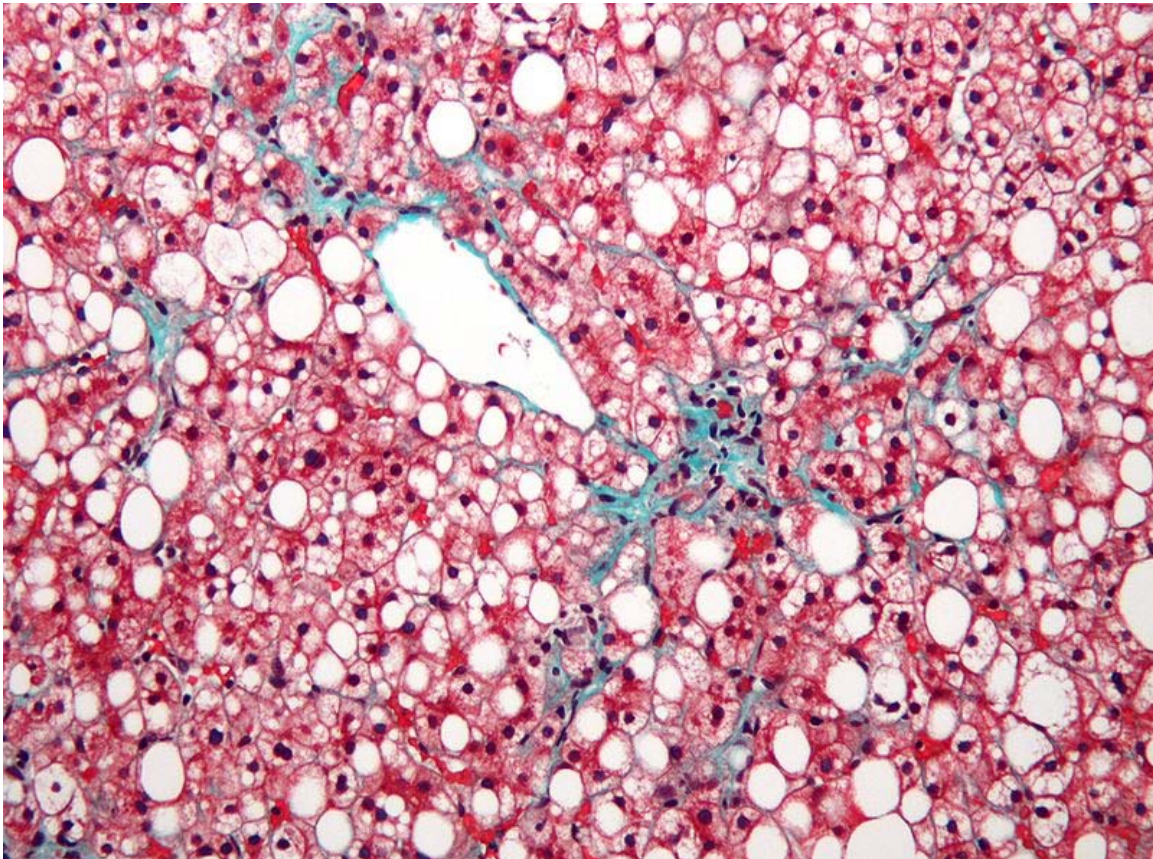
Those who are obese during pregnancy have a greater risk of have a child with a number of congenital malformations including: neural tube defects such as anencephaly and spina bifida, cardiovascular anomalies, including septal anomalies, cleft lip and palate, anorectal malformation, limb reduction anomalies, and hydrocephaly.

## ***Gastrointestinal***

### **Gastroesophageal reflux disease**

Several studies have show that the frequency and severity of GERD symptoms are higher in those who are obese.

### **Fatty liver disease**



Non-alcoholic fatty liver disease

## ***Neurology***

### **Stroke**

Ischemic stroke is increased in both men and women who are obese. For women with BMI of greater than 30 their risk of ischemic stroke was 1.7 times greater. While men with a BMI of greater than 30 had a risk of stroke 2.0 times greater.

### **Dementia**

Those who are obese have a rate of dementia 1.4 times greater than those of normal weight.

## Multiple sclerosis

Women that are obese at age 18 have a greater than twofold increased risk of MS.

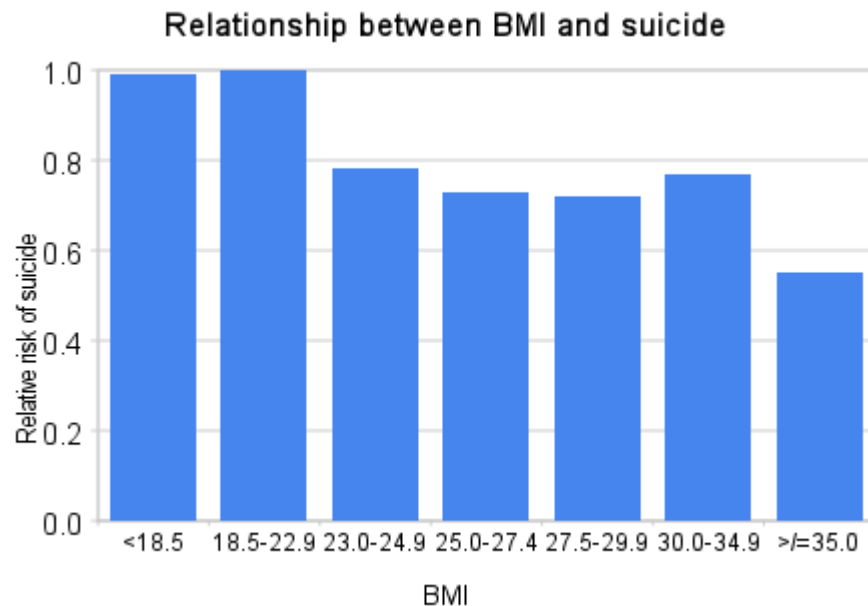
## Oncology

Many cancers occur at increased frequency in those who are overweight or obese. A study from the United Kingdom found that approximately 5% of cancer is due to excess weight. These cancers include:

- breast, ovarian
- esophageal, colorectal
- liver, pancreatic
- gallbladder, stomach
- endometrial, cervical
- prostate, kidney
- non-Hodgkin's lymphoma, multiple myeloma

## Psychiatry

### Depression



Risk of suicide decreases with increased body mass index in the United States

Obesity has been associated with depression. The relationship is strongest in those who are more severely obese, those who are younger, and in women. Suicide rate however decreases with increased BMI.

## **Social stigmatization**

In the United States young women who are overweight complete 0.3 year less school, are 20% less likely to get married, and make \$6,710 less than their normal weight counterparts.

## **Respirology**

### **Obesity hypoventilation syndrome**



CPAP machine commonly used in OHS

Obesity hypoventilation syndrome is defined as the combination of obesity, hypoxia during sleep, and hypercapnia during the day, resulting from hypoventilation. Based on its definition it occurs only in the obese.

### **Chronic lung disease**

Obesity is associated with a number of chronic lung diseases including: Asthma and COPD. It is believed that a systemic pro-inflammatory state induced by some causes of obesity may be contributing to airway inflammation and thus leading to asthma.

## ***Rheumatology and Orthopedics***

### **Gout**

Compared to men with a BMI of 21 - 23, men with a BMI of 30 - 35 have 2.3 times more gout and men with a BMI of greater than 35 have 3.0 times more gout. Weight loss decreases these risks.

### **Poor mobility**

There is a strong association between obesity and musculoskeletal pain and disability

### **Osteoarthritis**

Increased rates of arthritis are seen in both weight bearing and non weight bearing joint. Those with a BMI greater than 26.4 had rate of osteoarthritis of the knees 6 times greater than those with a BMI of less than 23.4, well rates of osteoarthritis in the hand was about 1.5 times greater.

### **Low back pain**

Obese individuals are twice to four times more likely to have lower back pain than their normal weight peers.

## ***Urology and Nephrology***

### **Erectile dysfunction**

One third of obese men with erectile dysfunction who lose weight have improvement in their sexual functioning.

### **Urinary incontinence**

Urge, stress, and mixed incontinence all occur at higher rates in the obese. The rates are about double that found in the normal weight population. Urinary incontinence improves with weight lose.

### **Chronic renal failure**

Obesity increases ones risk of renal failure by three to four times.

## Chapter 10

# Parental Obesity

**Maternal obesity** refers to obesity (often including being overweight) of a woman during pregnancy. **Parental obesity** refers to obesity of either parent during pregnancy.

Maternal obesity has a significant impact on maternal metabolism and offspring development. Insulin resistance, glucose homeostasis, fat oxidation and amino acid synthesis are all disrupted by maternal obesity and contribute to adverse outcomes. Modification of lifestyle is an effective intervention strategy for improvement of maternal metabolism and the prevention of adverse outcomes.

Obesity is defined as having a Body Mass Index (BMI) of 30 or greater. A 5-foot-5-inch tall woman would be considered obese if she weighs 180 pounds or more and a 5-foot-8-inch tall woman would be considered obese if she weighs 200 pounds or more.

### ***Effects on the fetus***

#### **Defects/ impairments**

Between 18 and 38% of pregnant women of American women are classified as obese. However, little is known about the link between maternal obesity and diabetic effects in offspring. Maternal obesity is associated with increased odds of pregnancies affected by congenital anomalies, including neural tube defects and spina bifida. The chances of having neural tube defects in the newborn of an obese woman has been shown to be twice that of a non-obese pregnant female. Some other anomalies that were increased among mothers with obesity included septal anomalies, cleft palate, cleft lip and palate, anorectal atresia, hydrocephaly, and limb reduction anomalies. Babies are also more likely to be admitted to neonatal intensive care units because of affects from the obese mother. Each year, nearly 2,500 babies are born with these defects, and many other affected pregnancies end in miscarriage and stillbirth.

#### **Mental or physical affects on the fetus**

Maternal obesity is linked with elective preterm delivery, neonatal death, and delivery of an extremely low birth weight infant. In follow-up studies of babies whose birth weights were below 1000g, it was shown that 40% to 45% of the survivors had severe neurodevelopmental impairments.

It has been demonstrated through a study on rats that when a pregnant mother ate a diet rich in fat, sugar, and salt, that mother's offspring was more likely to overeat and have a preference for junk food. Even when the offspring were not given the option of junk food, their bodies metabolized food differently than offspring whose mother ate healthier. Offspring of mothers who ate badly had higher levels of cholesterol and triglycerides in their bloodstream and higher risk of heart disease. In addition, these offspring had higher levels of glucose and insulin, which indicate development of type 2 diabetes. The rats were studied through adulthood and were found to be fatter than the offspring whose mothers ate healthier. This study showed that the diet of mothers not only effects the offspring's chemical physiology but also their likelihood of becoming even more unhealthy through their natural preference to bad habits.

### **Paternal obesity effects on the fetus**

Researchers from the NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducted a study and found that early-onset paternal obesity is connected with an increased risk of liver disease in their kin. Researchers found that obese fathers had an elevated level of serum alanine aminotransferase (ALT), a liver enzyme, compared to fathers who were not obese. They did a secondary analysis that excluded obese offspring. Children who were a normal weight but had obese fathers still had elevated ALT levels, which indicated that a child's ALT levels are not dependent upon the child's own BMI.

### ***Obesity effects on the mother***

#### **Disease**

Obese women have an increased risk of pregnancy-related complications, including hypertension, gestational diabetes, and blood clots. Maternal obesity is also known to be associated with increased rates of complications in late pregnancy such as cesarean delivery, and shoulder dystocia. In addition, morbidly obese women who have not had children before are at increased risk of all-cause preterm deliveries. It is well recognized that obese women are at increased risk of preeclampsia and that women who have never been pregnant are at higher risk of preeclampsia than women who have had children in the past.

### **Effects of negative diets**

Poor glycemic control can lead to neural tube defects. The usual increase in insulin resistance seen in late pregnancy is enhanced in obese mothers, causing an postprandial increase in glucose, lipids, and amino acids, as well as excessive fetal exposure to fuel sources. This, in turn, increases fetal size, fat storage, and potential risk for disease. For mothers, impaired glucose tolerance and hyperlipidemia are more common among obese mothers.

## ***Modifying the risks***

There are many options available in treating obesity, such as: altering one's diet and exercising regularly. Moderate forms of exercise, such as walking, can lead to healthy weight loss. Some people who are obese turn to gastric bypass surgery in order to reduce their appetites. It is always advised to consult a physician regarding any obesity treatment.

It is recommended that obese women should try to lose weight before becoming pregnant, yet women should not diet during pregnancy because sufficient nutrition is important for pregnant women and women planning pregnancy. Women with gastric banding can have normal pregnancies and better outcomes than women who do not have the surgery, but in most cases, doctors have agreed that pregnancy should wait until surgery-related weight loss has stabilized. Clinicians have been encouraged to talk to women who are pregnant or may become pregnant about getting enough folic acid, quitting smoking, and avoiding alcohol. Women are also recommended to have appropriate calorie intake and exercise adequately.

## ***Nutrition recommendations***

Nutrition in pregnancy includes avoiding foods that are high in saturated or trans fats or that are high in sugar, such as potato chips and other processed foods. Enhance your diet with whole grains, vegetables, fruits and lean proteins. Foods that contain factors such as choline, folic acid, and omega-3 fatty acids are important for the proper development of the fetus. Foods such as soybeans, grape juice, and cabbage are a high source of choline; eggs, yeast, mushrooms, citrus fruits, green vegetables, milk, chicken, tuna, and salmon contain folic acid. Omega-3 fatty acids can be found in flaxseed oil, cottage cheese, or yogurt. Vitamin D can be obtained from food sources or by adequate exposure to natural sunlight.

Pregnant women that ate more sweets, such as candy and processed juices, in early pregnancy were at higher risk of gaining excessive weight. A healthy, well-balanced diet during pregnancy can also help to minimize some pregnancy symptoms such as nausea and constipation.

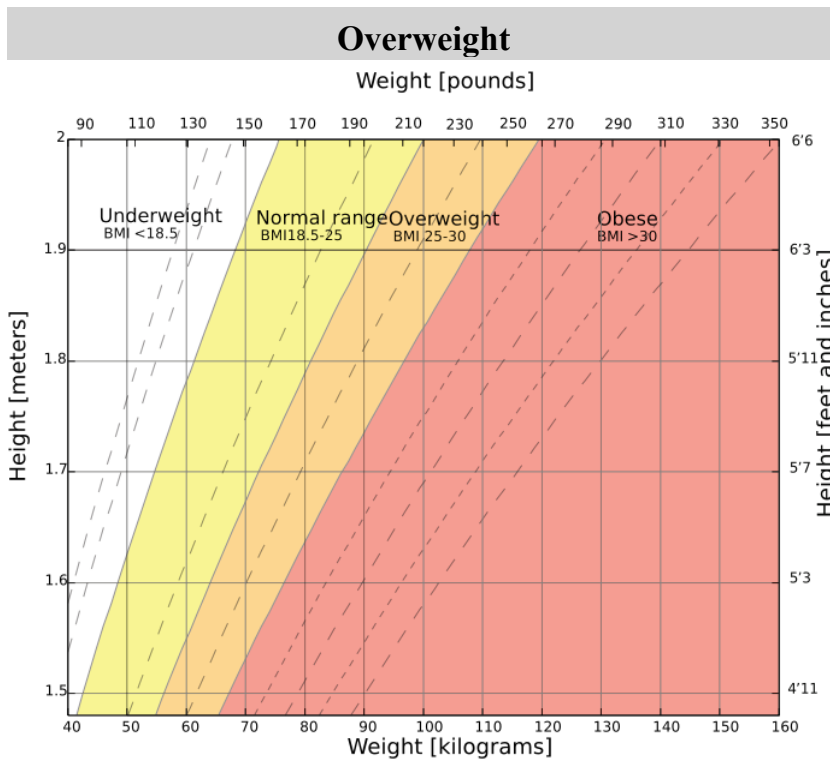
## ***Exercise recommendations***

During pregnancy, doctors recommend light exercise. Doctors state that exercise can help the comfort of the mother and the well-being of the unborn child. Some benefits include, but are not limited to: reduced back pain, decrease in constipation, less likely to gain excess weight, decreased chance of gestational diabetes, easier labor, quicker recovery, and better physical and emotional health of the baby.

If negative signs and symptoms occur after exercising, pregnant females should stop immediately. Some signs include: dizziness, faintness, headache, shortness of breath, uterine contractions, vaginal bleeding, fluid leaking, or heart palpitations.

# Chapter 11

# Overweight



The overweight range according to the Body Mass Index (BMI) is the area on the chart where BMI > 25.

**ICD-10** E66.

**ICD-9** 278.02

**MeSH** D050177

**Overweight** is generally defined as having more body fat than is optimally healthy. Being overweight is a common condition, especially where food supplies are plentiful and lifestyles are sedentary. As much as 64% of the United States adult population is considered either overweight or obese, and this percentage has increased over the last four decades.

Excess weight has reached epidemic proportions globally, with more than 1 billion adults being either overweight or obese. Increases have been observed across all age groups.

A healthy body requires a minimum amount of fat for the proper functioning of the hormonal, reproductive, and immune systems, as thermal insulation, as shock absorption for sensitive areas, and as energy for future use. But the accumulation of too much storage fat can impair movement and flexibility, and can alter the appearance of the body.

## ***Classification***

The degree to which a person is overweight is generally described by body mass index (BMI). Overweight is defined as a BMI of 25 or more, thus it includes pre-obesity defined as a BMI between 25 and 30 and obesity as defined by a BMI of 30 or more. Pre obese and overweight however are often used interchangeably thus giving overweight a common definition of a BMI of between 25 -30. There are however several other common ways to measure the amount of adiposity or fat present in an individual's body.

- Body mass index

The body mass index (BMI) is a measure of a person's weight taking into account their height. It is given by the formula: BMI equals a person's weight (mass) in kilograms divided by the square of the person's height in metres. The units therefore are  $\text{kg/m}^2$  but BMI measures are typically used and written without units.

BMI provides a significantly more accurate representation of body fat content than simply measuring a person's weight. It is only moderately correlated with both body fat percentage and body fat mass ( $R^2$  of 0.68.) It does not take into account certain factors such as pregnancy or bodybuilding; however, the BMI is an accurate reflection of fat percentage in the majority of the adult population.

- Body volume index

The body volume index (BVI) was devised in 2000 as a computer, rather than manual, measurement of the human body for obesity and an alternative to the BMI

Body volume index uses 3D software to create an accurate 3D image of a person so BVI can differentiate between people with the same BMI rating, but who have a different shape and different weight distribution.



An obese man on a motorcycle



### Childhood obesity

BVI measures where a person's weight and the fat are located on the body, rather than total weight or total fat content and places emphasis on the weight carried around the abdomen, commonly known as central obesity. There has been an acceptance in recent years that abdominal fat and weight around the abdomen constitute a greater health risk.

- Simple weighing

The person's weight is measured and compared to an estimated ideal weight. This is the easiest and most common method, but by far the least accurate, as it only

measures one quantity (weight) and often does not take into account many factors such as height, body type, and relative amount of muscle mass.

- Skinfold calipers or "pinch test"

The skin at several specific points on the body is pinched and the thickness of the resulting fold is measured. This measures the thickness of the layers of fat located under the skin, from which a general measurement of total amount of fat in the body is calculated. This method can be reasonably accurate for many people, but it does assume particular patterns for fat distribution over the body which may not apply to all individuals, and does not account for fat deposits which may not be directly under the skin. Also, as the measurement and analysis generally involves a high degree of practice and interpretation, for an accurate result it must be performed by a professional and cannot generally be done by patients themselves.

- Bioelectrical impedance analysis

A small electrical current is passed through the body to measure its electrical resistance. As fat and muscle conduct electricity differently, this method can provide a direct measurement of the body fat percentage, in relation to muscle mass. In the past, this technique could only be performed reliably by trained professionals with specialized equipment, but it is now possible to buy home testing kits which allow people to do this themselves with a minimum of training. Despite the improved simplicity of this process over the years, however, there are a number of factors which can affect the results, including hydration and body temperature, so it still needs some care when taking the test to ensure that the results are accurate.

- Hydrostatic weighing

Considered one of the more accurate methods of measuring body fat, this technique involves complete submersion of a person in water, with special equipment to measure the person's weight while submerged. This weight is then compared with "dry weight" as recorded outside the water to determine overall body density. As fat is less dense than muscle, careful application of this technique can provide a reasonably close estimate of fat content in the body. This technique does, however, require expensive specialized equipment and trained professionals to administer it properly.

- Dual energy X-ray absorptiometry (DEXA)

Originally developed to measure bone density, DEXA imaging has also come to be used as a precise way to determine body fat content by using the density of various body tissues to identify which portions of the body are fat. This test is generally considered to be very accurate, but requires a great deal of expensive medical equipment and trained professionals to perform.

The most common method for discussing this subject and the one used primarily by researchers and advisory institutions is BMI. Definitions of what is considered to be overweight vary by ethnicity. The current definition proposed by the US National Institutes of Health (NIH) and the World Health Organization (WHO) designates whites, Hispanics and blacks with a BMI of 25 or more as overweight. For Asians, overweight is a BMI between 23 and 29.9 and obesity for all groups is a BMI of 30 or more.

BMI, however, does not account extremes of muscle mass, some rare genetic factors, the very young, and a few other individual variations. Thus it is possible for an individuals with a BMI of less than 25 to have excess body fat, while others may have a BMI that is significantly higher without falling into this category. Some of the above methods for determining body fat are more accurate than BMI but come with added complexity.

If an individual is overweight and has excess body fat it could, but won't always, create or lead to health risks. Reports are surfacing, however, that being mildly overweight to slightly obese – BMI being between 24 and 31.9 – may be actually beneficial and that people with BMI between 24 and 31.9 could actually live longer than normal weight or underweight persons.

### ***Health-related implications***



Animals can suffer from obesity as well. This German Shepherd dog is noticeably overweight.

While the negative health outcomes associated with obesity are accepted within the medical community, the health implications of the overweight category are more controversial. The generally accepted view is that being overweight causes similar health problems to obesity, but to a lesser degree. Adams et al. estimated that the risk of death increases by 20 to 40 percent among overweight people, and the Framingham heart study found that being overweight at age 40 reduced life expectancy by three years.

Flegal et al., however, found that the mortality rate for individuals who are classified as overweight (BMI 25 to 30) may actually be lower than for those with an "ideal" weight (BMI 18.5 to 25).

Being overweight has been identified as a cause of cancer, and is projected to overtake smoking as the primary cause of cancer in developed countries as cases of cancer linked to smoking dwindle.

Psychological well-being is also at risk in the overweight individual due to social discrimination. However, children under the age of eight are normally not affected.

Being overweight does not increase mortality in older people.

## **Causes**

Being overweight is generally caused by the intake of more calories (by eating) than are expended by the body (by exercise and everyday living). Factors which may contribute to this imbalance include:

- Alcoholism
- Eating disorders (such as binge eating)
- Genetic predisposition
- Hormonal imbalances (e.g. hypothyroidism)
- Insufficient or poor-quality sleep
- Limited physical exercise and sedentary lifestyle
- Poor nutrition
- Metabolic disorders, which could be caused by repeated attempts to lose weight by weight cycling
- Overeating
- Psychotropic medication (e.g. olanzapine)
- Smoking cessation and other stimulant withdrawal
- Stress

People who have insulin dependant diabetes and chronically overdose insulin may gain weight, while people who already are overweight may develop insulin tolerance, and in the long run type II diabetes.

## ***Treatment***

A large number of people undergo some form of treatment to attempt to reduce their weight, usually either in an attempt to improve their health, to improve their lifestyle, or for cosmetic reasons. The generally recommended treatment for being overweight is a modified or controlled diet in conjunction with increased physical exercise. For those who are obese rather than overweight, more intensive therapies such as anti-obesity drugs and/or bariatric surgery are sometimes used.

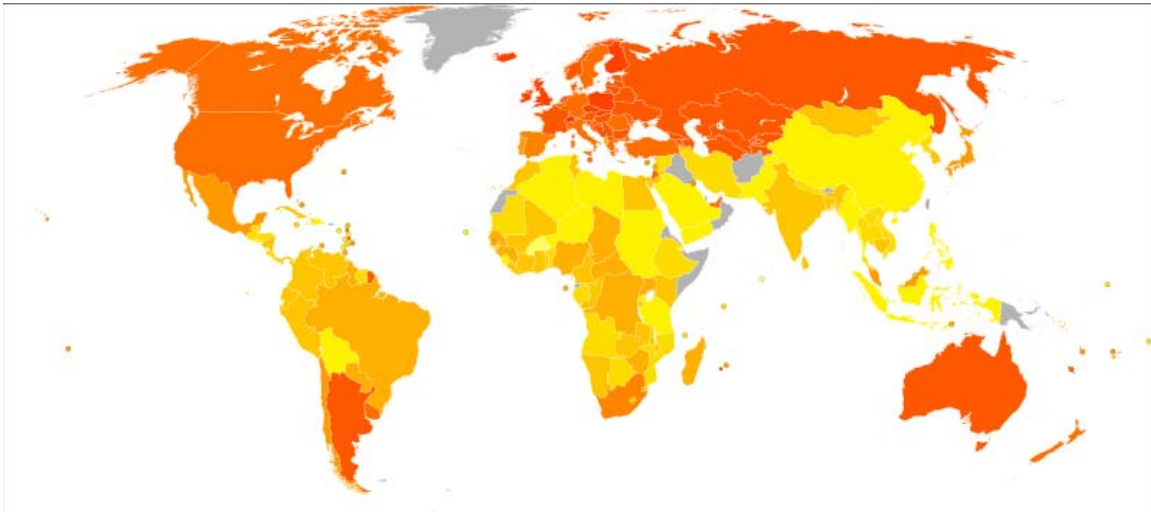
Recent evidence indicates that the spice turmeric may help prevent growth of new fat tissue without making other changes to the diet. The evidence is based on studies with mice. Researchers next will attempt studies in humans.

Studies suggest that reducing calorie intake by itself (dieting) may have short-term effects but does not lead to long-term weight loss, and can often result in gaining back all of the lost weight and more in the longer term. For this reason, it is generally recommended that weight-loss diets not be attempted on their own but instead in combination with increased exercise and long-term planning and weight management.

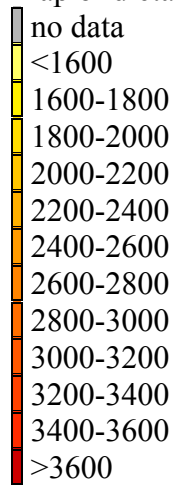
The health benefits of weight loss are also somewhat unclear. While it is generally accepted that for significantly obese patients, losing weight can reduce health risks and improve quality of life, there is some evidence to suggest that for merely overweight patients, the health effects of attempting to lose weight may actually be more detrimental than simply remaining overweight. Moreover, for all individuals, repeatedly losing weight and then gaining it back ("weight cycling" or "yo-yo dieting"), is believed to do more harm than good and can be the cause of significant additional health problems. This is caused by the loss of more muscle than fat.

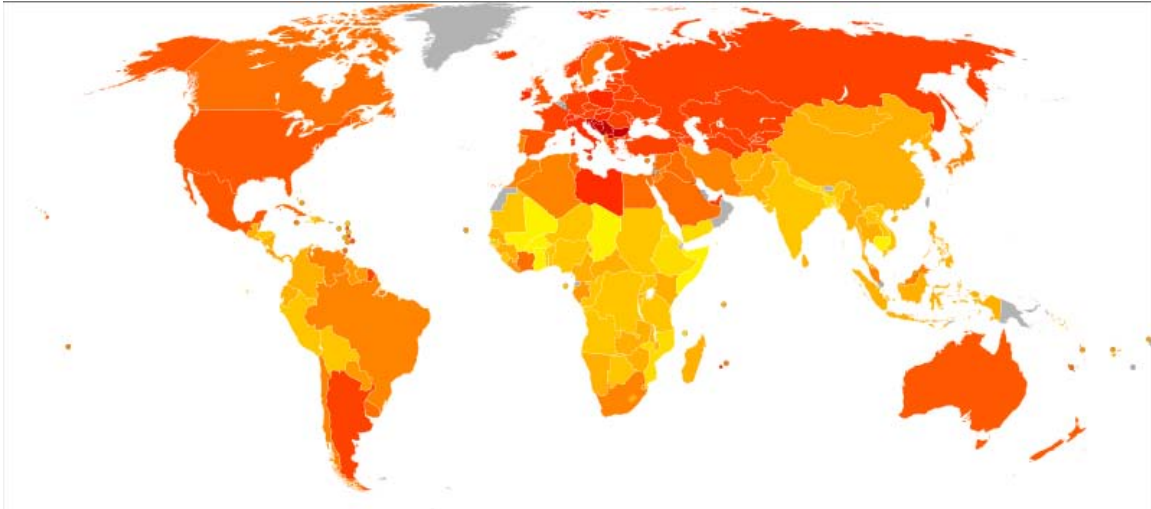
## Chapter 12

# Diet and Obesity

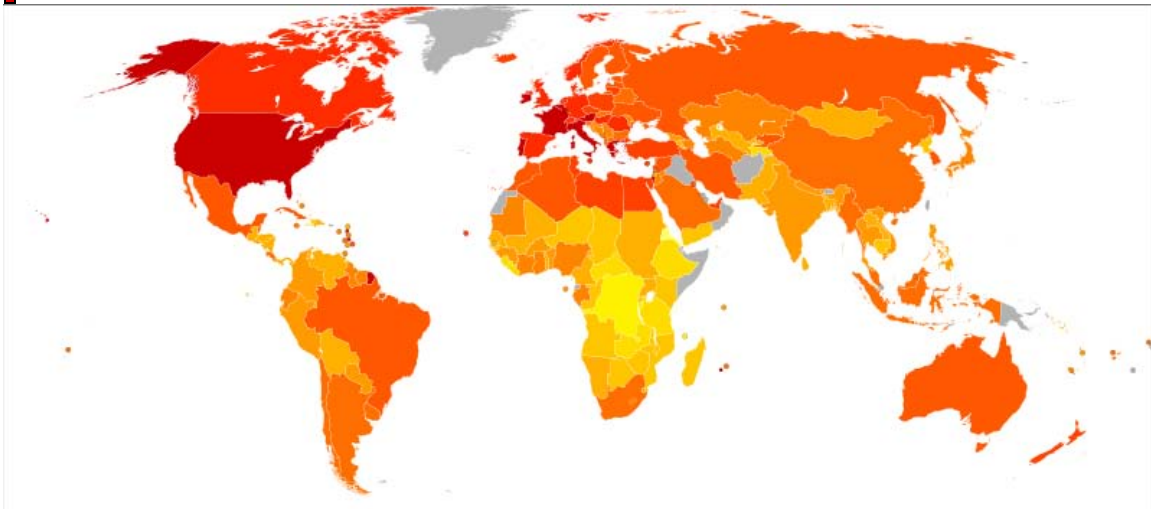
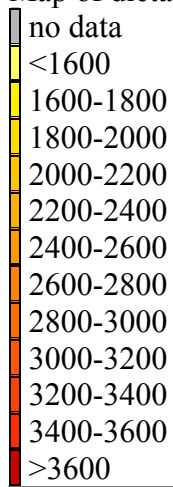


Map of dietary energy availability per person per day in 1961 (kcal/person/day).

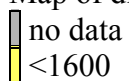


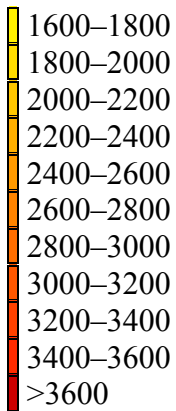


Map of dietary energy availability per person per day in 1979-1981 (kcal/person/day).



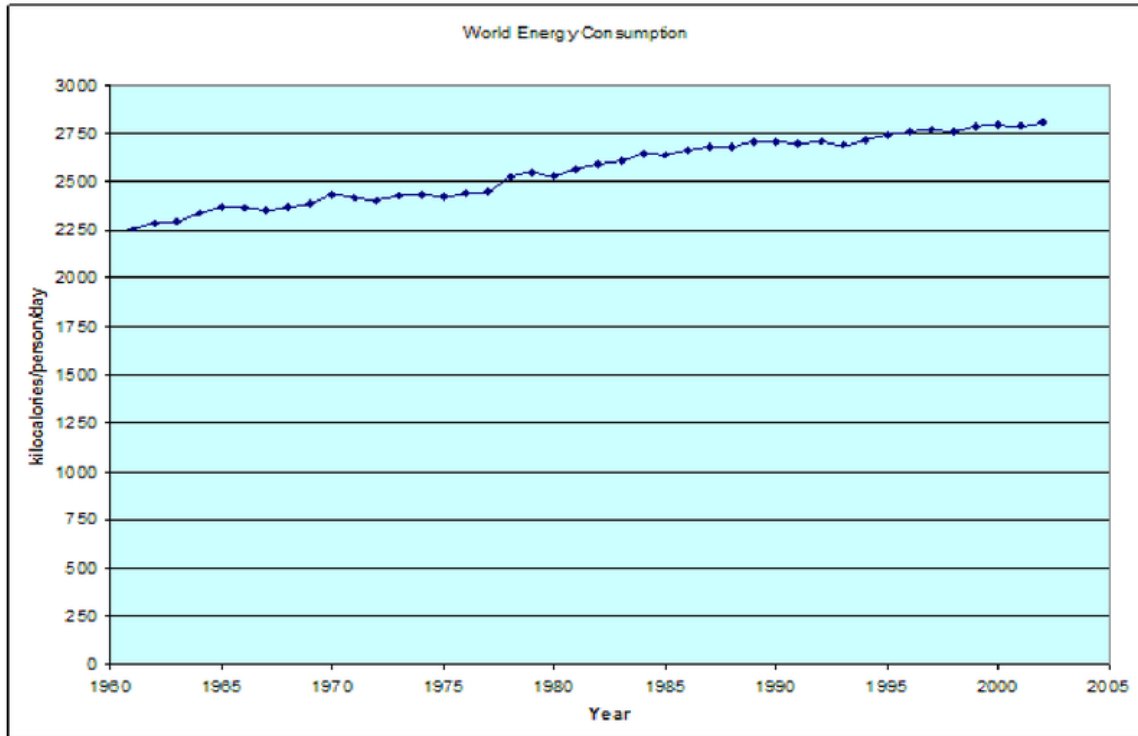
Map of dietary energy availability per person per day in 2001-2003 (kcal/person/day).





Diet plays an important role in the genesis of obesity. Personal choices, advertising, social customs and cultural influences, as well as food availability and pricing all play a role in determining what and how much we eat.

### ***Dietary energy supply***



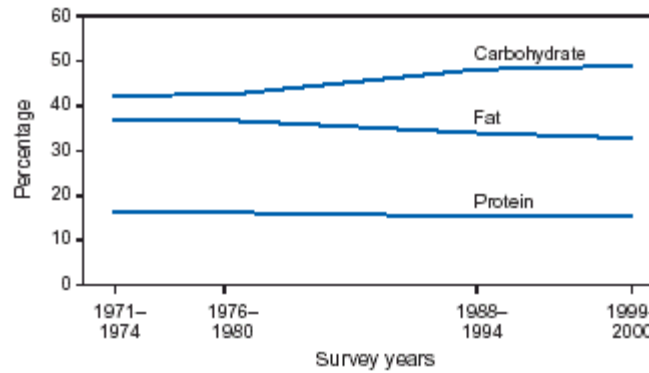
Average per capita energy consumption of the world from 1961 to 2002

The dietary energy supply is the food available for human consumption, usually expressed in kilocalories per person per day. It gives an overestimate of the total amount of food consumed as it reflects both food consumed and food wasted. The per capita dietary energy supply varies markedly between different regions and countries. It has also changed significantly over time. From the early 1970s to the late 1990s, the average calories available per person per day (the amount of food bought) has increased in all part

of the world except Eastern Europe and parts of Africa. The United States had the highest availability with 3654 calories per person in 1996. This increased further in 2002 to 3770. During the late 1990s, Europeans had 3394 calories per person, in the developing areas of Asia there were 2648 calories per person, and in sub-Saharan Africa people had 2176 calories per person.

### **Average calorie consumption**

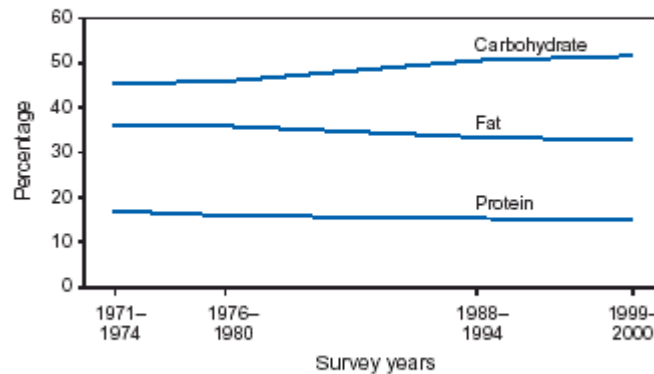
FIGURE 1. Percentage of kilocalories from macronutrient intake among men aged 20–74 years\*, by survey years — National Health and Nutrition Examination Surveys (NHANES), United States, 1971–2000



\*Age adjusted by direct standardization to the 2000 U.S. Census population by using age groups 20–39, 40–59, and 60–74 years.

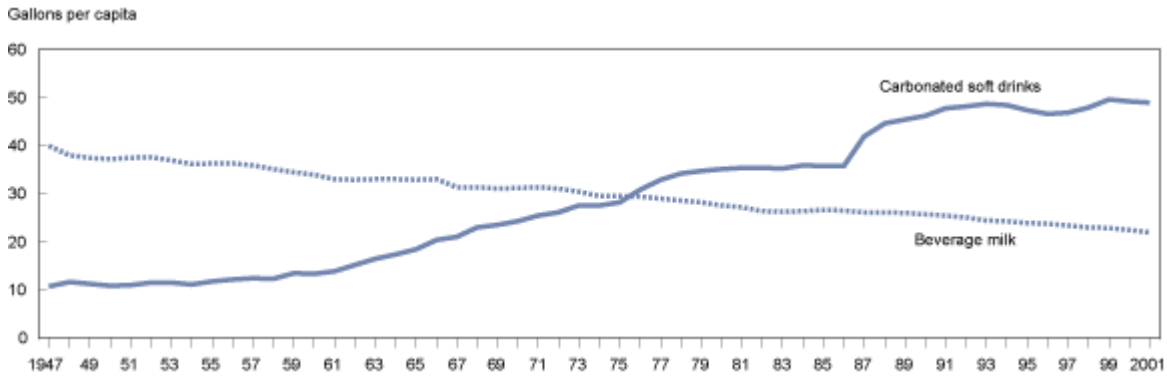
Change over time of the macronutrient composition of the US male diet

FIGURE 2. Percentage of kilocalories from macronutrient intake among women aged 20–74 years\*, by survey years — National Health and Nutrition Examination Surveys (NHANES), United States, 1971–2000



\*Age adjusted by direct standardization to the 2000 U.S. Census population by using age groups 20–39, 40–59, and 60–74 years.

Change over time of the macronutrient composition of the US female diet



USDA chart showing the increase in soda consumption and the decrease in milk consumption from 1947 to 2001.

In the period 1971 – 2004, the average number of calories which women consumed in the United States increase by 335 calories per day (1542 calories in 1971 and 1877 calories in 2004). For men the average increase was 168 calories per day (2450 calories in 1971 and 2618 calories in 2004). Most of these extra calories came from an increase in carbohydrate consumption rather than an increase in fat consumption. The primary sources of these extra carbohydrates were sweetened beverages, which now accounts for almost 25 percent of daily calories in young adults in America. As these estimates are based on a person's recall, they may underestimate the amount of calories actually consumed.

### ***Fast food***

As societies become increasingly reliant on energy-dense fast-food meals, the association between fast food consumption and obesity becomes more concerning. In the United States consumption of fast food meal has tripled and calorie intake from fast food has quadrupled between 1977 and 1995. Consumption of sweetened drinks is also believed to be a major contributor to the rising rates of obesity.

### ***Portion size***



A comparison of a typical cheeseburger 20 years ago (left) which had 333 calories with a modern cheeseburger (right) which contains 590 calories as per the National Heart, Lung, and Blood Institute

The portion size of many prepackage and restaurant foods have increased in both the United States and Denmark since the 1970s. Fast food serving for example 2 to 5 times larger than they were in the 1980s. Evidence has shown that larger portions of energy-dense foods lead to greater energy intake and thus to greater rates of obesity.

### ***Social policy and change***

Agricultural policy and techniques in the United States and Europe have led to lower food prices. In the United States, subsidization of corn, soy, wheat, and rice through the U.S. farm bill has made the main sources of processed food cheap compared to fruits and vegetables.

### ***Metabolism***

Evidence does not support the commonly expressed view that some obese people eat little yet gain weight due to a slow metabolism. On average obese people have a greater energy expenditure than normal weight or thin people. This is because it takes more energy to maintain an increased body mass. Obese people also underreport how much food they consume compared to those of normal weight. Tests of human subjects carried out in a calorimeter support this conclusion.

## Chapter 13

# Sedentary Lifestyle



Increases in sedentary behaviors such as watching television are characteristic of a sedentary lifestyle



A typical couch potato

**Sedentary lifestyle** is a medical term used to denote a type of lifestyle with no or irregular physical activity. A person who lives a sedentary lifestyle may colloquially be known as a **couch potato**. It is commonly found in both the developed and developing world. Sedentary activities include sitting, reading, watching television and computer use for much of the day with little or no vigorous physical exercise. A sedentary lifestyle can contribute to many preventable causes of death.

### ***Health effects***

A lack of physical activity is one of the leading causes of preventable death worldwide.

A sedentary lifestyle and lack of physical activity can contribute to or be a risk factor for:

- Anxiety
- Cardiovascular disease
- Mortality in elderly men by 30% and double the risk in elderly women
- Depression
- Diabetes
- Colon cancer
- High blood pressure

- Obesity
- Osteoporosis
- Lipid disorders
- Kidney Stones

## **Solutions**

One response that has been adopted by many organizations concerned with health and environment is the promotion of active travel, which seeks to promote walking and cycling as safe and attractive alternatives to motorized transport. Given that many journeys are for relatively short distances, there is considerable scope to replace car use with walking or cycling, though in many settings this may require some infrastructure modification.

## **History**

It is characterized by sitting or remaining inactive for most of the day with little or no exercise.

### **Historical Trend:**

Scavenging, to subsistence, to savannas, to sedentism, to steak houses, to supersizing, to *Dancing With The Stars*. That sums up a good portion of the last few million years of Western human roots. For millions of years, human types moved their bodies in meaningful ways. They were active all those years and then, over a few decades starting shortly after the Second World War, they stopped moving. It was as though a plague descended upon humanity. A plague named addiction. At the same daily calorie intake rose and Westerners increased the consumption of non-nutritive food high in sugar and corn syrup, fat, and salt.

Is a sedentary lifestyle an addiction? If you try to get someone to stop this pattern you will have your answer.

For their own health and happiness, those afflicted with the plague could remind themselves that movement is a wondrous thing and the best recreational activity individuals, friends, and families can do. And it's number one on the wellness checklist. Yes, may even trump diet but it's better not to think that way. Better to just do the right thing with everything. Don't try to do it, there is no value there. The magic is in doing it.

Starting in the 20th century, wellness and medicine have grown into not always profitable gigantic industries, in attempts to deal with (critics say "contribute to") the pandemic of unwell people. As the piles of data and articles deluge the throngs of overburdened and inactive public, an obvious and sensible option emerges. Instead of being consumed by all of this data, people would be better off the couch or desk, engaged in movement.

Lack of exercise causes muscle atrophy, i.e. shrinking and weakening of the muscles and accordingly increases susceptibility to physical injury. Additionally, physical fitness is correlated with immune system function; a reduction in physical fitness is generally accompanied by a weakening of the immune system. A review in Nature Reviews Cardiology suggests that since illness or injury are associated with prolonged periods of enforced rest, such sedentariness has physiologically become linked to life-preserving metabolic and stress related responses such as inflammation that aid recovery during illness and injury but which due to being nonadaptive during health now lead to chronic diseases.

Despite the well-known benefits of physical activity, many adults and many children lead a relatively sedentary lifestyle and are not active enough to achieve these health benefits.

In the 2008 United States American National Health Interview Survey (NHIS) 36% of adults were considered inactive. 59% of adult respondents never participated in vigorous physical activity lasting more than 10 minutes per week.

## Chapter 14

# Exercise Trends

Worldwide there has been a large shift towards less physically demanding work. This has been accompanied by increasing use of mechanized transportation, a greater prevalence of labor saving technology in the home, and less active recreational pursuits. At least 60% of the world's population does not get sufficient exercise. This is true in almost all developed and developing countries, and among children.

These exercise trends are contributing to the rising rates of chronic diseases including: obesity, heart disease, stroke and high cholesterol. Active transport ( walking, bicycling, etc. ) has been found to be inversely related to obesity in Europe, North America, and Australia. Thus exercise has been associated with a decrease in mortality.

### ***Causes of lack of exercise***

One of the causes most prevalent in the developing world is urbanization. As more of the population moves to cities, population over-crowding, increased poverty, increased levels of crime, high-density traffic, low air quality and lack of parks, sidewalks and recreational sports facilities leads to a less active lifestyle.

Physical inactivity is increasing or high among many groups in the population including: young people, women, and the elderly.

A number of factors has been associated with physical inactivity at a population level including: female gender, older age, living with a partner, smoking, little schooling and poverty.

Studies in children and adults have found an association between the number of hours of television watched and the prevalence of obesity. A 2008 meta analysis found that 63 of 73 studies (86%) showed an increased rate of childhood obesity with increased media exposure, and rates increasing proportionally to time spent watching television.

### ***Symptoms***

Noncommunicable diseases, partly due to a lack of exercise, are currently the greatest public health problem in most countries around the world. Each year at least 1.9 million

people die as a result of physical inactivity, which makes inactivity one of the leading preventable causes of death worldwide.

## **Countries**

### **Australia**

Australian children between 1961 and 2002 have had a marked decline in their aerobic fitness.

### **Canada**

Obese people are less active than their normal weight counterparts. In Canada, 27.0% of sedentary men are obese as opposed to 19.6% of active men. Lean people are more fidgety than their obese counterparts; this relationship is maintained even if normal weight people eat more or the obese person loses weight.

National data indicates that only 10% of Canadian youth are meeting the guideline for screen time of less than 2 hours per day. As well, although 2/3 of families live close enough for their children to bike or walk to school, only 1/3 report actually walking to school and 80% report never having cycled to school.

### **Asia and China**

A study from China found urbanization reduces daily energy expenditure by about 300–400 kcal and going to work by car or bus reduced it by a further 200 kcal.

A rapid decline in physical activity has occurred between the 1980s and the 2000s. The decline in physical activity is attributed to increasing technology in the workplace and changing leisure activities. In 1989 65% of Chinese had jobs that required heavy labor. This decreased to 51% in the year 2000.

Among Asian children between 1917 and 2003 little change has been seen in power and speed however endurance has decreased substantially in the last 10–15 years.

### **Denmark**

Between 1986 and 1998 school boys in Denmark have become less fit and more fat. This change was not observed among the girls.

### **Finland**

In Finland leisure-time physical activity has increased, while occupational and commuting physical activity has decreased from 1972 to 2002. Leisure-time physical activity increased from 66% (1972) to 77% (2002) in men and from 49% (1972) to 76% (2002) in women. Physically demanding work decreased from 60% (1972) to 38% (2002)

in men and from 47% (1972) to 25% (2002) in women. Daily commuting activity decreased from 30% (1972) to 10% (2002) in men and from 34% (1972) to 22% (2002) in women.

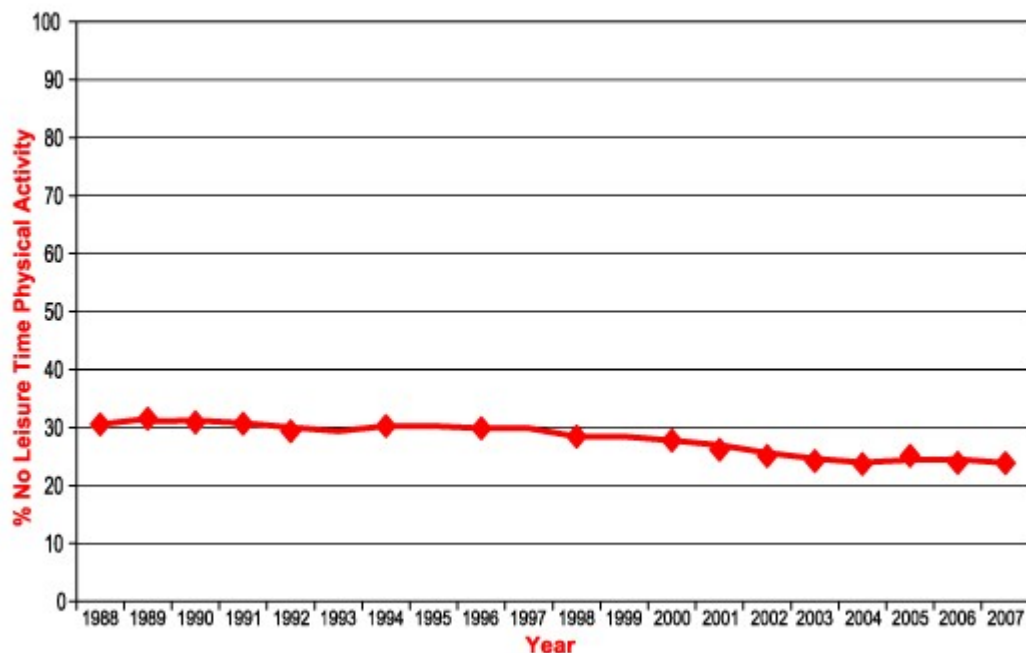
## South America

Over 60% of the population of Brazil, Chile, and Peru do not meet the recommended levels of physical activity needed to maintain health. A study of a southern Brazilian population found that >80% of the population was physically inactive.

## Sweden

A study of Swedish males found a significant decrease in total physical exercise even though recreational exercise has increased. This was due to a decrease in work place exercise and physical exercise in transportation.

## United States



Graph showing the trend in the proportion of the U.S. population which reported no leisure-time physical activity, 1988 - 2007.

Americans have become less physically active overall between 1955 and 2005. While the rate of leisure-time physical activity has not changed significantly there has been a decrease in work-related activity, human powered transportation, activity in the home, and increasing sedentary activity. During 2000 and 2005 the number of adults who were never physically active increased from 9.4% to 10.3% while the number who were engaged in the highest level of physical activity decreased from 18.7% to 16.7%.

Pertaining to leisure-time physical activity, people involved in no activity increased from 38.5% to 40.0% while those who spent most of their day sitting increased from 36.8% to 39.9%.

In 2000 the CDC estimated that more than 40% of the US population was sedentary, another 30% was active but not sufficiently and less than 30% had an adequate level of physical activity. There has been a trend toward decreased physical activity in part due to increasingly mechanized forms of work, changing modes of transportation, and increasing urbanization. Obesity rates have increased in relation to expanding suburbs. This has been attributed to increased time spent commuting, leading to less exercise and less meal preparation at home. Driving one's children to school has become increasingly popular. In the USA the proportion of children who walk or bike to school declined between 1969 (42%) and 2001 (16%) resulting in less exercise.

## **UK**

In England both walking and cycling have declined since 1975 being replaced by motorized transport. The average British citizen in the year 2005 walks 317 km (197 miles) per year, a fall of 106 km (58 miles) since 1975. Similar trends are seen in the United States. In 1983 9% of all trips were on foot. This decreased to 7% in 1990.

## ***Children***

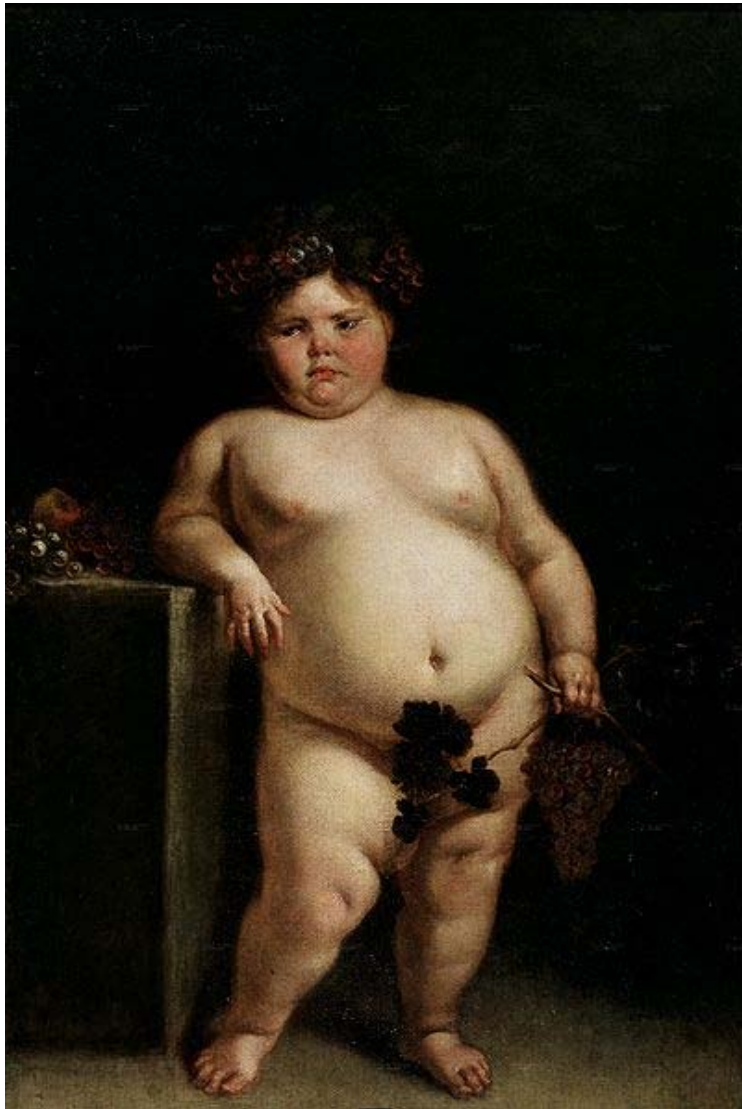
Physical activity among children in activities from self propelled transport, to school physical education, and organized sports is declining in many countries. A 2008 meta analysis found that 63 of 73 studies (86%) showed an increased rate of childhood obesity with increased media exposure, and rates increasing proportionally to time spent watching television.

## ***Public health measure***

Many measures have been attempted to address low levels of physical activity. Some of these include: Walking bus, Riding school bus, Mall walking, and Girls on the Run.

## Chapter 15

# Genetics of Obesity



A 1680 painting by Juan Carreno de Miranda of a girl presumed to have Prader-Willi syndrome

Like many other medical conditions, obesity is the result of an interplay between genetic and environmental factors. Polymorphisms in various genes controlling appetite and metabolism predispose to obesity when sufficient calories are present. The percentage of obesity that can be attributed to genetics varies depending on the population examined from 6% to 85%. As of 2006 more than 41 of these sites have been linked to the development of obesity when a favorable environment is present.

## Genes

Although genetic deficiencies are currently considered rare, variations in these genes may predispose to common obesity. Many candidate genes are highly expressed in the central nervous system.

Several additional loci have been identified. Also, several quantitative trait loci for BMI have been identified.

Confirmed and hypothesized associations include:

Condition	OMIM	Locus	Notes
leptin deficiency	164160	7q31.3	
leptin receptor deficiency	601007	1p31	
prohormone convertase-1 deficiency	600955	5q15-q21	
proopiomelanocortin deficiency	609734	2p23.3	
melanocortin-4 receptor polymorphism (MC4R)	155541	18q22	
<i>BMIQ1</i>		7q32.3	near D7S1804
<i>BMIQ2</i>		13q14	near D13S257
<i>BMIQ3</i>		6q23-q25	near D6S1009, GATA184A08, D6S2436, and D6S305
<i>BMIQ4</i>		11q24	near D11S1998, D11S4464, and D11S912
<i>BMIQ5</i>		16p13	near ATA41E04
<i>BMIQ6</i>		20pter-p11.2	near D20S482
INSIG2		2q14.1	
FTO		16q12.2	Adults who were homozygous for a particular <i>FTO</i> allele weighed about 3 kilograms more and had a 1.6-fold greater

rate of obesity than those who had not inherited this trait. This association disappeared, though, when those with *FTO* polymorphisms participated in moderately intensive physical activity equivalent to three to four hours of brisk walking.

TMEM18	2p25.3
GNPDA2	4p13
NEGR1	1p31.1
BDNF	11p13
KCTD15	19q13.12
SH2B1	16p11.2
MTCH2	11p11.2
PCSK1	5q15-q21
NPC1	18q11-q12

Some studies have focused upon inheritance patterns without focusing upon specific genes. One study found that 80% of the offspring of two obese parents were obese, in contrast to less than 10% of the offspring of two parents who were of normal weight.

The thrifty gene hypothesis postulates that certain ethnic groups may be more prone to obesity in an equivalent environment. Their ability to take advantage of rare periods of abundance by storing energy as fat would be advantageous during times of varying food availability, and individuals with greater adipose reserves would be more likely survive famine. This tendency to store fat, however, would be maladaptive in societies with stable food supplies. This is the presumed reason that Pima Indians, who evolved in a desert ecosystem, developed some of the highest rates of obesity when exposed to a Western lifestyle.

Numerous studies of laboratory rodents provide strong evidence that genetics plays an important role in obesity.

### **Genetic syndromes**

Obesity is also a major feature in several syndromes, such as Prader-Willi syndrome, Bardet-Biedl syndrome, Cohen syndrome, Ayazi syndrome, and MOMO syndrome. (The term "non-syndromic obesity" is sometimes used to exclude these conditions.) In people with early-onset severe obesity (defined by an onset before 10 years of age and body mass index over three standard deviations above normal), 7% harbor a single locus mutation.

## Chapter 16

# Management of Obesity

The main treatment for obesity consists of dieting and physical exercise. Diet programs may produce weight loss over the short term, but maintaining this weight loss is frequently difficult and often requires making exercise and a lower calorie diet a permanent part of a person's lifestyle. Success rates of long-term weight loss maintenance with lifestyle changes are low ranging from 2–20%.

One medication, orlistat (Xenical), is current widely available and approved for long term use. Weight loss however is modest with an average of 2.9 kg (6.4 lb) at 1 to 4 years and there is little information on how these drugs affect longer-term complications of obesity. Its use is associated with high rates of gastrointestinal side effects.

The most effective treatment for obesity is bariatric surgery. Surgery for severe obesity is associated with long-term weight loss and decreased overall mortality. One study found a weight loss of between 14% and 25% (depending on the type of procedure performed) at 10 years, and a 29% reduction in all cause mortality when compared to standard weight loss measures. However, due to its cost and the risk of complications, researchers are searching for other effective yet less invasive treatments.

Studies have found significant benefits in mortality in certain populations from weight loss. In a prospective study of obese women with weight related diseases, intentional weight loss of any amount was associated with a 20% reduction in mortality. In obese women without obesity related illnesses a weight loss of greater than 9 kg (20 lb) was associated with a 25% reduction in mortality. A recent review concluded that certain subgroups such as those with type 2 diabetes and women show long term benefits in all cause mortality, while outcomes for men do not seem to be improved with weight loss. A subsequent study has found benefits in mortality from intentional weight loss in those who have severe obesity.

### ***Dieting***

Diets to promote weight loss are generally divided into four categories: low-fat, low-carbohydrate, low-calorie, and very low calorie. A meta-analysis of six randomized controlled trials found no difference between three of the main diet types (low calorie, low carbohydrate, and low fat), with a 2–4 kilogram (4.4–8.8 lb) weight loss in all

studies. At two years these three methods resulted in similar weight loss irrespective of the macronutrients emphasized.

Very low calorie diets provide 200–800 kcal/day, maintaining protein intake but limiting calories from both fat and carbohydrates. They subject the body to starvation and produce an average weekly weight loss of 1.5–2.5 kilograms (3.3–5.5 lb). These diets are not recommended for general use as they are associated with adverse side effects such as loss of lean muscle mass, increased risks of gout, and electrolyte imbalances. People attempting these diets must be monitored closely by a physician to prevent complications.

## ***Exercise***

With use, muscles consume energy derived from both fat and glycogen. Due to the large size of leg muscles, walking, running, and cycling are the most effective means of exercise to reduce body fat. Exercise affects macronutrient balance. During moderate exercise, equivalent to a brisk walk, there is a shift to greater use of fat as a fuel. To maintain health the American Heart Association recommends a minimum of 30 minutes of moderate exercise at least 5 days a week.

A meta-analysis of 43 randomized controlled trials by the Cochrane Collaboration found that exercising alone led to limited weight loss. In combination with diet, however, it resulted in a 1 kilogram weight loss over dieting alone. A 1.5 kilogram (3.3 lb) loss was observed with a greater degree of exercise. Even though exercise as carried out in the general population has only modest effects, a dose response curve is found, and very intense exercise can lead to substantial weight loss. During 20 weeks of basic military training with no dietary restriction, obese military recruits lost 12.5 kg (27.6 lb). High levels of physical activity seem to be necessary to maintain weight loss. A pedometer appears useful for motivation. Over an average of 18-weeks of use physical activity increased by 27% resulting in a 0.38 decreased in BMI.

Signs that encourage the use of stairs as well as community campaigns have been shown to be effective in increasing exercise in a population. The city of Bogota, Colombia for example blocks off 113 kilometers (70 miles) of roads every Sunday and on holidays to make it easier for its citizens to get exercise. These pedestrian zones are part of an effort to combat chronic diseases, including obesity.

## ***Weight loss programs***

Weight loss programs often promote lifestyle changes and diet modification. This may involve eating smaller meals, cutting down on certain types of food, and making a conscious effort to exercise more. These programs also enable people to connect with a group of others who are attempting to lose weight, in the hopes that participants will form mutually motivating and encouraging relationships.

A number of popular programs exist, including Weight Watchers, Overeaters Anonymous, and Jenny Craig. These appear to provide modest weight loss (2.9 kg,

6.4 lb) over dieting on one's own (0.2 kg, 0.4 lb) over a two year period. Internet-based programs appear to be ineffective. The Chinese government has introduced a number of "fat farms" where obese children go for reinforced exercise, and has passed a law which requires students to exercise or play sports for an hour a day at school.

In a structured setting, 67% of people who lost greater than 10% of their body mass maintained or continued to lose weight one year later. An average maintained weight loss of more than 3 kg (6.6 lb) or 3% of total body mass could be sustained for five years.

## Medication



Orlistat (Xenical) the most commonly used medication to treat obesity and sibutramine (Meridia) a recently withdrawn medication due to cardiovascular side effects

Only one anti-obesity medications orlistat (Xenical) is currently approved by the FDA for long term use. It reduces intestinal fat absorption by inhibiting pancreatic lipase. Rimonabant (Acomplia), a second drug, works via a specific blockade of the endocannabinoid system. It has been developed from the knowledge that cannabis smokers often experience hunger, which is often referred to as "the munchies". It had been approved in Europe for the treatment of obesity but has not received approval in the United States or Canada due to safety concerns. European Medicines Agency in October 2008 recommended the suspension of the sale of rimonabant as the risk seem to be greater than the benefits. Sibutramine (Meridia), which acts in the brain to inhibit deactivation of the neurotransmitters, thereby decreasing appetite was withdrawn from the UK market in January 2010 and United States and Canadian markets in October 2010 due to cardiovascular concerns.

Weight loss with these drugs is modest. Over the longer term, average weight loss on orlistat is 2.9 kg (6.4 lb), sibutramine is 4.2 kg (9.3 lb) and rimonabant is 4.7 kg (10.4 lb). Orlistat and rimonabant lead to a reduced incidence of diabetes, and all three drugs have some effect on cholesterol. However, there is little information on how these drugs affect the longer-term complications or outcomes of obesity. In 2010 it was found that sibutramine increases the risk of heart attacks and strokes in people with a history of cardiovascular disease.

There are a number of less commonly used medications. Some are only approved for short term use, others are used off-label, and still others are used illegally. Most are appetite suppressants that act on one or more neurotransmitters. Phendimetrazine (Bontril), diethylpropion (Tenuate), and phentermine (Adipex-P) are approved by the FDA for short term use, while bupropion (Wellbutrin), topiramate (Topamax), and zonisamide (Zonegran) are sometimes used off-label. Recombinant human leptin is very effective in those with obesity due to congenital complete leptin deficiency via decreasing energy intake and possibly increases energy expenditure. This condition is, however, rare and this treatment is not effective for inducing weight loss in the majority of people with obesity. It is being investigated to determine whether or not it helps with weight loss maintenance.

The usefulness of certain drugs depends upon the comorbidities present. Metformin (Glucophage) is preferred in overweight diabetics, as it may lead to mild weight loss in comparison to sulfonylureas or insulin. The thiazolidinediones, on the other hand, may cause weight gain, but decrease central obesity. Diabetics also achieve modest weight loss with fluoxetine (Prozac), orlistat and sibutramine over 12–57 weeks. Preliminary evidence has however found higher number of cardiovascular events in people taking sibutramine versus control (11.4% vs. 10.0%). The long-term health benefits of these treatments remain unclear.

Fenfluramine and dexfenfluramine were withdrawn from the market in 1997, while ephedrine (found in the traditional Chinese herbal medicine *má huáng* made from the *Ephedra sinica*) was removed from the market in 2004. Dexamphetamines are not approved by the FDA for the treatment of obesity due to concerns regarding addiction and abuse potential. The use of these drugs is not recommended due to potential side effects. However, people do occasionally use these drugs illegally.

## **Surgery**

Bariatric surgery ("weight loss surgery") is the use of surgical intervention in the treatment of obesity. As every operation may have complications, surgery is only recommended for severely obese people (BMI > 40) who have failed to lose weight following dietary modification and pharmacological treatment. Weight loss surgery relies on various principles: the two most common approaches are reducing the volume of the stomach (e.g. by adjustable gastric banding and vertical banded gastroplasty), which produces an earlier sense of satiation, and reducing the length of bowel that comes into contact with food (gastric bypass surgery), which directly reduces absorption. Band

surgery is reversible, while bowel shortening operations are not. Some procedures can be performed laparoscopically. Complications from weight loss surgery are frequent.

Surgery for severe obesity is associated with long-term weight loss and decreased overall mortality. One study found a weight loss of between 14% and 25% (depending on the type of procedure performed) at 10 years, and a 29% reduction in all cause mortality when compared to standard weight loss measures. A marked decrease in the risk of diabetes mellitus, cardiovascular disease and cancer has also been found after bariatric surgery. Marked weight loss occurs during the first few months after surgery, and the loss is sustained in the long term. In one study there was an unexplained increase in deaths from accidents and suicide, but this did not outweigh the benefit in terms of disease prevention. When the two main techniques are compared, gastric bypass procedures are found to lead to 30% more weight loss than banding procedures one year after surgery.

The effects of liposuction on obesity are less well determined. Some small studies show benefits while others show none. A treatment involving the placement of an intragastric balloon via gastroscopy has shown promise. One type of balloon led to a weight loss of 5.7 BMI units over 6 months or 14.7 kg (32.4 lb). Regaining lost weight is common after removal, however, and 4.2% of people were intolerant of the device.

### ***Clinical protocols***

Much of the Western world has created clinical practice guidelines in an attempt to address rising rates of obesity. Australia, Canada, the European Union, and the United States have all published statements since 2004.

In a clinical practice guideline by the American College of Physicians, the following five recommendations are made:

1. People with a BMI of over 30 should be counseled on diet, exercise and other relevant behavioral interventions, and set a realistic goal for weight loss.
2. If these goals are not achieved, pharmacotherapy can be offered. The person needs to be informed of the possibility of side-effects and the unavailability of long-term safety and efficacy data.
3. Drug therapy may consist of sibutramine, orlistat, phentermine, diethylpropion, fluoxetine, and bupropion. For more severe cases of obesity, stronger drugs such as amphetamine and methamphetamine may be used on a selective basis. Evidence is not sufficient to recommend sertraline, topiramate, or zonisamide.
4. In people with a BMI over 40 who fail to achieve their weight loss goals (with or without medication) and who develop obesity-related complications, referral for bariatric surgery may be indicated. The person needs to be aware of the potential complications.
5. Those requiring bariatric surgery should be referred to high-volume referral centers, as the evidence suggests that surgeons who frequently perform these procedures have fewer complications.

A clinical practice guideline by the US Preventive Services Task Force (USPSTF) concluded that the evidence is insufficient to recommend for or against routine behavioral counseling to promote a healthy diet in unselected people in primary care settings, but that intensive behavioral dietary counseling is recommended in those with hyperlipidemia and other known risk factors for cardiovascular and diet-related chronic disease. Intensive counseling can be delivered by primary care clinicians or by referral to other specialists, such as nutritionists or dietitians.

Canada developed and published evidence-based practice guidelines in 2006. The guidelines attempt to address the prevention and management of obesity at both the individual and population levels in both children and adults. The European Union published clinical practice guidelines in 2008 in an effort to address the rising rates of obesity in Europe. Australia came out with practice guidelines in 2004.

## **Research**

Lorcaserin has been found to be effective in the treatment of obesity with a weight loss of 5.8 kg at one year as opposed to 2.2 kg with placebo. It however, failed to get FDA approval in 2010 due to concerns regarding cancer. Temporary, controllable gastric pseudo-bezoars (swallowable, swellable foreign bodies in the stomach meant to reduce gastric volume from inside the organ) are being tested. Treatment with naltrexone plus bupropion in a phase three trial resulted in a weight loss of 5–6% versus 1% for a placebo. Another combination that is in trials is phentermine and topiramate (Qnexa). In October 2010 the FDA refused approval due to inadequate evidence regarding potential birth defects and cardiac side effects.

## Chapter 17

# Anti-Obesity Medication



Orlistat (Xenical) the most commonly used medication to treat obesity and sibutramine (Meridia) a recently withdrawn medication due to cardiovascular side effects

**Anti-obesity medication** or weight loss drugs are all pharmacological agents that reduce or control weight. These drugs alter one of the fundamental processes of the human body, weight regulation, by either altering appetite, metabolism, or absorption of calories. It is common for them to be tried and if there is little or no benefit from them to discontinue treatment. The main treatment modalities for overweight and obesity remain dieting and physical exercise.

Only one anti-obesity medication orlistat (Xenical) is currently approved by the FDA for long term use. It reduces intestinal fat absorption by inhibiting pancreatic lipase. Rimonabant (Acomplia), a second drug, works via a specific blockade of the endocannabinoid system. It has been developed from the knowledge that cannabis smokers often experience hunger, which is often referred to as "the munchies". It had been approved in Europe for the treatment of obesity but has not received approval in the United States or Canada due to safety concerns. The European Medicines Agency in October 2008 recommended the suspension of the sale of rimonabant as the risks seem to be greater than the benefits. Sibutramine (Meridia), which acts in the brain to inhibit deactivation of the neurotransmitters, thereby decreasing appetite was withdrawn from the United States and Canadian markets in October 2010 due to cardiovascular concerns.

Because of potential side effects, it is recommended that anti-obesity drugs only be prescribed for obesity where it is hoped that the benefits of the treatment outweigh its risks.

### ***Mechanisms of action***

Anti-obesity drugs operate through one or more of the following mechanisms:

- Suppression of the appetite. Catecholamines and their derivatives (such as phentermine and other amphetamine-based drugs) are the main tools used for this, although other classes of drugs such as anti-depressants and mood stabilizers have been anecdotally used for appetite suppression (see: bupropion and topiramate). Drugs blocking the cannabinoid receptors may be a future strategy for appetite suppression.
- Increase of the body's metabolism.
- Interference with the body's ability to absorb specific nutrients in food. For example, Orlistat (also known as Xenical and Allī) blocks fat breakdown and thereby prevents fat absorption. The OTC fiber supplements glucomannan and guar gum have been used for the purpose of inhibiting digestion and lowering caloric absorption

Anorectics are primarily intended to suppress the appetite, but most of the drugs in this class also act as stimulants (dextroamphetamine, e.g.), and patients have abused drugs "off label" to suppress appetite (e.g. digoxin).

### ***History***

The first described attempts at producing weight loss are those of Soranus of Ephesus, a Greek physician, in the second century AD. He prescribed elixirs of laxatives and purgatives, as well as heat, massage, and exercise. This remained the mainstay of treatment for well over a thousand years. It was not until the 1920s and 1930s that new treatments began to appear. Based on its effectiveness for hypothyroidism, thyroid hormone became a popular treatment for obesity in euthyroid people. It had a modest effect but produced the symptoms of hyperthyroidism as a side effect, such as

palpitations and difficulty sleeping. Dinitrophenol (DNP) was introduced in 1933; this worked by uncoupling the biological process of oxidative phosphorylation in mitochondria, causing them to produce heat instead of ATP. The most significant side effect was a sensation of warmth, frequently with sweating. Overdose, although rare, led to a rise in body temperature and, ultimately, fatal hyperthermia. By the end of 1938 DNP had fallen out of use because the FDA had become empowered to put pressure on manufacturers, who voluntarily withdrew it from the market.

Amphetamines (marketed as Benzedrine) became popular for weight loss during the late 1930s. They worked primarily by suppressing appetite, and had other beneficial effects such as increased alertness. Use of amphetamines increased over the subsequent decades, culminating in the "rainbow pill" regime. This was a combination of multiple pills, all thought to help with weight loss, taken throughout the day. Typical regimens included stimulants, such as amphetamines, as well as thyroid hormone, diuretics, digitalis, laxatives, and often a barbiturate to suppress the side effects of the stimulants. In 1967/1968 a number of deaths attributed to diet pills triggered a Senate investigation and the gradual implementation of greater restrictions on the market. This culminated in 1979 with the FDA banning the use of amphetamines, then the most effective of the diet drugs, in diet pills.

Meanwhile, phentermine had been FDA approved in 1959 and fenfluramine in 1973. The two were no more popular than other drugs until in 1992 a researcher reported that the two caused a 10% weight loss which was maintained for more than two years. *Fen-phen* was born and rapidly became the most commonly prescribed diet medication. Dexfenfluramine (Redux) was developed in the mid-1990s as an alternative to fenfluramine with less side-effects, and received regulatory approval in 1996. However, this coincided with mounting evidence that the combination could cause valvular heart disease in up to 30% of those who had taken it, leading to withdrawal of *Fen-phen* and dexfenfluramine from the market in September 1997.

Ephedra was removed from the US market in 2004 over concerns that it raises blood pressure and could lead to strokes and death.

### ***Contemporary anti-obesity drugs***

Some patients find that diet and exercise is not a viable option; for these patients, anti-obesity drugs can be a last resort. Some prescription weight loss drugs are stimulants, which are recommended only for short-term use, and thus are of limited usefulness for extremely obese patients, who may need to reduce weight over months or years.

#### **Orlistat**

Orlistat (Xenical) reduces intestinal fat absorption by inhibiting pancreatic lipase. Orlistat may cause frequent, oily bowel movements (steatorrhea), but if fat in the diet is reduced, symptoms often improve. Originally available only by prescription, it was approved by the FDA for over-the-counter sale in February 2007. On May 26, 2010, the U.S. Food

and Drug Administration (FDA) has approved a revised label for Xenical to include new safety information about cases of severe liver injury that have been reported rarely with the use of this medication.

## **Sibutramine**

Sibutramine (Reductil or Meridia) is an anorectic or appetite suppressant, reducing the desire to eat. Sibutramine may increase blood pressure and may cause dry mouth, constipation, headache, and insomnia.

Sibutramine has been withdrawn from the market in the United States, the UK, the EU, Australia, Canada and Hong Kong. Its risks (non-life threatening MI and stroke) have been shown to outweigh the benefits.

## **Rimonabant**

Rimonabant (Acomplia) is a recently developed anti-obesity medication. It is a cannabinoid (CB1) receptor antagonist that acts centrally on the brain thus decreasing appetite. It may also act peripherally by increasing thermogenesis and therefore increasing energy expenditure.

Weight loss with Rimonabant however has not been shown to be greater than other available weight-loss medication. Due to safety concerns, primarily psychiatric in nature, the drug has not received approval in the United States or Canada, either as an anti-obesity treatment or as a smoking-cessation drug.

Sanofi-Aventis has received approval to market Rimonabant as a prescription anti-obesity drug in the European Union, subject to some restrictions, however, in October 2008, the European Medicines Agency (EMA) recommended that Acomplia no longer be available in UK. One month later, Sanofi-Aventis decided it would no longer study rimonabant for any indication.

## **Metformin**

In people with Diabetes mellitus type 2, the drug metformin (Glucophage) can reduce weight.

## **Exenatide**

Exenatide (Byetta) is a long-acting analogue of the hormone GLP-1, which the intestines secrete in response to the presence of food. Among other effects, GLP-1 delays gastric emptying and promotes a feeling of satiety. Some obese people are deficient in GLP-1, and dieting reduces GLP-1 further. Byetta is currently available as a treatment for Diabetes mellitus type 2. Some, but not all, patients find that they lose substantial weight when taking Byetta. Drawbacks of Byetta include that it must be injected subcutaneously twice daily, and that it causes severe nausea in some patients, especially when therapy is

initiated. Byetta is recommended only for patients with Type 2 Diabetes. A somewhat similar drug, Symlin, is currently available for treating diabetes and is in testing for treating obesity in non-diabetics.

## **Pramlintide**

Pramlintide (Symlin) is a synthetic analogue of the hormone Amylin, which in normal people is secreted by the pancreas in response to eating. Among other effects, Amylin delays gastric emptying and promotes a feeling of satiety. Many diabetics are deficient in Amylin. Currently, Symlin is only approved to be used along with insulin by Type 1 and Type 2 diabetics. However, Symlin is currently being tested in non-diabetics as a treatment for obesity. A drawback is that Symlin must be injected at mealtimes.

## **Other drugs**

ZGN-433, is undergoing initial human trials, starting in early 2011.

Lorcaserin, a serotonin-blocking drug, is undergoing FDA trials, as of 2009.

Human growth hormone is also said to increase fat loss and increase strength.

Dinitrophenol (DNP) is another agent that increases strength and promotes fat loss.

Other weight loss drugs have also been associated with medical complications, such as fatal pulmonary hypertension and heart valve damage due to Redux and Fen-phen, and hemorrhagic stroke due phenylpropanolamine. Many of these substances are related to amphetamine.

Unresearched nonprescription products or programs for weight loss are heavily promoted by mail and print advertising and on the internet. The US Food and Drug Administration recommends caution with use of these products, since many of the claims of safety and effectiveness are unsubstantiated. Individuals with anorexia nervosa and some athletes try to control body weight with laxatives, diet pills or diuretic drugs, although these generally have no impact on body fat. Products that work as a laxative can cause the blood's potassium level to drop, which may cause heart and/or muscle problems. Pyruvate is a popular product that may result in a small amount of weight loss. However, pyruvate, which is found in red apples, cheese, and red wine, has not been thoroughly studied and its weight loss potential has not been scientifically established.

## ***Alternative medicine***

Alternative medicine has insufficient evidence to support its use.

## ***Side effects***

Some anti-obesity drugs have severe or life-threatening side effects, fen-phen being a famous example. These side effects are often associated with their mechanism of action. In general, stimulants carry a risk of high blood pressure, faster heart rate, palpitations, closed-angle glaucoma, drug addiction, restlessness, agitation, and insomnia.

Another drug, orlistat, blocks absorption of dietary fats, and as a result may cause oily spotting bowel movements (steatorrhea), oily stools, stomach pain, and flatulence. A similar medication, designed for patients with Type 2 diabetes, is Acarbose which partially blocks absorption of carbohydrates in the small intestine, and produces similar side effects including stomach pain, and flatulence.

## ***Limitations of current knowledge***

The limitation of drugs for obesity is that we do not fully understand the neural basis of appetite and how to modulate it. Appetite is clearly a very important instinct to promote survival. Arguably any drug that would abolish appetite may carry a high mortality risk and may be unsuitable for clinical use.

Because the human body uses various chemicals and hormones to protect its stores of fat (a reaction probably useful to our ancestors when food was scarce in the past,) there has not yet been found a 'silver bullet', or a way to completely circumvent this natural habit of protecting excess food stores. Because of this, anti-obesity drugs are not a practical long-term solution for people who are overweight.

In order to circumvent the number of feedback mechanisms that prevent most monotherapies from producing sustained large amounts of weight loss, it has been hypothesized that combinations of drugs may be more effective by targeting multiple pathways and possibly inhibiting feedback pathways that work to cause a plateau in weight loss. This was evidenced by the success of the combination of phentermine and fenfluramine or dexfenfluramine, popularly referred to phen-fen, in producing significant weight loss but fenfluramine and dexfenfluramine were pulled from the market due to safety fears regarding a potential link to heart valve damage. The damage was found to be a result of activity of fenfluramine and dexfenfluramine at the 5-HT<sub>2B</sub> serotonin receptor in heart valves. Newer combinations of SSRIs and phentermine, known as phenpro, have been used with equal efficiency as fenphen with no known heart valve damage due to lack of activity at this particular serotonin receptor due to SSRIs. There has been a recent resurgence in combination therapy clinical development with the development of 3 combinations: Qnexa (topiramate + phentermine), Empatic (bupropion + zonisamide) and Contrave (bupropion + naltrexone).

## ***Future developments***

Other classes of drugs in development include lipase inhibitors, similar to orlistat. Another lipase inhibitor, called GT 389-255, is being developed by Peptimmune

(licensed from Genzyme). This is a novel combination of an inhibitor and a polymer designed to bind the undigested triglycerides therefore allowing increased fat excretion without side effects such as oily stools that occur with orlistat. The development seems to be stalled as Phase 1 trials were conducted in 2004 and there has been no further human clinical development since then.

Another potential long-term approach to anti-obesity medication is through the development of ribonucleic acid interference (RNAi). Animal studies have illustrated that the deletion of the RIP140 gene in mice by genetic knockdown results in the lack of fat accumulation, even when mice are fed a high fat diet. Experiments conducted by Professor Malcolm Parker of Imperial College show that by silencing RIP 140, a nuclear hormone co-repressor which regulates fat accumulation, animal models exhibit a lean profile throughout their life, are resistant to diet-induced obesity, and show an enhanced metabolic rate. CytRx Corporation is developing RNAi therapeutics against this drug target for the treatment of obesity and type 2 diabetes. Similarly, another nuclear hormone receptor co-repressor, SMRT, has demonstrated an opposing effect in genetically engineered mice. Dr. Russell Nofsinger and Dr. Ronald Evans of the Salk Institute showed that disruption of the molecular interaction between SMRT and their nuclear hormone receptor partners leads to increased adiposity and a decreased metabolic rate. These studies suggest that new drugs targeting the molecular interaction between nuclear hormone receptors and their regulatory cofactors could provide a useful new category of therapeutic targets to be developed in an effort to control obesity.

Another approach is to induce a sense of satiety by occupying space in the gastric and intestinal cavities. One clinical trial involves a hydrogel made of indigestible, food-grade materials. Another pilot study uses pseudobezoars.