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INNOVATIONS | NUTRITION UPDATES AND APPLICATIONS

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Does Birth Determine Girth?

At least four factors that contribute to energy utilization (calorie burning) have been identified.

For many years conventional wisdom held body weight was directly related to how closely the number of calories a person consumed matched the amount of calories he/she burned. If this basic energy balance equation were true, then weight control should be a simple matter of balancing calorie intake and expenditure. Despite dozens of reducing diets and a wide selection of home exercise equipment, the rate of obesity in the American population has escalated rapidly since the early 1960s. As the legions of obese Americans and the number of unsuccessful dieters expanded, scientists and lay people alike rejected the old "calories-in versus calories-out equation" in search of a better explanation of why some people seem to gain weight just looking at sweets while others appear to stay sleek for a lifetime.

What needs evaluation is not the equation so much as the factors that influence energy intake and expenditure.

Scientists have identified both genetic traits and psychological factors that can increase a person's risk of developing obesity. In the process they have come to the conclusion that the basic energy balance equation "Body Weight = Calories Consumed - Calories Expended" is fairly accurate. What needs evaluation is not the equation so much as the factors that influence energy intake and expenditure.

Factors that Influence Energy Balance

Only one factor, calorie consumption, contributes to energy intake. At least four factors that contribute to energy utilization (calorie burning) have been identified. They are **basal metabolic rate** or **BMR** (rate at which energy is expended to keep a resting, awake body alive), **dietary-induced thermogenesis** (the amount of calories burned during digestion and absorption of food), voluntary activity, and **adaptive thermogenesis** (the body's ability to burn more calories in a cold

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environment when overfed). As yet, however, no one understands what regulates each of these factors, nor is it known how these factors affect each other or energy balance as a whole. Both nature (genetics) and nurture (environment) have been cited as the primary regulators of energy balance (2-4, 17). Neither theory by itself provides a totally satisfactory explanation. The contemporary view is that a given person's energy balance results from a complex combination of genetic and environmental regulatory messages.

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How Can Genetics Influence the Development of Obesity?

Genetically determined obesity has been clearly demonstrated in certain strains of laboratory and domestic animals (17). The role of genetics in the development of human obesity is not as clearly established, however. To date, 27 inherited disorders that produce obesity as well as other symptoms have been identified. The occurrence of these disorders is quite rare, in some cases affecting only a few individuals. Research indicates that for most individuals there is not a clear cause-and-effect relationship between genetics and body weight. Rather, genetics influences body weight, fat distribution patterns, metabolic efficiency, and appetite, but each of these factors is also modified by environmental conditions. For most of us our body weight is a combination of nature and nurture.

Lower-body obesity seems to be more strongly controlled by female sex hormones than by genetics.

Research indicates that genetics influences body weight, fat distribution patterns, and metabolic efficiency.

Familial Body Weight Patterns Research has confirmed what many casual observers have known for years: the tendency to be tall or short, plump or lean tends to run in families. There are three basic types of human physiques (see figure 1), *ectomorph, mesomorph,* and *endomorph.* **Ectomorphs** have long and thin builds, as a result of their elongated, slender bones, narrow hips and chests. At the other end of the spectrum are the stockily built **endomorphs**. They owe their soft and rounded appearance to short, stubby bones, wide chests and hips, short necks, and round heads. People with **mesomorphic** physiques fall between these two extremes. Their build is often described as solid and muscular (25). Investigators have found people with an ectomorphic build have an easier time maintaining a healthy body weight than do people with other types of physiques. Possibly it is because their bodies have greater surface area, which in turn makes them less energy efficient. In other words, ectomorphs lose more energy just staying warm and performing basic functions, like breathing, than do their more compactly built peers. Genes as well as sex hormones influence body fat distribution patterns (see figure 2). A high level of the male sex hormone, *testosterone,* favors storage of fat in the upper body and abdominal area resulting in the typical “apple on a stick” appearance of many overweight men. Research has demonstrated a strong familial tendency toward abdominal obesity in both males and females in certain families (13, 20), suggesting upper-body obesity is favored by genetics as well as male sex hormones. Conversely, the female sex hormones, *estrogen* and *progesterone,* favor lower-body obesity, resulting in the pear-like shape of most females. Lower-body obesity seems to be more strongly controlled by female sex hormones than by genetics. Obese men very rarely have a pear-shaped build. Additionally, women who had pear-shaped builds during their reproductive years tend to store fat in their abdominal area post menopause. This redistribution in fat stores is linked to the drop in female hormones.

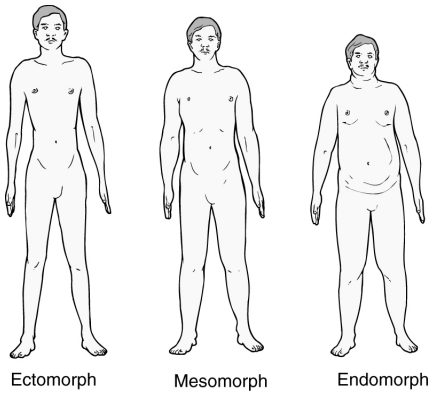

Figure 1 The three basic body physiques. How would you classify your own physique?

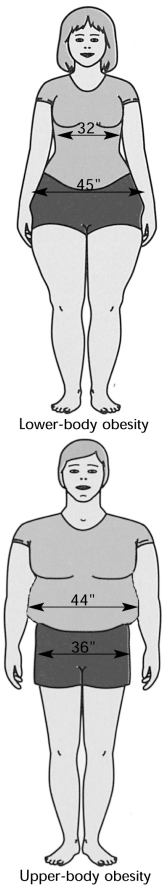

Figure 2 Lower-body obesity is described as pear-shaped, while upper-body obesity is described as apple-shaped.

The Power of Lean Genes Outweighs the Power of Fat Ones

Studies show the body weights of adopted children are typically more similar to the weight patterns of their biological families than they are to those of their adopted families.

The high incidence of obesity in certain families, ethnic groups, and sets of twins has often been cited as evidence that genetics is the predominant determinate of energy balance. For some scientists the most compelling evidence that "birth determines girth" are studies that show the body weights of adopted children are typically more similar to the weight patterns of their biological families than they are to those of their adopted families. Identical twins, even when raised apart, are twice as likely as fraternal twins to have a similar body weight (5,6). Other experts aren't convinced. Using a type of statistics known as *meta-analysis* to simultaneously examine the data from many familial body-weight studies, they have shown the genetics for leanness are actually stronger than are those for obesity. In other words, you may have trouble gaining weight if you are naturally lean, but changing your lifestyle can help you trim down if you've grown plump (12,19). They also concluded people don't inherit obesity. Rather, they inherit a tendency to become fat if they follow a particular lifestyle (19).

Metabolic Efficiency Favors Obesity

Genetically obese rodents use fewer calories for basic metabolic functions than do their lean counterparts. This ability to do more with less is termed ***thrifty metabolism***. Thrifty genes provide an evolutionary advantage by promoting fat storage during times of plenty. It appears some people share this thrifty tendency. When pairs of identical twins were fed 1000 extra calories a day for 100 days some pairs gained less than 10 pounds whereas other pairs gained as much as 30 pounds. The difference in weight gain seemed to be due to metabolic differences in the way extra calories were utilized. It appeared that some twins had very thrifty metabolisms and readily stored extra calories as fat, whereas other twins tended to burn off the extra energy (6).

Metabolic spendthrifts seem to burn off those extra calories by making more heat or fidgeting non-stop. A portion of the calories we eat are used to keep us warm. The cooler the environment the more calories are used for this purpose. Some people seem to make more heat when they overeat, regardless of the temperature. This process, known as *adaptive thermogenesis*, is initiated by activating proteins known as ***uncoupling proteins***. When fat is burned for energy some of it is given off as heat and some is captured as ATP. When uncoupling proteins shift into action they shunt fat to heat production instead of ATP formation. (28). Other people resist putting on pounds because they burn off hundreds of extra unwanted calories with excessive *fidgeting*. This discovery is part of a research program labeled NEAT — for Non-Exercise Activity Thermogenesis, which is evaluating how activities of everyday living burn calories (14).

Appetite Regulators

Genetics also appears to influence how much food a person consumes. It is well established that humans are genetically programmed to like the sweet and salty flavors and to favor fat-rich foods (10). Leptin, melanin and orexins are among the hormones newly recognized as playing a role in food intake.

Leptin, a hormone discovered in the mid-1990s, made headlines when scientists observed genetically obese mice had a much lower level of leptin in their blood than did normal-weight mice. Equally exciting was the discovery that injecting leptin into fat mice suppressed their appetite and brought about rapid weight loss. Leptin, which is produced by adipose cells, appears to work on the appetite center of the hypothalamus as a primitive check and balance to fat storage. In normal-weight mice leptin levels increase as body weight increases, thereby limiting their appetite and the development of obesity. To the disappointment of many chronic dieters, leptin injections did not reduce the weight of most obese people (21). Only two instances of a genetic defect resulting in leptin deficiency have been found in humans. In both cases extremely overweight youngsters were found to have very little leptin in their blood. Without leptin their appetites went unchecked, and they ate constantly (8).

To the disappointment of many chronic dieters, leptin injections did not reduce the weight of most obese people.

Leptin doesn't always cause the predicted response, however. Despite having high levels of leptin in their blood, many obese people go right on eating (21). The biology behind this puzzling finding may soon be unraveled. Researchers recently found leptin activity increased in adipose (fat) cells of obese rats when food was plentiful—assuring fat storage — and fell when food was limited. The researchers termed this a thrifty leptin gene and reasoned that in affluent societies where food is plentiful, a thrifty leptin gene would predispose people to weight gain and to become obese (26). Scientists at Harvard University reported leptin has opposing effects on different neurons in the hypothalamus (the part of the brain linked to appetite regulation). One bundle of neurons is inhibited by leptin, leading to obesity. The other cluster is activated by leptin, which could lead to starvation. They also noted leptin targets cells that contain neuropeptides implicated in regulating behaviors like eating and sleeping cycles. Leptin may affect appetite through indirect as well as direct mechanisms (7).

Animals treated with orexin consumed eight to ten times more food than normal within a few hours.

Melanin, one of the substances effected by leptin, is involved in the regulation of a variety of functions including sleeping and eating cycles. Animals who cannot produce the melanin-concentrating hormone MCH lose their appetite and remain lean (24). Animals with a defect in a related protein known as MC4R, short for *melanocortin-4 receptor,* become obese through chronic overeating. French and British researchers have identified two families, some of whose members carry a dominantly inherited mutation in their MC4R gene. Like the research animals, they never seem to stop eating and become significantly obese as a result (29).

In early 1998 researchers in the United States identified a new class of hormones that appears to regulate hunger and satiety. They christened these new compounds ***orexins***, after the Greek word *orexis*, meaning appetite. They also identified a gene that codes for production of orexins. Animals treated with orexin consumed eight to ten times more food than normal within a few hours. Rodents deprived of food for two days produced much larger quantities of orexins than usual in their brain. It is unclear whether orexins have the same activity in humans, or how they interact with other appetite-regulating substances like hormones and neurotrans-mitters. The researchers speculate that a lack of the hormone leptin, which suppresses hunger, may prompt the brain to produce orexins, which cause hunger (23).

A variety of **neurotransmitters** (also known as *neuropeptides*) that seem to stimulate the feeding response have been identified. As with the hormones leptin and orexin, just how these

peptides are regulated is unclear. Some researchers have suggested that the mere presence of food may stimulate the release of these peptides, which in turn stimulates appetite. Experts who favor this theory contend that this was a type of early failsafe mechanism to encourage people to eat when food was plentiful, so they'd have adipose reserves to draw from when food inevitably became scarce again. Some neurotransmitters like neuropeptide Y stimulate appetite in general. The action of other peptides seems to be quite specific. The peptide *galanin,* for example, stimulates fat intake. A high-fat diet, in turn, stimulates galanin release. The more fat consumed the more fat is desired (1, 22). Peptides with the opposing action, such as *serotonin*, have also been identified. Serotonin, often described as the "feel good chemical," creates a sense of well being and suppresses appetite-driven, but not hunger-driven, eating. This ability to quell appetite without creating total anorexia has made serotonin the target of diet drugs fen-Phen and Meridia. Both of these drugs elevate serotonin levels.

Environmental factors like food intake and activity levels alter what nature provides.

Three new McDonald's restaurants open every day.

Nurture — The Role of Environment

Nature may determine our body type and dictate where we store fat, but environmental factors like food intake and activity levels alter what nature provides. Many experts have pointed out that the rate at which obesity is increasing in the U.S. population far outstrips the rate at which genetic changes occur, hence environmental factors must have a more significant role in the development of obesity than do genetic factors. The prevalence of obesity has increased dramatically since 1980. And obesity is on the rise in country after country, as each becomes more like America in terms of its food, work, and leisure patterns (2,15).

The prevalence of obesity has increased dramatically since 1980.

According to Dr. William Dietz, director of the Nutrition and Fitness Lab at the Centers for Disease Control, the increase in obesity in the United States parallels an increase in portion sizes, high-calorie convenience foods, laborsaving devices, and time spent in sedentary activities, like watching TV, playing video games, or surfing the web (2). Furthermore, unrelated people sharing a common environment often show similar patterns in body weight. For example, the phenomena known as the "freshman 15" refers to the well-documented tendency for college freshmen to gain weight when they are exposed to the pressures of adjusting to college life and choosing a healthy diet when confronted with many high-calorie options. Likewise, husbands and wives frequently achieve a similar degree of plumpness or leanness, presumably because of their shared lifestyle (2).

Are People Being Driven to Dine? The food industry spends billions of marketing dollars each year to keep people focused on food, through aggressive advertising and by improving availability. Food is everywhere. Vending machines, drive-through windows, and mini-markets in gas stations are commonplace. And it is not healthy foods like carrots and apples that are promoted. According to Kelly Brownell, professor of psychology, epidemiology, and public health at Yale University and a recognized expert on obesity, the situation is bound to get worse before it gets better. Three new McDonald's restaurants open every day, and a chief corporate goal is to have no American more than four minutes from a McDonald's (15).

The food industry also entices people to eat more food at each dining opportunity with super-sized portions and multiple-unit marketing schemes. Bigger portions are good business for the food industry. Consumers perceive them as a better value. Since food itself is relatively cheap, serving more of it is an easy way to increase profits. Only about 20 cents of every food dollar goes to the actual cost of the food. The remainder is spent on packaging, transportation, advertising, and marketing. These non-food costs don't change much as the serving size increases. Bigger portions equal bigger profits, but they also help create bigger people. Despite professing concern about their weight, most people eat more when they are

served more. In general, people will eat 25% more of any food packaged in a large container. If the food happens to be a highly palatable one like chips, popcorn, or candy, they tend to eat 50% more (27). Manufacturers and grocers also rely on the lure of multiple-unit pricing to stimulate consumption. Most people are very susceptible to marketing suggestions. They buy more of an item when the price reads "2 for $1.00" instead of "50 cents each." Quantity limits such as "limit 6 per customer" and suggested quantities like "buy one for now and one for the freezer" also cause consumers to adjust their expectations and purchases upward (15).

Most people eat more when they are served more.

Nurture Reshaping Nature

Some lifestyle choices can promote weight gain or facilitate weight loss by altering the underlying physiology.

How and why do people learn to overeat to sooth their stress?

The Brain-Body Connection

One of the newest areas of inquiry and one of the most difficult to evaluate is the role the brain plays in determining health. Some of our physiological responses are strictly dictated by our genes; others seem to be modifiable by experience.

Stress is a good example of the brain-body connection and its impact on eating. Stress can stimulate the appetite. Whether trying to juggle too many responsibilities or trying to cope with a traumatic event, many people report they "pig-out" when they feel "stressed-out" (9). How and why do people learn to overeat to sooth their stress? It seems food, mating, and mood-altering drugs, like cocaine or alcohol, stimulate a common brain pathway that triggers release of pleasure-producing neurotransmitters, such as dopamine and serotonin. This may explain why it is possible to become addicted to food (22).

Building up muscle tissue favors fat use and weight loss.

For others, eating seems to be a habit. An international team of researchers led by a group from MIT is exploring the changes that take place in the brain as a new habit is acquired. They have found when a new behavior is learned, nerve cell responses in the brain are reorganized into a set pattern. When the brain is confronted with a familiar task it runs on autopilot using these stored behavioral routines. The investigators have also found animals given addictive drugs develop stereotyped patterns of behavior, suggesting an intriguing link between habit and addiction (11). The tendency to run on autopilot explains why dieters often regain weight. Unless they are vigilant about their food and activity choices and alter their environmental cues, they are apt to fall back into their old familiar habits and pile on the pounds once again.

Body Composition

Certain lifestyle choices can alter energy utilization by altering body composition. Behaviors that promote excess adipose tissue favor fat storage whereas behaviors that promote muscle tissue development favor fat utilization. Fat cell numbers increase during key periods of rapid growth, like infancy and puberty. Fat cell numbers also increase whenever rapid weight gain causes all existing fat cells to reach their maximal storage capacity. Once established, excess fat cells can't be removed by dieting. They can only be shrunk. An enzyme, *LPL* (lipoprotein lipase), which is on the cell's surface, promotes the storage of energy as fat. The more fat cells a person has the higher their *LPL* level. Some scientists believe people with an excess of fat cells have a hard time losing weight and keeping it off because their body produces excess *LPL*, which favors fat storage (17).

Building up muscle tissue, on the other hand, favors fat use and weight loss. People who are active build up muscle tissue and increase the ability of their muscle fibers to burn fat for fuel. The more muscle tissue a person has the greater his/her BMR. The combined increases in BMR, fat utilization, and calories lost through exercise help active people maintain a healthy body weight, and underscore the importance of physical activity in weight loss and maintenance (17).

Some researchers have suggested the high degree of post-diet weight regain is due to the fact that BMR falls during dieting and remains depressed post-dieting. Meta-analysis of twelve published studies on post-diet BMR, as well as two new studies, refutes the idea that dieting significantly lowers BMR. Because BMR is partly influenced by body weight, a decline in BMR is to be anticipated whenever someone loses a considerable number of pounds (17,18). Weight regain appears to be due more to behavioral choices than biological factors.

Common genes don't always yield common results.

When Nature and Nurture Combine

A decline in BMR is to be anticipated whenever someone loses a considerable number of pounds.

After evaluating the relationship between **BMI** (body mass index) and inheritance in individuals participating in a familial heart disease study, researchers concluded 41% to 59% of the differences in body weight between people of the same height, age, gender, and overall health status could be attributed to inherited characteristics. In other words, if you are 10 pounds heavier than an appropriately matched control individual, 4.1 to 5.9 pounds of your excess weight are probably due to inherited characteristics. The rest is related to lifestyle choices (3). It also appeared that there was more than genetic factors involved in the development of obesity (4).

Common genes don't always yield common results, however. Environmental factors strongly influence the extent of obesity in *genetically susceptible* people. The researchers analyzed the emotional well-being, calorie intake, and energy expenditure of 145 sets of siblings raised in the same household. One sibling in each set was severely obese, the other had a healthy body weight. Obese siblings scored lower on tests of emotional well-being, including perceived health, than the normal-weight siblings. The obese siblings also consumed significantly more total calories, calories from fat, and expended considerably less energy than their slender relations (16).

It's not just nature or nurture, or a simple combination of both, that determines a person's body weight. Rather, scientists have found that a complex interaction of numerous genetic and environmental factors influence weight. Body weight seems to depend on an individual's genetic makeup coupled with his/her emotional and intellectual response to environmental conditions. As demonstrated by the thin and obese sibling study described above (16), for some people nature and nurture combine harmoniously, yielding a healthy body weight, whereas for others these factors collide, resulting in weight gain.

ACTIVITIES

1. Dr. Kelly Brownell of Yale University has proposed a "bad foods tax" to reduce the rate of obesity and obesity-related diseases in the United States. Dr. Brownell contends this approach is no different than taxing cigarettes to make smoking less attractive. What do you think? Write a brief essay either supporting or rejecting his proposal.

2. Visit the Johns Hopkins' **IntelliHealth Fattest Foods** site and take the "Find the Fattest Foods, but Calories Still Count" quiz. **http://www.intelihealth.com/IH/ihtIH/EMIHC000/408/20920.html**

3. Test your knowledge of portion size at the **phys.com** site. **http://www.phys.com/b_nutrition/02solutions/05portion/finalkey.htm**

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