Exercise and Diet: Different Tools for Different Jobs

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Excessive body weight is detrimental to health and survival, with the exception of rare circumstances in which obesity plays a protective role: a phenomenon known as the "obesity paradox."[1-4] The list of co-morbidities related to obesity is long and includes: type 2 diabetes, hypertension, coronary artery disease, congestive heart failure, pulmonary embolism, stroke, asthma, sleep apnea, back pain, osteoarthritis, hepatic steatosis, cholelithiasis, and various malignancies.[5] The negative impact of obesity on mental health is substantial as well.[6] Yet the prevalence of obesity has been rapidly increasing, reaching the level of a global epidemic.[7-8] Moreover, despite the apparent plethora of scientific research on obesity, its clinical management remains extremely difficult and frustrating.[9]

Misconceptions About Exercise

Initially, clinicians based their understanding of obesity on the simplistic paradigm of imbalance between energy intake and output. In this model, caloric content of diet represented the energy input, while "burning calories" through physical exertion corresponded to energy output. Therefore, it seemed that simply decreasing caloric intake and/or increasing energy output by exercise should be an easy cure for obesity. Surprisingly, giving the logical advice to "eat less, exercise more" failed miserably to deliver the expected weight loss. Clearly, biological organisms are not basic thermodynamic systems, which would conform to the first law of the thermodynamics with mathematical precision. There are myriad confounding factors that influence energy homeostasis in humans. These include genetics, the complexity of appetite regulation, the psychology of eating habits, and survival biomechanisms that favor the energy gains over losses. Unlike in the inanimate thermodynamic system tested in the laboratory, there is no equipotency between the effects of caloric restriction and exercise-induced energy losses in the organism living in the real world. Any diet resulting in a decrease in caloric load will cause a notable weight loss.[10] However, even the most strenuous exercise produces an effect much lower than predicted.[11-12] This asymmetry is very counterintuitive. Unsurprisingly, the myth about the equivalency between restricting energy input and increasing energy output in weight control persists. Despite educational campaigns, many clinicians, fitness coaches, and patients wrongly believe that intensive exercise is better than or as good as diet for losing weight.[12]

There are several reasons why exercise programs should not be the primary strategy for weight control, although methods of decreasing body weight by limiting energy input are fraught with problems. Compliance with calorie-restrictive diets is difficult, especially in the long run. The body's survival mechanisms favor energy accumulation over losses. There are hedonic eating mechanisms in addition to simple homeostatic processes involved in a control of food intake.[13-14] The human neuroendocrine system is set to provide the reward for eating and punishment for starvation. All those reasons may create the impression, for the unsophisticated observer, that calorie restrictive diets do not work in the real world. Such diets do work but are very difficult to follow because of those physiological determinants. Many attempts have been made to override the problems with calorie-restrictive diets. Pharmacological and surgical interventions have been developed to decrease energy intake by appetite suppression or by interfering with absorption of nutrients. Their goal was to override the pre-set tendency to noncompliance with calorie-restrictive regimens. Unfortunately, the efficacy and safety of pharmacological therapies of obesity have been disappointing. The methods of bariatric surgery have proven to be more effective, but are expensive, burdensome, and risky.

These disappointments renewed interest in the use of exercise as the primary measure of weight control. Theoretically, such an approach offers numerous advantages. In a contrast to dietary restriction, exercise triggers reward systems resulting in mild euphoria.[15-16] Beneficial effects of regular exercise on physical and mental health, independent of weight loss, are well documented.[15,17,18] It would appear that putting the emphasis on the exercise as the primary method of weight control would be a win-win situation. However, as was shown during the studies of the trendy paleo-lifestyle concept, such theory-driven conclusions may be very wrong.

Debunking the Paleo Myth

The evolutionary discordance hypothesis (EDH) attempted to explain the recent obesity epidemic by propounding that advanced civilization has reduced the level of physical activity, and therefore, decreased energy expenditure.[19-20] This notion is plausible since the rise in the prevalence of obesity correlates with the increase in sedentary lifestyle brought about by society's technological advances. Similarly, EDH proposed that qualitative and quantitative changes in diet caused by civilization's advancements should be blamed for proliferation of numerous chronic conditions in addition to obesity, such as diabetes, hypertension, and heart disease.[20] Some authors theorized that if only humans could return to "the good old days unspoiled by technology," the general health of the population would improve. However, other researchers noted that this reasoning may be too simplistic, since based on available historical records, mortality was very high in the remote past. Therefore, most people would simply die before they could develop the many chronic diseases that plague today's societies.

Many self-appointed health advocates started to promote the idea that the Paleolithic era was a golden age of humanity.[21-22] According to them, in those ancient times the lifestyle of humans was the healthiest. The level of physical activity was high while the diet was healthy, since it was protein-fat based and contained almost no simple sugars. Those speculations about diet, however, may not be correct. There are tribes around the word that still live in isolated settings similar to those of that period. Using cutting-edge research methodology, Pontzer et al. have extensively studied such tribes of hunters-gatherers.[23-26] Their findings contradict many stereotypes regarding Paleolithic communities. Moreover, those findings provided the impetus for additional research that solved the enigma of asymmetry between effects of exercise and diet on weight loss.

Pontzer's group started by examining energy homeostasis in the African Hadza tribe, which lives in conditions similar to those in the Paleolithic era.[27] The following are the highlights of their most pertinent findings.

The total energy expenditure (TEE) of Paleolithic-like people is not different from 21st century city dwellers, because energy expenditure is constrained. While the daily level of active exertion of hunters-gatherers from the Hadza tribe was much higher than that of Westerners, this was compensated by the lowering of their basic metabolic rate (BMR) and non-exercise activity thermogenesis (NEAT). In result, Hadzas, despite being more physically active than modern Americans, burned exactly the same number of calories.[23-24] This breakthrough discovery led to additional studies of TEE, which revealed that, contrary to conventional wisdom, TEE does not increase in a linear additive fashion.[25, 26, 28] The traditional additive TEE model, which assumed that increase in physical activity translates into the linearly proportional energy output, had to be replaced by the constrained TEE model. In the latter paradigm, TEE initially increases with physical activity, but it plateaus at a certain point.[25] Therefore, the body "constrains" its energy losses by maintaining TEE within a restricted range.[25-26] This is achieved by the compensatory decrease in the components of TEE that are not related to physical activity, namely BMR and NEAT. Hadzas are lean, but not because they are burning a lot of calories due to high level of physical activity. They simply do not overeat.

The Paleolithic diet is not low in sugar. Paleolithic health theorists have overlooked the role of honey. Bees are as prevalent in the areas inhabited by Hadzas as they were in the Paleolithic period. Foraging honey is much simpler for hunter-gatherers than hunting. For Hadzas, honey is one of the staples of their diet.[29] They consume on average more than 1-2 liters of honey per day. Honey is a super-saturated sugar solution containing mainly fructose and glucose, but only small amounts of protein, enzymes, vitamins, and minerals. This unexpected excess of simple sugar in the diet of hunter-gatherers did not have any impact on rate of obesity or rate of diabetes. Hadzas' diet contained a lot of sugar, but their total daily caloric intake was much lower than that of Westerners. Again: they did not overeat.

Paleolithic-like hunter-gatherers do not have shortened lives. Hadzas live to their 60s or 70s.[23-24] This perhaps has to do more with the favorable climate than with diet or exercise.[27] In Tanzania, Hazdas' homeland, February is the hottest month, with an average temperature of 82°F, while the coldest is July at 75°F. December has the most daily sunshine hours (10). The wettest month is April with an average of 401 mm of rain. Therefore, this climate is neither too cold, too hot, nor too humid.

The benefits of a Paleolithic lifestyle do not outweigh its drawbacks. Hadzas are slimmer than Westerners and have lower incidence of diabetes, hypertension, and cardiovascular pathologies,[30] but they have much higher incidence of communicable diseases, such as chronic microbial infections and parasitic infestations.[23-24] While the majority of those diseases are not lethal, the high pathogen burden typical for hunter-gatherers substantially decreases their quality of life.

All those findings were confirmed by studying other remote tribes (Shuar and Tsimane) living in South America.[31-32]

Realistic Benefits of Exercise

The above research shows that exercise alone is clearly not the solution for the world obesity epidemic. Nevertheless, it is still a very useful tool for clinicians, though it can be used properly or misused. The adage *modus omnibus in rebus* (moderation in all things) also applies to exercise regimens.

The terminology related to exercise requires clarification. Exercise is not synonymous with physical activity.[18] Physical activity constitutes any bodily movement resulting from the function of skeletal muscle that increases the energy output beyond the basal level. Physical activity can be related to transportation, occupation, housework, or leisure. The term "exercise" denotes a deliberately structured type of physical activity that is planned, recurring, and performed specifically to maintain or enhance various aspects of physical fitness.[33]

Exercise has many strong, well-evidenced benefits in addition to its modest impact on obesity. Systematic exercise decreases all forms of mortality in all individuals, male and female.[17,34] This beneficial effect of exercise is initially linear, but it may plateau with time.[33] It starts at a relatively low level of effort. Even so-called weekend warriors, who engage in only one to two short-lasting exercise periods (no longer than 75 minutes) per week have a substantial decrease in all-cause, cardiovascular, and cancer-related mortality in comparison to sedentary subjects.[35]

A sensible exercise regimen is an obligatory part of a lifestyle modification regimen in prevention and treatment of diabetes. As little as 150 minutes per week of moderate-intensity exercise resulted in beneficial effects in adults with pre-diabetes.[36] Similarly, such a moderate level of exercise was demonstrated to improve insulin sensitivity in children.[37] The beneficial impact of exercise on metabolism extends also to the prevention of gestational diabetes mellitus.[38] A moderate exercise program of at least 8 weeks' duration can lower HbA1c by an average of 0.66% in patients with type 2 diabetes, even without a significant change in body mass index (BMI).[39] Due to increased cardiovascular fitness, greater muscle strength and improved insulin sensitivity, regular exercise also benefits patients with type 1 diabetes independently of weight loss.[39]

Formal exercise programs have been shown to be beneficial in primary and secondary prevention of coronary disease.[17,33] Adhering to the regular exercise correlates inversely with the frequency of cardiac events and cardiovascular deaths.[40] Even moderate exercise reduces the risk of cerebrovascular events.[41,42] Those effects of exercise are independent of weight loss and are likely mediated by its beneficial impact on lipoproteins,[43] hemostatic factors,[44] inflammatory responses,[45] and blood pressure.[46]

Exercise decreases the risk of developing breast, endometrial, prostate, intestinal, and pancreatic cancers.[47] Exercise programs increase survival rate and alleviate cancer-related fatigue in patients with malignancies.[48,49] Therefore, exercise should be a part of oncological therapies.

People who follow a moderate exercise program have lower incidence of infections and respond better to stress as compared with those who lead a sedentary life.[45,50,51] Those effects are mediated by modulation of the sympathetic nervous system, hypothalamic-pituitary-adrenal axis, and action of stress proteins (e.g. Hsp72).[51] Sensible exercise restores immuno-neuroendocrine stabilization in patients whose inflammatory and stress responses have been deregulated due to a chronic illness or acute trauma.[51]

Weight-bearing exercise (WBE), sometimes referred to as "boning up," is a proven preventive and therapeutic measure for osteoporosis.[52,53] A "minimum of 30 minutes of physical activity (such as brisk walking) on most, if not all, days of the week" is recommended by the U.S. Surgeon General.[33] It was believed that pressure exerted on bones during exercising stimulated bone formation. However, the mechanism of beneficial effects of WBE in osteoporosis is more complex. The actual impact of WBE on increasing the areal bone density is quite small.[33,54,55] It appears that WBE reduces the risk of fractures in patients with osteoporosis primarily by increasing muscular strength and thus decreasing the risk of falls.[33,54,55]

Sarcopenia, the age-related degenerative loss of skeletal muscle mass, quality, and strength, which may lead to frailty and disability in the elderly, may be slowed by exercise, likely through the action of apelin.[56,57]

Regular exercise prevents and improves symptoms of cholelithiasis, as confirmed by a large prospective cohort study. Independently of weight loss, 30 minutes of endurance-type training five times per week has decreased the emergence of symptomatic cholelithiasis by 34%.[58]

When combined with a cognitive-behavioral smoking cessation program, vigorous but not moderate exercise improves short-and long-term smoking cessation results.[59,60] It also improves physical endurance and well-being in ex-smokers.[59,60]

Both moderate and vigorous exercise improves executive function in young and older, otherwise healthy adults, regardless of baseline cognitive status.[61,62]

Regular exercise causes a mild euphoria and reduces anxiety and depressive symptoms, improving the physical and psychological quality of life.[33,63,64] Those well-known effects of exercise are mediated by the release of endorphins and endocannabinoids.[15,16]

Risks of Exercise

Like any therapeutic intervention, exercise programs are not risk-free. In most patients, any plausible risks of routine exercise do not offset its benefits. Nevertheless, physicians should be aware of the potential drawbacks of exercise and consider them while making recommendations.

Musculoskeletal injuries are the most common risk of exercise.[33] These include acute sprains and tears, chronic strains, inflammatory states such as bursitis or tendonitis, overt traumatic or latent stress fractures, and various traumatic and ischemic neuropathies.[65] Risk is related to age, physical and mental status, comorbidities, type of exercises (e.g. contact sports vs. casual walking), and duration of exercise.[33] When recommending exercise, it is important to let patients know that too much of a good thing can be harmful, and that it is better to be safe than sorry. Types of exercise that are too strenuous for a specific patient should be discouraged, and the use of protective devices encouraged.

Asymptomatic exercise-related muscular damage, with subclinical myoglobinemia, myoglobinuria, and increased creatine kinase level, is quite common.[33,66] This phenomenon is usually clinically irrelevant and self-limiting. It can cause a false alarm when those abnormalities are detected accidentally and misinterpreted as signs of serious pathologies. However, overt severe rhabdomyolysis (SR) may occur when the supply of energy to the muscular tissue becomes too limited to meet its demands. This can occur in healthy subjects upon extreme exertion, especially during very hot and humid weather. SR can be triggered by moderate effort in patients affected by vascular conditions, myopathies, or hemoglobinopathies such as sickle cell anemia. SR is a life-threatening condition and may lead to compartment syndrome, acute renal failure, and serious electrolyte abnormalities (e.g. hyperkalemia, metabolic acidosis).[33,66]

Cardiovascular events are less common but constitute the most serious risks of exercise. They include arrhythmia, sudden cardiac arrest, and myocardial infarction.

Exercise-induced arrhythmias typically occur in patients with underlying heart problems. Unfortunately, many such patients have latent genetic conditions, which are asymptomatic until they start to exercise.[67,68] The most common exercise-induced arrhythmias such as atrial fibrillation and flutter can present with multiple dramatic symptoms, but they are not lethal and respond well to treatment.[68] It is noteworthy that sinus bradycardia and atrioventricular conduction blocks are common in athletes but usually cause no symptoms and likely represent a form of adaptation.[68]

Sudden cardiac death (SCD) triggered by exercise is the most devastating albeit very uncommon complication. Its pathogenetic mechanisms involve arrhythmias (e.g. ventricular tachycardia and ventricular fibrillation), coronary artery disease, structural heart disease, congenital abnormalities (e.g. hypertrophic cardiomyopathy) and myocarditis.[33,69]

Because of the risk of myocardial infarctions, cardiologists frequently call exercise a "two-edged sword" in patients affected by coronary artery disease. On one hand, strenuous exercise in previously untrained people with coronary artery disease increases the risk of myocardial infarction. On the other hand, a moderate and gradual exercise program reduces its risk.[33,68]

Transient, reversible bronchoconstriction that develops after strenuous exercise is called exercise-induced bronchoconstriction (EIB).[70] It has a vast spectrum of pathologies. It may occur in apparently healthy people who respond to exercise with bronchoconstriction either due to a genetic condition, or secondary to injury caused by excessive exercise.[71] Typically, however, it occurs in patients with symptomatic asthma.[33] Exercise in asthma can also be seen as a "two-edged sword." Vigorous exertion can trigger asthmatic episodes in sedentary patients. However, a progressive exercise regimen may prevent EIB by reducing the minute ventilation required for a given level of exercise and therefore attenuating the bronchospastic stimulus.[33]

It is well recognized that an excessive exercise regimen may induce oligomenorrhea, amenorrhea, and infertility in women. The so called "female athlete triad" seen in young women consists of disordered eating, amenorrhea, and osteoporosis.[72] It is less appreciated that intense exercise may also induce hypogonadism in males.[73]

Hyperthermia and hypothermia are very common and preventable problems, which could deter sedentary patients who start an exercise program.[33] Hyperthermia can cause a wide range of complications from mild fatigue through cardiovascular problems, to heat stroke and death.[74] Hypothermia can negatively impact the immune system, resulting in frostbite and cold sores, and can also cause cardiac problems. Elderly and chronically ill patients should be advised to exercise in air-conditioned facilities during extreme weather. Wearing proper exercise attire (e.g. "dressing in layers") is a common-sense measure that is often neglected.

Severe hypoglycemia is uncommon in non-diabetic individuals, due to a redundant counter-regulatory system. However, mild to moderate lowering of blood glucose occurs frequently during intense exercise (e.g. marathon run), due to a discrepancy between increased fuel demand and a limited supply of glucose from glycogenolysis and gluconeogenesis. This exercise-induced hypoglycemia (EIH) results in severe fatigue, impairs thermoregulatory adaptation, and has a negative impact on muscle metabolism.[75] It is preventable by adequate pre-exercise feeding with complex carbohydrates ("carb loading"). Exercise may induce severe hypoglycemia in diabetic patients, especially those with type 1 diabetes who are affected by hypoglycemia-associated autonomic failure.[76] Proper adjustment of diabetes management as well as hypoglycemic reaction preparedness (e.g. glucose pills, glucagon kit) are necessary.[77]

Dehydration and dyselectrolytemia are very common during exercise.[78] Severe hyponatremia and hypokalemia occur frequently in athletes participating in endurance events (e.g. marathons, triathlons, cycling, or swimming).[33] Some clinicians believe that these electrolyte imbalances are responsible for exercise-associated muscle cramps (EAMC).[78] However, this notion has been negated by recent studies.[79]

Independent of their connection to EAMC, dehydration and dyselectrolytemia can exert various negative effects on the cardiovascular and nervous systems, causing disturbing symptoms. Consequently, the use of various over-hyped rehydrating with "sports drinks" became an essential part of exercise programs.[80] Such "sports drinks" are flavored, sweetened beverages containing numerous non-essential electrolytes, vitamins, and "performance enhancers" (e.g. caffeine, amino acids). Evidence for this approach is lacking.[81] Since the research regarding value of "sports drinks" is inconclusive, the most sensible approach is to encourage the judicious use of simple rehydration fluids containing only water, sodium, and potassium.

The Alzheimer dementia paradox was noted in the Dementia and Physical Activity (DAPA) trial, in which the mean score on the Alzheimer's Disease Assessment Scale-Cognitive Sub-scale (ADAS-cog) became worse for subjects affected by dementia who underwent a much more strenuous exercise regimen than is routinely recommended.[82] It is difficult to reconcile why moderate exercise in healthy individuals is protective against cognitive decline, while vigorous exercise in patients with dementia has a detrimental effect. It has been suggested that this outcome may be secondary to periodic hypoxemia associated with vigorous exercise. Veracity of this hypothesis remains to be established.

The elite athlete paradox is the observation that elite athletes who engage in extremely intense forms of physical training are more susceptible to infection and have decreased levels of well-being. This phenomenon results most likely from the exaggerated anti-inflammatory effects of exercise, which lead to maladaptive immunosuppression.[45]

Conclusions

In contrast to the predictions of theoretical models, energy loss is constrained but energy gain is not in human metabolism. This explains the counterintuitive asymmetry between the disappointing effects of exercise and the good results of strict adherence to calorie-restrictive diets in the management of obesity. Despite all the benefits of exercise, "one cannot outrun the bad diet."[26] While exercise is a helpful adjuvant to weight control and a part of lifestyle modification strategies to improve general health, strict compliance with a calorie-restrictive diet—not vigorous exercise—should be the mainstay of obesity management. Diet and exercise are different tools for different jobs.

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