

Effect of regular exercise on health and disease

Kursat Karacabey

Gaziantep University, School of Physical Education and Sports, Gaziantep, Turkey

Correspondence to: Dr. Kursat Karacabey
Gaziantep University, The School of Physical Education and Sports
(Beden Egitimi ve Spor Y.O)
TR 27100, Gaziantep, TURKEY
TEL: +90 0342 3601616 ext 1400
FAX: +90 0342 3600751
EMAIL: kkaracabey@hotmail.com

Submitted: October 10, 2005

Accepted: October 15, 2005

Key words: **physical activity: immune system: diseases: exercise**

Neuroendocrinol Lett 2005; **26**(5):617-623 **PMID:** 16264392 NEL260505A30 ©Neuroendocrinology Letters www.nel.edu

Abstract

It is known for a long time that exercise increases physical adequacy, has beneficial effects on the general health condition as well as a playing preventing role against various disease states.

To decrease the risk of disease and maintain good health, the natural defense system of the organism needs to be strengthened. It is thought that in addition to increasing the body's resistance to disease through the strengthening of the immune system, decreases the convalescence time, increases work efficiency and improves the sportive performance of the individual all which would contribute positively to the national economy.

The positive effects of regular exercising of aerobic nature such as strengthening of the immune system, protection against diseases as well as its positive effects on quality of life will help to emphasize the importance of physical exercise and improve the general view of sports by society.

Introduction

It is a well known truth that there exists a large group of individuals who are willing to participate in regular exercise programs but who for various reasons are not able to do so. Even some individuals from this group have for a particular time in their lives participated in one form of sportive events and still look back to such days. These individuals, though well aware of the benefits of exercise in daily life, are still not able to see this dream materialize. The remaining group however, is not aware of the benefits of physical activity.

In the end, it can be said that in the society there exists individuals who are just waiting for a spark or driving force to join in regular exercise programs.

Also, those who happen to take part in activities of any kind can be in need of the driving force to keep them going. Just as teachers try to convince their students to exercise, so do families to their children and doctors to their patients. However, most often their efforts are in vain. To be able to instill this driving force, individuals in general are encouraged to do so for their own benefit. In rare cases, however, events likely to affect the point of view of the individual to be motivated are conveyed. This is because an individual at conflict with his/her driving force is preoccupied with his own thoughts of what is appropriate and acts accordingly [43].

Exercise and Diseases

In exercise the factors that affect the immune response and at the same time responsible for its benefits can be grouped into four. These are; improving the general well being of individuals, protecting the health of the sportsman/sportswoman, treatment of patients with cancer or AIDS, and psychoneuroimmunology applied to investigate the immunology of behavior [39,40]. In the light of this information, it is clear that beneficial effects of exercise on individual health state presents 3 aspects while increasing sportive performance stands only points, and this highlights the importance of exercise with respect to the public health. Moderate level of regular exercise has been demonstrated to play an important role in the prevention and treatment of diseases like heart disease, obesity, non-insulin dependent diabetes mellitus (Type II DM), hypertension, and osteoporosis as well as controlling body weight and increasing the resistance of the organism against stress [21,43]. Recently, investigators have focused their studies on diseases with factors dependent on lifestyle (like cancer). Predictions of lower cancer incidence among individuals engaged in regular exercise have been effective on this issue [28].

Lifestyle factors can interact to augment or weaken the immune system response. Diet, stress and physical activity constitute these factors. Inadequate nutrition and deficiency of appropriate nutrients might also weaken the immune system. Factors like sleep, diet, and stress are now regarded as the basic components of physical exercise that affect our life [32].

Undoubtedly, dissemination of information about the benefits of exercise and its effect on the immune system on regular basis will be all important to the health of mankind.

Exercise and Mental Health

Physical activity also improves depression, and anxiety and to a lesser degree panic disorders. Exercise raises the perceived energy level and self confidence and improves the feeling of positive approach of the patient [18].

Mental stress, inadequate nutrition, rapid weight loss, poor hygiene and impaired immunity may occur together. Each one of the above factors acts in synergism with the stress of exercise on the immune system in sportsmen/women exposed to vigorous exercise.

Mental stress may weaken the immune system [3,33,47]. Changing a home, divorce, family problems and extreme anxiety have also been shown to weaken the immune system [47]. Moderate activity lifestyle, avoidance of stress and adequate resting time are the most powerful weapons that lend support to the immune system.

The benefits of physical exercise on mental health and perceived energy are more prompt and dramatic in development than physical health to patients [17].

Epidemiological studies have shown exercise to be linked to a reduced depressive and anxiety symptoms.

Exercise has also been found to be related to positive affect and personal good feeling. However, the effect of exercise on sleep and several mental diseases like eating problems, schizophrenia, dementia, personality changes and substance abuse have not been widely studied [4,8].

Inasmuch as studies showing the protective effect of exercise against depression are available many more are still required [4]. Paffenbarger et al., in their study in which diagnosis was made either by a doctor or reported by the subjects themselves in 1988 found depression to be related inversely to exercise. Men who exercised for three hours or more per week were found to have relative risk of depression 27% lower than that for those who never engaged in sporting activities [45].

In general inactive individuals are reported to exhibit more depressive symptoms than active individuals. Reports on the protective effect of exercise against development of depression have all been positive [45]. Efforts have been made to explain the effect of physical activity from various psychological, physiological and biochemical view points. Exercise increases the persons feeling of power psychologically. A small but significant relation has been found between exercise and self esteem. With exercise the attention of the patient is shifted from anxiety and feelings of guilt to something else. Also, improvement in the health, physique, and flexibility and responsibility of the individual positively affects his/her spirit [4,39].

In addition to this, there are findings that the beta endorphin and mono-amine concentrations increase with exercise and as a result of the increase in body temperature muscle tone falls which is interpreted by the individual to be psychological relief [17,39].

Exercise and Upper Respiratory Tract Infections (URTI)

In all epidemiological, clinical and experimental studies moderate exercise has been demonstrated to lead to a fall in the incidence of upper respiratory tract infections [9,12,13,16,20]. In a study in which subjects exercised for 15 weeks by walking, a fall in the incidence of URTI among women in the study group was observed [36]. In vigorous exercise however, an increase in URTIs was observed [40,46,49]. Here, the desired exercise type is a regular, moderately intense exercise performed over a long time period.

In individuals leading sedentary lives whereas URTIs occur to a certain degree it is decreased in those engaged chronically in moderate degree exercise but increased in those engaging in exercising vigorously. At least for this reason, exercise and the immune system are important [9,14,31,34,38]. URTIs are responsible for great work force and financial losses as well as time and when severe enough may even cause loss to life.

Cancer and Exercise

Within the last 10 years the effect on cancer and its various types have been the focus of several studies [19,29]. Experimental studies have also found exercise to increase the resistance against tumorigenesis [30,43]. In one study that examined the effect of energy balance on these effects the investigator suggested that with exercise the increased energy requirement retards the growth of the tumor [43,54]. In addition to that the basic mechanism is thought to be immunologic.

Findings supporting the fact that physical activity leads to low colorectal cancer are available. The relative risk of colon cancer is reportedly 1.3 to 2 times higher in sedentary individuals than their active counterparts. In the Harvard study male individuals with age at enrollment between 30 and 79 were followed for intervals of 11 and 14 years and their activities at leisure including climbing of stairs, walking and engagement in sporting activities were noted. According to these results those involved actively in sports (> 2500 kcal/week) or moderate activity had a risk of colon cancer reduced to more than half that for inactive individuals [30]. Physical activity reduces the incidence of breast and other urogenital cancers in women [29,30]. Inasmuch as the relationship between the development of cancer in other body parts and exercise have not been studied widely, data showing a reduction in lung, thyroid, the gastrointestinal system and haematopoietic system cancers with exercise are available [43,52].

Results of studies conducted on breast and colon cancer at the University of California seem undebatable; according to this study the risk of breast cancer among women engaged in regular exercise was significantly lowered. Women engaged in regular exercise of 1–3 hours duration every week had a 30% reduction while those performing for 4 hours and over had a 55% reduction in the risk of breast cancer [55].

Exercise and the Endogenous Opiate System

Aerobic exercise enhances the secretion of endogenous opiates like endorphin and met-enkephalin. These hormones provide a state of good self feeling and euphoria [8]. In well trained sportsmen they create the urge to exercise. This is like a vicious cycle and is held responsible for the “exercise withdrawal syndrome”. Stress is thereby eliminated. These hormones also have direct effects on the immune system [47].

Hypertension and Exercise

Scientific studies report regular exercise as protecting the elasticity of arteries. Blood flow is regulated and blood pressure thereby regulated. Individuals leading sedentary lives have a 35% higher risk of developing hypertension than sporting individuals [2,48]. No one with hypertension should engage in an exercise program without first consulting a doctor. Vigorous exercise does not reduce the blood pressure like moderate exercise. In one study moderate exercise (jogging for 2 km a day)

was equally effective in regulating the blood pressure in about one half of the patients on drugs. Also, relaxation exercises contribute to blood pressure reduction as moderate exercise [22]. In individuals who exercise regularly through isotonic exercise an increase in the vasodilator prostaglandins, and a fall in the plasma renin activity and plasma viscosity has been demonstrated. In hypertensive isotonic exercise that includes more muscle movements is recommended [26,43].

General inactivity, like high blood pressure, poor cholesterol control and cigarette smoking is one of the four major risk factors for cardiovascular disease and its equivalents [21]. The frequency of exercise is more important than its duration [44]. Children should be encouraged to exercise to prevent against possible heart disease in their future lives.

Cholesterol and Coronary Artery Diseases

Individuals leading active lives have a more than 45% reduction in the risk of coronary disease than those leading sedentary lives [25]. Regular aerobic exercise including walking jogging, swimming, cycling and aerobic dancing is the best method of controlling levels. For a significant change in the level of cholesterol exercise need to be continued for at least a year.

Burning approximately 250 kilocalories per day (approximately 45 minutes of brisk walking) protects significantly against coronary arterial diseases [43]. Resistance (weight lifting) exercises additionally contribute to lowering of the ‘bad’ cholesterol level. Exercise increases the oxidation of ‘bad’ cholesterol [27]. Triglyceride levels which become elevated after meals can be reduced by a 90 minute aerobic exercise [27,29].

Osteoarthritis

Osteoarthritis a disease characterized by progressive loss in joint cartilage with reactive changes in subchondral bone and periarticular areas of joints occurring in the back, knees, pelvis and fingers. This disease is most common among individuals of age 70 years and above [15]. It limits the physical activity of affected person significantly. Pain, bradypragia (tutuluk), fatigue and fear of injury make exercise less attractive to individuals. Exercise stamina helps in developing muscle power and elasticity, and also helps protect against bradypragia and pain, weight loss and regulation of body weight. In inactive individuals the bone mineral density is lower than in exercising bones which adapt to bear the stress of exercise [43,49].

Arthritis patients should avoid highly vibrant sports activities like jogging, tennis and basketball. Three exercise types are recommended for arthritis patients; aerobic fitness (involving movement of all joints), resistance training and stretching exercise [15,49]

Osteoporosis

This is a metabolic bone disease characterized by an absolute reduction in bone mass. Loss in bone tissue increases the risk of fracture. Sixty percent of women above 60 years and 30% of men are at risk of osteoporotic fractures [8].

Prevention and treatment of osteoporosis is divided into three sections; initially (calcium-intake), hormonal treatment (and other drugs) and exercise. Whereas calcium-rich diet and hormone/drug treatment are well understood exercise still remain to be comprehended. According to results of studies conducted increase in mineral density and reduction in the decrease in bone loss have been reported.

Exercise has been very effective in arresting the development of osteoporosis. Women need to start exercising from adolescence when bone mass starts to increase reaching peak levels at 20–30 years. Isometric exercise is beneficial to all including those aged 90 years [43,53].

Weight-bearing type exercises are very effective in preventing osteoporosis. This type of exercise includes that carrying the body against the pull of gravity. Jogging, walking aerobic stepping exercise, dancing, tennis and basketball are among this type of sports. This kind of exercise is important for the formation of bone mass and contributes to ensuring that bone mass reaches its maximum level.

Severe exercise reduces the levels of female hormones (estrogen-progesterone). Low levels of these hormones may lead to interruptions in the menstrual cycle. The best benefit is obtained through long-term regular walking. Careful weight lifting can also be beneficial to old women. Less stressing exercise regulates muscles of balance and strength. Weight bearing type exercise through the application of tension to muscles and bones leads to a 2.8% increase in the bone density [8,43]

Exercise leads to an increase in the formation of more bone mass in childhood and adolescence while protecting against osteoporosis in adulthood [43].

Exercise and Coronary Heart Disease

Most of the positive developments of exercise on the health status of man have been conducted on the prevention of coronary heart disease (CHD) [2,42]. Review of epidemiological studies on this issue revealed a strong but inverse relationship between exercise and CHD. In some study groups more than one follow-up studies have been conducted. In older studies lower CHD risk has been described in individuals involved in active sports than in those leading sedentary lives with the relationship being an inverse one without any dose-response curve shown. Recent studies, on the other hand, show an inverse dose-response curve for the relationship between exercise and CHD [43,53].

Exercise improves oxygen supply to the myocardium by limiting the progression of atherosclerosis and through the formation of collateral coronary arteries or by enlargement of the diameter of the lumen of

the coronary arteries close to the center [42,55]. Also, thorough exercise induces potential positive changes in the blood coagulation-fibrinolysis activity and plasma lipoprotein profiles which in turn lead to an increase in the coronary blood flow. Exercise by causing a fall in the resting heart beat and systolic blood pressure leads to reduction in the myocardial oxygen demand [27,37]. Exercise also reduces obesity, a CHD risk factor and the incidence of type 2 DM as well as redistribution of body fat [7,53,51].

Exercise and Diabetes Mellitus

Diabetes Mellitus which is not a single disease entity is a disease group characterized by an absolute or relative insulin deficiency and affects about 150 million people worldwide [11]. Type 1 diabetes is defined as deficient insulin in the blood due to an autoimmune-mediated destruction of the beta cells of the pancreas [5,7].

Physical activity is recommended for both healthy and diabetic patients [1]. In type 1 diabetics exercise together with improved blood sugar control retards the progression of the thickening process of the basal membranes of blood capillaries, decreases the arterial pulse volume and increases the fat-free body mass as well as the work capacity [7,43].

Enormous evidence supporting the relationship between physical activity and type 2 diabetes mellitus is available. Societies in which the traditional lifestyle has been changed including regular physical exercise the prevalence of Type 2 diabetes mellitus has been found to be overwhelmingly great. Comparative studies showing the importance of lifestyle has demonstrated that individuals who migrate from a technologically less developed to a more developed country have a higher prevalence of Type 2 DM than their unmigrated native ethnic group [7,24,35].

Primary prevention is very important in diabetes. This type of prevention which is simple and cheap can protect individuals at risk against development of diabetes or delay in the appearance of its clinical symptoms. In China, lifestyle changes (including appropriate diet, increased physical activity and weight loss) among a population with high risk of diabetes, through an educational support program demonstrated a one-third fall in development of diabetes within the 6-year study period [7,43].

Studies in general have shown that exercise helps in protecting against development of Type 2 DM through its facilitatory action on insulin sensitivity. Exercise has been suggested to improve the abnormal glucose intolerance that results from insulin resistance rather than the deficiency in insulin per se [6,44]. For this reason, exercise in type 2 DM would be more beneficial during the early stages of DM when insulin treatment is not required [7].

Exercise protects against type 2 DM or delays its development by reducing the total body fat or specifically the intraabdominal fat which is known to be a risk factor of insulin resistance [35].

Exercise plays a decisive role in regulating blood sugar levels in diabetes mellitus patients. For this reason, to minimize the risk of hypoglycemia in patients receiving insulin treatment, special care should be taken to make adjustment for exercise by reducing the dose appropriately. Exercise should always be however, considered complimentary to intensive insulin and dietary therapy for the long term metabolic control of blood sugar and prevention of microvascular complications [7,43].

Exercise and Hyperlipidemia

Hypercholesterolemia is an important risk factor for coronary heart disease [21,27]. Due to the relationship between lipid and lipoprotein diseases and atherosclerosis, especially coronary heart disease, this topic is the focus of studies in recent years. In clinical studies decreasing the high plasma levels of low density lipoprotein cholesterol (LDL-C) has resulted in significant reduction in both the mortality and morbidity of CHD [29]. Increasing the low levels of high density lipoprotein cholesterol (HDL-C) through regular exercise is the cheapest, simplest and safest way known to date. Regular aerobic exercise can decrease body weight, blood pressure, total serum cholesterol and triglyceride levels, LDL levels and an increase in the antiatherogenic HDL cholesterol levels [27]. Epidemiological studies have shown an increase in the risk of coronary heart disease as the total cholesterol and low density lipoprotein levels rise among populations [10]

Acute and chronic exercise results in major falls in the levels of lipid and lipoproteins (*Table 1*)^{3T}.

Long distance runners and other endurance athletes generally have been found to have high HDL-C levels, especially in the HDL₂ fraction (20%–30% more than healthy non-athlete individuals) [27]. Cross-sectional studies have shown a dose-response relationship between exercise and the plasma HDL-C levels. In order to increase HDL-C exercise more vigorous than that required to maintain a feeling of good health is needed [51]

Addition of diet to an exercise program would definitely lead to a change in the lipid and lipoprotein type. While serious fat restriction results in more reduction in serum cholesterol and triglyceride levels, a lesser fall probably also occurs in the HDL level. Women with low HDL cholesterol levels due to weight losing diets out-

number men and exercise in such individuals have been found to contribute to increasing the HDL cholesterol and a fall in the LDL and triglyceride levels [27,51].

Available information reports of a fall in CETP (cholesterol ester transport protein) as being another mechanism through which exercise induces changes in lipid fractions [43,51].

Exercise and Obesity

Obesity, one of the major problems of our time (50) is a chronic disease resulting from the interplay between a person's genes and several environmental factors. It occurs as a result of changes in lifestyles to less active sedentary lives and poor nutrition that accompany technological advancement and remains an important public health problem worldwide. Obesity is a condition of excess fat defined as a body mass index (BMI) of 30 and above [23,43].

That exercise results in loss of body weight is a well known fact. Exercise without dietary restriction has been reported to lead to an average of 0.2 ± 0.4 kg per week (2,50). According to the results of another study in which exercising subjects were followed for a period of 4–6 months the loss in body weight was 2.4 kg more than that in the controls [23]. In contrast, in another study with obese women on no dietary restriction, exercising for 90 minutes 4–5 times a week at 55% their maximal oxygen consumption rate showed improvement in their aerobic capacity while their body weight increased by 2.3–2.8 kg after 6 months of exercising [29]. Despite numerous studies demonstrating that exercise alone without dietary restriction in obese patients improves cardiovascular and aerobic capacity and insulin tolerance [41], conflicting results have been reported on decreased body weight, body fat content, and body mass index. According to results from our study, therapies that combine exercise with dietary restriction can be speculated to be more effective than either treatment protocols individually. According to results from scientific studies the latest approaches to the treatment of obesity has been shifted to long-term application of dietary restriction and exercise in a combined fashion to yield more meaningful and successful results.

Table 1. ^{3T} Effects of Acute and Chronic Exercise on Lipids [51].

	EFFECTS OF EXERCISE	
	ACUTE EXERCISE	CHRONIC EXERCISE
Triglycerides	Decreased	Decreased
Total Cholesterol	No Major changes	Moderately elevated or no change
VDL-C	Reduced	Moderately reduced or no change
HDL-C	Increased	Increased

Results and recommendations

Regular and effective exercise programs are important and one of the most economic ways of protecting against diseases and supporting treatment as well as improving endurance training in developing countries like ours. However, maintaining a regular, effective and continuous exercise program is not as easy as it seems. Families, schools, institutions, city and town councils, health officers, politicians responsible for health, the media houses, and foremost primary care workers as well as all health workers have crucial roles to play.

It is important for sports scientists and physicians to receive education on exercise counseling. This is because if better physical capacity and life styles are the targets then knowing the personal goals and desires, the physical state at the present time, family structure, environment the person lives in, and the opportunities available should be known. In short, in order to help in the issue of starting and continuing an exercise program he/she needs to be evaluated biopsychosocially.

Considering diseases associated with exercise, it is important to educate primary health care workers on the benefits of providing protection against disease in healthy young adolescents with positive family histories and for continuation of motivation and support for treatment in those with chronic disease.

To decrease the risk of illness and to remain healthy, the natural defense system of the organism needs to be strengthened. For this purpose, individuals can select this natural option of regular exercise to regulate the body's natural defense system just as they can make use of routine high-cost drugs to strengthen their immune systems. Through strengthening of the immune system, it is our thought that exercise might help in contributing positively to the national economy by reducing recovery times, increasing work efficiency and raising the sportive performance of individuals.

REFERENCES

- American College of Sports Medicine and American Diabetes Association joint position statement: Diabetes mellitus and exercise 1997; **29**(12):1-6.
- Anderssen S, Holme I, Urdal P, Hjermann I. Diet and exercise intervention have favourable effects on blood pressure in mild hypertensives: the Oslo Diet and Exercise Study (ODES). Blood Press 1995; **4**:343-9.
- Arent SM, Rogers TJ, Landers DM. Determining a Causal Link Between Physical activity and selected mental health variables. Medicine & Science in Sports & Exercise. 2002; **34**:1:5.
- Artal M, Sherman C. Exercise against depression. The Physician and Sportsmedicine 1998; **26**: No. 10.
- Atalay M and David E. Laaksonen diabetes, oxidative stress and physical exercise Journal of Sports Science and Medicine 2002; **1**:1-14.
- Belke, Darrel D, Terje S. Larsen, E. Michael Gibbs, And David L. Severson. Glucose metabolism in perfused mouse hearts over-expressing human GLUT-4 glucose transporter. The American Physiological Society 2000; Abstracts 7:0247E.
- Birrer RB, Sedaghat VD. Exercise and diabetes mellitus. The Physician and Sportsmedicine. 2003; **31**: No. 5.
- Blair SN, Kohl HW, Paffenbarger RS JR, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA 1989; **3**:262(17):2395-401.
- Callow KA. Effect of specific humoral immunity and some non-specific factors on resistance of volunteers to respiratory coronavirus infection. J Hyg 1999; **5**:173-80.
- Carr DB, Bullen BA, Skrinar GS, Arnold MA, Rosenblatt M, Beitins IZ, Martin JB, McArthur JW. Physical conditioning facilitates the exercise-induced secretion of beta-endorphin and beta-lipotropin in women. N Engl J Med 1981; **3**:305(10):560-33.
- Chicharro J L, A López-Calderon, J Hoyos, A I Martín-Velasco, G Villa, M A Villanúa And A Lucía. Effects of an endurance cycling competition on resting serum insulin-like growth factor I (IGF-I) and its binding proteins IGFBP-1 and IGFBP-3 Br J Sports Med 2001; **35**:170-173.
- Daniel König, Dominik Grathwohl, Christoph Weinstock, Hinnak Northoff, And Aloys Berg.: Upper Respiratory Tract infection in athletes: influence of lifestyle, type of sport, training effort and immunostimulant intake. Exercise Immunology Review 2000; **6**:102-20.
- David B. Pyne; Warren A. McDonald; Maree Gleeson; Adrian Flanagan; Robert L. Clancy; Peter A. Fricker.; Mucosal immunity, respiratory illness and competitive performance in elite swimmers. Med Sci Sports Exerc 2001; **33**:348-353.
- David C. Nieman . Current perspective on exercise immunology. Curr Sports Med Rep 2003; **2**(5):239-42.
- Ettinger WH, Afbale RF. Physical disability from knee osteoarthritis: the role of exercise as an intervention. Med Sci Sports Exerc 1994 ; **26**(12):1435-40.
- Fitzgerald L. Overtraining increases susceptibility to infection. Int J Sports Med 1991; **12**(Suppl 1);5-8.
- Fontaine KR. Physical activity improves mental health. The Physician and Sportsmedicine. 2000; **28** - No. 10.
- Gauvin L, Spence JC. Physical activity and psychological well-being: knowledge base, current issues, and caveats. Nutr Rev. 1996; **54**:553-65.
- Giovannucci EL, Liu Y, Leitzmann MF, Stampfer MJ, Willett WC. A prospective study of physical activity and incident and fatal prostate cancer. Arch Intern Med. 2005; **9**:165(9):1005-10.
- Gleeson M. Mucosal immunity and respiratory illness in elite athletes. Int J Sports Med 2000; **21** Suppl 1:533-43.
- Guyton A.C.: Textbook of Medical Physiology 3, 1989.
- Hagberg JM, Montain SJ, Martin WH 3rd, Ehsani AA. Effect of exercise training in 60- to 69-year-old persons with essential hypertension. Am J Cardiol 1989; **64**(5):348-53.
- Hammer RL, Barrier CA, Roundy ES, Bradford JM, Fisher AG. Calorie-restricted low-fat diet and exercise in obese women. Am J Clin Nutr 1989; **49**(1):77-85.
- Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS Jr. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. N Engl J Med. 1991; **18**:325(3):147-52.
- Ivey FM, Macko RF, Ryan AS, Hafer-Macko CE. Cardiovascular health and fitness after stroke. Top Stroke Rehabil 2005; **12**(1):1-16.
- Jirayos C, David TL. Exercise in treating hypertension. The Physician and Sportsmedicine 2002; **30**:3.
- Laaksonen DE, Atalay M, Niskanen LK, et al. Aerobic exercise and the lipid profile in type 1 diabetic men: a randomized controlled trial. Med Sci Sports Exerc 2000; **32**(9):1541-1548.
- Lamarche B, Despres JP, Pouliot MC, Moorjani S, Lupien PJ, Theriault G, Tremblay A, Nadeau A, Bouchard C. Is body fat loss a determinant factor in the improvement of carbohydrate and lipid metabolism following aerobic exercise training in obese women? Metabolism 1992; **41**(11):1249-56.
- Lane K, Worsley D, McKenzie D. Exercise and the lymphatic system: implications for breast-cancer survivors. Sports Med. 2005; **35**(6):461-71.
- Lee IM, Sesso HD, Oguma Y, Paffenbarger RS. Physical activity, body weight, and pancreatic cancer mortality. Br J Cancer 2003; **88**(5):679-83.
- Liesen H. Sports Immunology. Sport Sci Rev 1992; **1**:94-116.
- Mackinnon LT. Immunity in athletes. Int J Sports Med 1997; **18** Suppl 1:562-8.
- Mackinnon LT. Chronic exercise training effects on immune function. Med Sci Sports Exerc 2000; **32**: 7:369-376.
- Mackinnon LT. Exercise and Immunology. Human Kinetics Books. 1992.

- 35 Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS, Rosner B, Hennekens CH, Speizer FE. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 1991; **28**:(338):774–8.
- 36 Maree G. Mucosal immune Responses and risk of respiratory illness in elite athletes. *Exercise Immunology Review* 2000; **6**:5–42.
- 37 Martin H, Aloys B, Hinnak N, Joseph K. Importance of TNF-A and leptin in obesity and insulin resistance: A Hypothesis on the impact of physical exercise. *Exercise Immunology Review* 1998; **4**:77–94.
- 38 Michael G. Biochemical and immunological Markers Of Over-Training. *Journal of Sports Science and Medicine* 2002; **1**:31–41.
- 39 Morgan WP. Physical activity and mental health In: Eckhert HM & Montayle HS (eds) *Exercise and health. Campaign Human Kinetics*, 1984. pp. 132–145.
- 40 Nixon S, O'Brien K, Glazier RH, Tynan AM. Aerobic exercise interventions for adults living with HIV/AIDS. *Cochrane Database Syst Rev*. 2002; **18**(2):CD001796.
- 41 Nyholm B, Nielsen MF, Kristensen K, Nielsen S, Ostergard T, Pedersen SB, Christiansen T, Richelsen B, Jensen MD, Schmitz O. Evidence of increased visceral obesity and reduced physical fitness in healthy insulin-resistant first-degree relatives of type 2 diabetic patients. *Eur J Endocrinol* 2004; **150**(2):207–14.
- 42 Onat A. Prevalence of cardiac diseases, new coronary cases and mortality due to cardiac diseases in adults. *Ohan Press Co* 2000:16–23. (In Turkish).
- 43 Ozcan S, Saatci E, Bozdemir N, Akpınar E, Ergun OG. Exercise, health, disease, public and health. *Archive* 2002; **11**:388–415. (In Turkish).
- 44 Ozmerdivenli R, Ilhan N, Karacabey K, Bicer Y. and Kutlu M. Effects of exercise types on free radical production and glucose utilization. *The Journal Of Physiology* 2000; **528**:49.
- 45 Paffenbarger RS, Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med* 1986; **6**:314(10):605–13.
- 46 Pedersen, B.K. and Bruunsgaard, H. How physical exercise influences the establishment of infections. *Sports Medicine* 1995; **19**: 393–400.
- 47 Perna FM, Schneiderman N, Laperriere A. Psychological stress, exercise and immunity. *Int J Sports Med* 1997; **18** Suppl 1:578–83.
- 48 Pescatello, LS. Exercise and hypertension: recent advances in exercise prescription. *Curr Hypertens Rep*. 2005; **7**(4):281–6.
- 49 Puett DW, Griffin MR. Published trials of nonmedicinal and non-invasive therapies for hip and knee osteoarthritis. *Ann Intern Med*. 1994; **15**(2):133–40.
- 50 Rippe JM, Hess S. The role of physical activity in the prevention and management of obesity. *J Am Diet Assoc*. 1998; **98**:(10 Suppl 2):S31–8.
- 51 Stone NJ, Blum CB, Winslow E. Management of lipids in clinical practice. *Turgut yayınevi ve Tic. A.S* 2000:185–190.
- 52 Schmitz KH, Ahmed RL, Hannan PJ, Yee D. Safety and efficacy of weight training in recent breast cancer survivors to alter body composition, insulin, and insulin-like growth factor axis proteins. *Cancer Epidemiol Biomarkers Prev* 2005; **14**(7):1672–80.
- 53 U.S Department of Health and Human Services. *Physical Activity and Health: A Report of the Surgeon General*. Atlanta, GA: Centers for disease control and prevention, National Center for chronic Disease Prevention and Health Promotion. 1996.
- 54 Visovsky C, Dvorak C. Exercise and cancer recovery. *Online J Issues Nurs* 2005; **28**:10(2):7.
- 55 Wilmore HJ, Costill LD. *Physiology Of Sport And Exercise*. Campaign, Human Kinetics Books 1999.