Relationship between physical activity and cardiovascular disease: selected historical highlights

REVIEWS

J SPORTS MED PHYS FITNESS 2007;47:84-90

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Selected historical highlights

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The full awareness that physical exercise represents a form of prevention and therapy for cardiovascular diseases is rather recent, considering that the discovery of blood circulation dates back to the 17th century and that the definition of major cardiovascular risk factors is an acquisition of the 20th century. In this paper a historical review has been undertaken so as to evidence major selected highlights of cardiovascular knowledge applied to physical activity from antiquity to the present day. Despite of the fact that the role of physical activity for the sake of a good body equilibrium is an ancient concept, as documented by the recurrent term "exercise" in the works of Hippocrates, only about 70 years have passed from the time when, in the '30s, myocardial infarction patients were strictly advised to observe a period of bed rest of at least 6 weeks; less than a century has passed since the so-called "chair therapy" constituted the cornerstone of the therapy of the cardiovascular patient. In the '40s and the '50s a certain amount of attentive mobilization proved to be beneficial, given that it was associated with a remarkable reduction of thromboembolic risk. In the '70s an increasing amount of clinical literature documented that even healthy subjects, remaining in bed for a long period, showed relatively rapidly signs of de-conditioning. In 1973 Kavanagh *et al.* demonstrated that the patients included in cardiac rehabilitation showed an improvement in their physical work capacity, an increase in their global cardiovascular function and went back more quickly and safely to their work environment, as compared with cardiac patients not performing rehabilitative physical exercise. The studies performed in the '70s provided the bases of modern cardiovascular rehabilitation, a multidimensional and integrated approach, one of whose pillars is structured physical activity.

KEY WORDS: Motor activity - Cardiovascular diseases, prevention and control - Rehabilitation - Evidence-based medicine - History of medicine.

Source of support: none. Funding to declare: none. Conflict of interest statement: none.

Acknowledgements.—The authors would like to thank Professor L. Camaiora, B.A., M.Phil., for her correction of the English.

Received on September 20, 2005.
Accepted for publication on December 21, 2006.

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Physical exercise in history

The full awareness that physical exercise represents a form of prevention and therapy for cardiovascular diseases is relatively recent, considering that the discovery of blood circulation dates back to the 17th century and that the definition of major cardiovascular risk factors is an acquisition of the 20th century.[1]

The role of physical activity for the sake of a good body equilibrium is, on the contrary, a more ancient concept: the term "exercise" is often mentioned in the works of Hippocrates, and in ancient Greece therapeutic exercise was prescribed by physicians and gymnasts.[2] In classical Greece the cult of the body, even before being offi-

cially sanctioned by the Olympic Games, was observed in gymnasia, precisely on the basis of the Platonic theory of the two-fold beauty of body and spirit.

In the Roman world Caelius Aurelianus assumed an extremely modern position towards physical therapy, including kinetic-therapy and water gym. The Ancient Romans paid great attention to gymnastics and to active and passive body movements (thermal baths are indicative of this concern).[3]

During the Middle Ages interest in physical exercise as a possible therapeutic tool declined, also on account of the dominant power of the Church, that emphasized and exalted the spiritual over the physical; however, at the practical level, sports practices were quite common, and hunting and tournaments constituted hard tests for knights.

A first reference text regarding therapeutic exercise dates back to the 16th century, namely, the *De arte Gymnastica* of Mercurialis.[4] In the course of the 16th century the formative function of physical activity was repeatedly stressed, thanks also to the philosopher Michel Eyquem de Montaigne.[1]

In the 18th century Andry De Boisregard greatly stimulated the structured evaluation of physical activity, linking physical exercise to the muscular-skeletal apparatus; in March 1723 he gave a lesson in the Medical School of Paris entitled "Is exercise the best means to maintain health?", beginning with the following sentence: "Among all the methods adopted to relieve and also to heal many physical disorders, none is better than exercise".[5]

During the 18th and the 19th centuries physical exercise recovered the dignity attained during classical times, and in the first years of the 19th century Pehr Henrik Ling established a gym hall in Stockholm, in which free body ("Swedish") gymnastics were performed.[6] When, at the end of the 19th century (1896) the institution of the modern Olympic Games certified the sportive and social relevance of physical activity, gymnastics underwent a great impulse, spreading into many different settings.

Atherosclerosis: 19th century pathogenic theories

In the course of the 19th century the in-depth study of the structural bases of the most frequent cardiovascular pathologic picture, namely, ischemic heart disease, permitted the achievement of "historical" acquisitions in the comprehension of the atherosclerotic phenomenon, the pathological process underlying the clinical expression of the disease itself.

Even if, already in the 18th century, the Italian clinician Giambattista Morgagni had recorded and described the common "induration" of the arteries of elderly people, and the not infrequent presence of "bony scales", the concept of the potential threat represented by calcified plaques dates back to the first half of the 19th century, first in a veterinary setting, and then with more and more frequent documentations in human beings. The term "atherosclerosis" was coined in 1833 by Johann F. Lobstein, who asked himself if this pathological picture were sustained by an inflammatory disease of the vessel wall, or if, on the contrary, it depended on modifications in the composition of the blood.[1]

The first pathogenic theory aimed at an explanation of the complex process of atherosclerosis was that formulated by Von Rokitansky (in 1852).[7] He proposed that the initial stimulus for atherosclerotic plaque formation derived from a new formation of thrombi on the endothelium, and not from initial lipid accumulation. In this hypothesis the subsequent aggregation of blood cells and lipid material became embedded in the arterial wall afterwards, evolving into an atherosclerotic plaque.

The other great pathogenic theory, attributed to Virchow (in 1858) and later to Aschow,[8] was instead centered on the lipid nature of the atherosclerotic plaque.[9] As a consequence of these theories it became usual practice, around the middle of the 19th century, to complete postmortem examinations by means of microscopic observation of tissues subjected to coloration, that permitted the understanding of the intrinsic process of myocardial infarction, at least from a pathophysiological point of view. In a brief space of time researchers were able to reproduce myocardial infarction on an experimental basis; at the conceptual level, on the contrary, the idea that coronary occlusion was not always the cause of death developed very slowly, and it was only in the 20th century, thanks to James Bryan Herrick and other researchers, who demonstrated the possibility of diagnosing myocardial infarction in living subjects too, that it was also realized that individuals could survive this cardiac disease.[1]

Since then the understanding of the genesis of cardiovascular diseases has made enormous progress. It

is precisely the better definition of the subtle mechanisms that lie at the basis of vascular pathology that, in a number of cases, has also allowed the shedding of light on the structure and physiological functions of the cardiovascular apparatus, and on the most effective interventions employable to maintain the cardiovascular function itself. Physical exercise is nowadays considered one of the best interventions in this perspective,[10] and in the next section the historical evolution of the concept of therapeutic exercise within the vascular setting and in the course of the last two centuries will be discussed.

Evolution of the concept of therapeutic exercise in the 19th and 20th centuries

At the end of the 18th century Tissot achieved notable progress in the understanding of the therapeutic role of physical exercise in the vascular context and specifically in the cerebrovascular one. Tissot had extremely modern ideas on the usefulness of respiratory exercises and also great confidence in the use of work and occupation as a kinetic-therapies, and he gave extremely precise indications regarding the management of hemiplegic subjects, indications that unfortunately remained neglected for a long time. The researcher was convinced that the key point in managing stroke patients was "the stimulation of an altered control of the brain, through the sustaining of its activity by means of every element of the body. Movement can be of help in this urgent necessity. Apoplectic individuals should not be left in bed for long periods. Such a position in fact enhances the tendency towards complete inactivity and towards sleep... We must try to awaken sensibility and movement... We must keep the patient busy, even to the point of irritating him... When the patient has recovered mastery of himself, he should undergo exercise".[11]

On the cardiovascular front it is in the 19th century that some forms of exercise are proposed in heart diseased subjects. In 1854 in Dublin, William Stokes advised his cardiopathic patients to take long walks and, when, in 1875, Oertel of Munich was advised to look after himself since he had a "fatty heart", he decided to do so by undertaking climbing.[12] Oertel extended this indication to other cardiopathic individuals, as well as suggesting walking for a number of hours a day on specific types of ground. Later the Schott brothers further developed the indication of exercise in subjects with heart disease by elaborating more than 20 patterns of exercises involving one limb after the other, thus constituting the initial phase of motor convalescence, which was to be successively completed with stages of walking-exercises on level ground, destined to increase on a daily basis (in 1916).[13]

The exercises foreseen for cardiac diseases were extended, at the beginning of the 20th century, to peripheral vascular pathologies as well. In the '20s, Buerger proposed a complex motor pattern for the therapy of the vascular diseases of the lower limbs, in which the force of gravity and the effect of posture were applied to the smooth musculature of vessels and to the blood column. The exercises taking their name from Buerger have for a long time been performed in the peripheral vascular pathology that also takes its name from this same researcher (Buerger disease). In his 1924 fundamental text Buerger wrote that the collateral circle had the role of re-establishing the blood flow between an occluded vessel and the tract of the same vessel distal to the occlusion.[14] Buerger tried to stimulate the formation of the collateral circle through exercises in which the limbs were sustained in an upright position at an angle of 60-90° for 30-180 s, or for the time necessary to obtain skin pallor of the limb. When pallor appeared the feet were put outside the bed for 2-5 min or for the time needed for the appearance of reactive hyperemia, and then the legs were posed in horizontal position for 3-5 min. This cycle was repeated 6-7 times each session and the complete sequence was repeated a number of times during the same day. With time, Buerger's method came to be less and less prescribed, and in 1936 Sylvan proposed a technique characterized by exercises involving the different muscular groups of the upper and lower limbs working against a weak resistance.[15] The rationale of this physical activity pattern was to be found in previous studies that indicated that muscular exercise recalls blood from internal organs to the muscles. Nevertheless, the idea of studying the muscular blood flow in the course of physical exercise had to face considerable technical obstacles.

In 1951, Veal *et al.* described the clinical picture of 11 subjects with massive vein occlusion and documented that the early beginning of active and passive exercises could save affected limbs from acute venous occlusion. Nine out of 11 patients had a positive response to a program based on the maximum elevation of the limb as a consequence of rapid and intense

exercises in flexion and in extension on the part of the knee and of the ankle.[16]

In 1969, Larsen *et al.* efficiently documented the role of physical exercise in intermittent claudication by examining Xenon-133 clearance from the gastrocnemius muscle during a walking test on a treadmill before beginning treatment with therapeutic exercises, subsequently re-proposing the test on a monthly basis for the whole 6-month length of their study.[17]

However, apart from the fundamental work of AV Hill in the '20s, it was in the '70s that the first experimental documentation of the variations of metabolic activity in the course of physical exercise was achieved. In 1974, Dahllof *et al.* described the favourable effects of physical exercise in increasing the walking autonomy, the concentration of muscle cholesterol and phospholipids, and the succinate-dehydrogenase activity, as well as in enhancing the speed rate of the incorporation of glycidic carbon in the form of glycogen.[18]

In conclusion, at the beginning of the '80s the available experimental evidence indicated that physical exercise had a positive effect on the increase of gait autonomy in peripheral arterial insufficiency and that the mechanisms underlying the improvement were likely to be multiple, and specifically centered on the development of the collateral circle, on the improvement of the distribution of blood flow to ischemic muscles, and on the augmentation of the use of oxygen on the part of muscular tissue.[19]

Definition of the protective function of physical activity with regard to coronary artery disease

One of the first structured demonstrations of the protective role of physical activity with reference to coronary artery disease dates back to approximately the middle of 20th century. In 1953 Morris *et al.* published in the *Lancet* a paper entitled "Coronary heart disease and physical activity of work", in which they documented that bus conductors working on the typical double-decker English buses presented an incidence in cardiac attacks lower than the drivers of the same buses, and precisely in a 1:2.2 proportion.[20] Following this fundamental research a number of studies consensually confirmed the initial evidence provided by Morris. Between the '60s and the '80s studies on railway men,[21] postmen,[22] manual workers,[23] insurance clients,[24] dock workers,[25] and clerks [19] showed that a reduced physical activity was associated with a higher incidence of ischemic heart disease, in a proportion ranging from 2:1 to 5:1, approximately. The research carried out in the above mentioned two decades (1960-1980) also documented that the incidence of sudden cardiac death proportionally decreased as consequence of an increased physical activity. The interesting studies above mentioned constituted the basis for modern preventive and therapeutic indications concerning physical exercise. These same past studies, however, were subject to criticism because of their tendency towards preselection phenomena. Other researchers, in effect, noted that individuals with a more robust constitution usually selected (and were selected for) a more intense working and leisure activity, and *vice versa*. As a matter of fact, the more recent studies here examined have considerably reduced the pre-selection possibility, thus confirming again the basic datum that a more intense daily physical activity is associated with a reduction of cardiovascular risk.

The studies mentioned above also tried to establish the physical activity threshold necessary to provide significant protection against coronary artery disease. The dock workers examined by Paffenbarger *et al.* needed at least 8 000 kcal (33 488 kJ) a week, with a minimum effort of about 5 kcal (20.9 kJ) a minute,[25] while in the bus conductors studied by Morris and others energy expenditure achieved a peak during the climbing of the stairs.[21] In the course of time the observations reported in the research papers became more numerous; just to quote an example, Morris referred that civil servants carrying out regular aerobic activity involving great muscular groups above a certain energy threshold had a reduced resting heart rate and a lower cardiac attack incidence. The University alumni investigated by Paffenbarger *et al.* showed remarkable protection if and when they achieved a total caloric expenditure of approximately 7 000 kcal (29 302 kJ) a week, of which at least 30% spent in a sport activity requiring an energetic expenditure of 5-10 kcal (20.9-41.9 kJ) a minute.

The evidence concerning the mechanisms underlying the protection provided by physical exercise with reference to coronary artery disease therefore dates back to the end of the '40s; more recently a large amount of data has become available for the central role of the endothelium, that at present is considered a mor-

phologically complete and functionally active organ. Great progress has therefore been made in the last 40 years, if we remember that, in the '60s, the Nobel Award winner Howard Walter Florey summarized the best available knowledge on the endothelium stating that it served to pave vascular conduits, and that its component cells had no other function.[1]

The historical bases of cardiovascular rehabilitation: the role of physical exercise

The '50s represent a fundamental period in the history of the relationship between physical activity and cardiovascular disease. In effect, until 50 years ago the standard treatment for patients suffering an acute myocardial infarction was a period of bed rest of at least 6 weeks, preferably in a hospital environment, followed by an even longer period of home care mobilization. The leading thought was that the infarcted needed rest; "too early" mobilization was considered risky since it could cause a rupture of the still unhealed left ventricle scar. The pioneer studies of Deitrick *et al.*[26] and Taylor *et al.*,[27] aimed at documenting that a prolonged rest period in bed, far from representing the best therapeutic intervention for infarcted patients, could determine negative physical effects on the functional recovery of the cardiac patient, were ignored by the international scientific community. In 1952 Levine *et al.*, in their paper intriguingly entitled "Armchair treatment of acute coronary thrombosis", published in the *JAMA*, suggested in a convincing way the importance of an early mobilization period (in their proposal 2 weeks after the acute clinical event) for the cardiac patient.[28] However, it was only in the '70s that the proposal of Levine *et al.* spread in a significant way in North America, also thanks to the increasing body of clinical literature documenting that even healthy (volunteer) subjects, if they stayed in bed for a long period, showed relatively rapid "de-conditioning" signs. This status was characterized by muscular hypotrophy, osteopenia and a worsening of cardiovascular performance, with an increase in rest and effort heart rate, a reduction in maximum oxygen consumption, in cardiac output and in cardiac volume.[29]

Between the '60s and the '70s it became clear in the English-speaking world that the rehabilitative technique based on early mobilization was associated with favorable effects not only from the functional point of view, but also from the psychological and the social ones. The patient in fact perceived early mobilization as a possible indicator of a speedy recovery, and such a reinforcement triggered and maintained improvement at the psychological and social levels. The avoidance of a negative de-conditioning was paralleled by an early return to work and to social and leisure activity. In the light of these findings the next step, in the recent history of the structured relationship between physical activity and cardiovascular disease, was the planning of rehabilitative programs centered on physical exercise.

In 1973, Kavanagh *et al.* clearly realized (and the title of their paper published in the *American Journal of Physical Medicine* "Importance of physical activity in post-coronary rehabilitation" is self-explaining in this regard) that patients included in cardiac rehabilitation showed an improvement in their physical work capacity, an increase in their global cardiovascular function and went back more quickly and safely to their work environment, as compared with cardiac patients not performing rehabilitative physical exercise.[30] From a clinical point of view, their heart rate and their arterial pressure were lower than those of sedentary cardiac patients. Their cardiac work diminished, as did their oxygen expenditure, with a subsequent increase in the threshold of effort anginal pain appearance.

At the end of the '70s research performed on animals showed that physical exercise could stimulate the collateral coronary circle, and at the same time other research studies confirmed in human beings that postinfarction physical training could reduce the rate of ventricular ectopic beats, depressive state and anxiety values, also increasing the compliance to a more healthy lifestyle.

Current therapeutic role of structured exercise in cardiovascular diseases

Despite of all the relevant scientific acquisitions obtained in the second half of the 20th century, and above discussed, in 1978 the 3rd edition of the reference text on "Therapeutic exercise" still reported a very limited number of bibliographical references concerning cardiovascular diseases. Cardiovascular rehabilitation is therefore an integrated process that has completely asserted itself, on the basis of increasing scientific evidence, only in the last quarter of the 20th century.[13]

Today the relationship between established cardiovascular disease and physical exercise can be described in terms of the need for a multidimensional cardiovascular rehabilitation, that is, a process through which the individual with cardiac disease tends to reach and to maintain a satisfactory level of health and of physical, psychological and social well-being. The complex of structured rehabilitation, shared by the patient with a multidisciplinary group of health operators, currently aims at encouraging patients in the appropriate modification of their lifestyle so as to prevent further clinical events and to re-insert them in their daily activities.[31]

Physical exercise is a cornerstone of cardiac rehabilitation and should be performed at least twice a week for life. The recommendations included in SIGN guidelines,[32] graduated on the basis of the strength of the evidence, foresee that, in the perspective of the performance of the physical exercise itself, mild-moderate risk patients should undergo a clinical stratification of their risk completed by cardiac ultrasound examination; such an assessment should be integrated by the treadmill test in high risk patients. Functional capacity should be evaluated before and at the end of physical exercise by means of valid and reliable measures. Physical exercise at the moment represents an element of the rehabilitation process strictly tied to educational, psychological and pharmacological interventions.[32]

SIGN guidelines propose 4 phases for the rehabilitative program of cardiac patients. The first, that of in-hospital stay, includes clinical assessment, the beginning of instruction and the subsequent correction of erroneous beliefs, the analysis of risk factors and the design of the postdischarge program. In the second, immediately subsequent to hospital discharge, are foreseen a continuous (personal and/or by phone call) support, psychological support, the prosecution of structured physical activity and the creation of a network of social and health contacts essential to the rehabilitative program itself. The third phase is characterized by the integration of structured physical exercise with psychological support and with the instructions regarding home lifestyle so as to re-insert the patients in their work and social environment if and when their conditions allow this, or in any case, to achieve maximum recovery of functional capacity in the most serious patients. The fourth phase is the long term one of maintaining physical activity and the appropriate modifications of lifestyle. As is evident from this summary of the four-step rehabilitative process, physical exercise currently represents a common denominator of every single phase of the recovery procedure of patients affected by cardiovascular diseases.[32]

Conclusions

Only about 70 years have passed from the time when, in the '30s, myocardial infarction patients were strictly advised to observe a period of bed rest for at least 6 weeks, and the so-called "armchair therapy" constituted the cornerstone of the treatment of the cardiovascular patient. In the '40s and the '50s the prescription of 3'-5' of careful mobilization a day, starting from a month after acute myocardial infarction, represented a first significant step forward. A certain amount of careful mobilization proved in effect to be beneficial, given that it was associated with a remarkable reduction in thromboembolic risk, without an increase in cardiac rupture risk. The overcoming of the unjustified excess of fear with regard to the mechanical complications was later associated with the defeat of the fear for arrhythmic complications, thanks to the definition of rehabilitative programs (planned and conducted by physicians only), integrated with electrocardiographic monitoring. Paralleling the recent development of multidimensional and complex cardiac rehabilitation programs, the role of the clinician has been flanked and integrated by that of other health professionals (nurses, rehabilitation therapists, sports scientists, dietitians, psychologists) who constitute the rehabilitative team as currently understood.

Many actors have therefore been appropriately placed in the context of the current cardiac rehabilitation scene; however, the leading figure still remains the patient, for whose functional, social, and psychological recovery physical exercise, after a long and difficult historic evolution, has now imposed itself as coprotagonist.

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