

# Exercise in hypertension: how to counter a pathophysiologic mechanism

Paolo Palatini

*Department of Clinical and Experimental Medicine, University of Padua, Padua, Italy*

(Ital Heart J 2000; 1 (Suppl 3): S69-S71)

## Address:

Prof. Paolo Palatini

*Clinica Medica 4  
Università degli Studi  
Via Giustiniani, 2  
35126 Padova*

## Introduction

The usefulness of physical training in the management of hypertension has been debated in numerous reviews and meta-analyses<sup>1</sup>. All scientific societies have clearly stated that aerobic exercise should be included in every non-pharmacological regimen, with or without concomitant drug therapy. However, controversy still exists as to how an exercise program should be tailored, especially as far as exercise intensity is concerned. A body of evidence supports the view that exercise in hypertension is more beneficial when performed at a low level of intensity (~50% VO<sub>2</sub> max) than at higher levels<sup>2</sup>. According to studies performed with ambulatory blood pressure (BP) measurement regular physical exercise can cause an average of 5 to 6 mmHg BP decrease, which together with the beneficial effect exerted on lipid levels and other metabolic parameters improves the risk profile of the hypertensive patient<sup>1</sup>.

There is still some controversy on the prevailing pathophysiologic mechanisms which account for the BP drop caused by physical training. Changes in the tone of the autonomic nervous system have often been observed in subjects who started an exercise program but the precise nature of these changes and their relationship with the BP lowering effect could not be clearly established<sup>1</sup>. Some authors found a down-regulation of beta- and alpha-adrenoceptors after physical training while others found opposite results<sup>1,3</sup>. Recently, among the possible mechanisms implicated in BP reduction with regular exercise the metabolic mechanism has gained more and more credit. Insulin sensitivity and glucose utilization showed a remarkable improvement in sub-

jects who started a program of endurance exercise<sup>1</sup>. A decreased activity of the renin-angiotensin system, and a decline in the erythrocyte sodium content are other described features in subjects undergoing regular exercise. According to Juhlin-Dannefelt, the BP lowering effect of physical training should be attributed to the increase in low-twitch skeletal muscle fibers produced by exercise which implies an increase in the muscle capillary bed<sup>1</sup>.

Although the results of the literature may often appear contradictory, they can be explained in the frame of a single pathogenetic mechanism that will be discussed below.

## Sympathetic overactivity, tachycardia, and cardiovascular disease

A number of prospective epidemiological studies suggest that a rapid heart rate is a risk factor for future hypertension<sup>4</sup>. This relation was found by Levy et al.<sup>5</sup> who described 22 741 US army officers, in whom transient tachycardia noted during a routine annual physical examination predicted the development of sustained hypertension at a future examination. Since then, numerous other reports have confirmed this finding, chiefly in young patients with borderline hypertension. A body of evidence suggests that fast heart rate is also a potent precursor of myocardial infarction. This association was found in a study of 10 000 Israeli male government employees and in the Glostrup County study where the predictive power of heart rate for coronary events was superior to that of cholesterol<sup>4</sup>. The relationship between high heart rate and development of myocardial infarction was later con-

firmed in the Chicago People Gas Co. Study<sup>6</sup>, and in the NHANES study<sup>7</sup> even after the data were adjusted for the level of physical activity. The results of the Framingham study confirmed the predictive value of heart rate for cardiovascular events, but a significant association was found only in men<sup>8</sup>. In the Framingham study heart rate appeared to be significantly related to coronary death and to sudden death even when many other risk factors were taken into account. The relation was stronger in men than in women; was present when either the general population or the hypertensive individuals were considered; and held true even when the subjects who had died during the first 2 years after the baseline evaluation had been eliminated. The heart rate-death relation was less impressive for stroke mortality, and no gender-related differences were found. In the Chicago studies, which were performed in male subjects, there was an association between heart rate and sudden death<sup>6</sup>. A relationship between fast heart rate and cardiovascular mortality has recently been found by our group also in elderly subjects. In the CASTEL study<sup>9</sup> we found an excess of mortality from sudden death and cardiovascular causes in general in 763 elderly men with baseline heart rate > 80 b/min followed for 12 years. The increased mortality rate in the subjects with tachycardia remained significant after adjusting for all the other main risk factors for atherosclerosis, and when the men, who had died within 2 years after baseline assessment, had been eliminated from the analysis. A similar but non significant association was found in 1175 elderly women.

### Role of exercise

The above description of the mechanisms that account for the relationship between sympathetic activity and cardiovascular disease is necessary to fully understand the beneficial effects of exercise in hypertensive patients. As stated above, regular training is accompanied by a marked reduction of the sympathetic tone, which has been documented with the reduction of heart rate, the decrease of plasma and urinary catecholamines, with spectral analysis of R-R interval, and with microneurographic techniques<sup>10</sup>. Another less known effect of sympathetic overactivity is its action on insulin sensitivity which has been found in several laboratory studies<sup>4</sup>. Chronic sympathetic stimulation reduces glucose utilization by skeletal muscle and in the long run can cause an insulin resistance state. The improvement in insulin sensitivity recently found in obese individuals undergoing a program of physical training can be explained through the depressant action of exercise on sympathetic activity. Blunted sympathetic activity can also account for the decrease in renin-angiotensin system activity often observed in trained individuals<sup>1,10</sup>. Sympathetic activation can increase sodium reabsorption by the kidney and facilitate the action of sodium on the arterial wall. However, it has been

shown that high sodium intake causes an increase in BP only in subjects with high sympathetic tone, while in subjects with normal or low sympathetic tone no effect of sodium intake on BP is apparent<sup>11</sup>. Overall, these data demonstrate the complexity of the relationship between sympathetic activity and many biochemical mechanisms and humoral systems that contribute to BP regulation, and explain why exercise-induced decline in sympathetic activity can decrease BP through a large variety of mechanisms.

### Exercise and blood pressure reactivity

Physical training is effective not only in lowering resting BP levels, but also in reducing BP reactivity to stressors<sup>2</sup>. The latter finding helps to explain the results of recent studies performed with ambulatory monitoring, which documented that in subjects who perform physical activity daytime BP is lower than that predictable on the basis of office BP<sup>1</sup>. If exercise can attenuate the BP response to stressful situations it may blunt BP peaks occurring during daily activities and reduce BP variability. Some studies suggest that increased BP variability favors the occurrence of target organ damage in hypertension<sup>12</sup>. Thus, a non-pharmacological measure which simultaneously decreases daytime BP levels and variability appears particularly beneficial.

The reduction of cardiovascular reactivity to stressors with low intensity physical activity may also account for the longer survival shown by individuals who perform leisure activities compared to professional athletes<sup>13,14</sup>. Although conclusive evidence is still lacking, some reports have demonstrated that calorie expenditure in mild sports activities decreases the risk of mortality, while competitive athletics are conferred little or no benefit<sup>13</sup>. In a recent report Shaper et al.<sup>14</sup> have documented that the risk of cardiovascular events was reduced in hypertensive subjects who performed physical activity at low levels of intensity, but this benefit was totally lost in subjects performing vigorous sports.

### References

1. Fagard R, Amery A. Physical exercise in hypertension. In: Laragh JH, Brenner BM, eds. Hypertension. New York, NY: Raven Press, 1995: 2367-88.
2. Rogers MW, Probst MM, Gruber JJ, Berger R, Boone JB. Differential effects of exercise training intensity on blood pressure and cardiovascular responses to stress in borderline hypertensive humans. *J Hypertens* 1996; 14: 1303-6.
3. Palatini P. Effectiveness of different programmes of exercise training in hypertension: commentary. *J Hypertens* 1996; 14: 1377-8.
4. Palatini P, Julius S. Heart rate and the cardiovascular risk. *J Hypertens* 1997; 15: 3-17.
5. Levy RL, White PD, Stroud WD, Hillman CC. Transient

- tachycardia: prognostic significance alone and in association with transient hypertension. *JAMA* 1945; 129: 585-8.
6. Dyer AR, Persky V, Stamler J, et al. Heart rate as a prognostic factor for coronary heart disease and mortality: findings in three Chicago epidemiologic studies. *Am J Epidemiol* 1980; 112: 736-49.
  7. Gillum RF, Makuc DM, Feldman JJ. Pulse rate, coronary heart disease, and death: the NHANES I epidemiologic follow-up study. *Am Heart J* 1991; 121: 172-7.
  8. Kannel WB, Kannel C, Paffenbarger RS Jr, Cupples LA. Heart rate and cardiovascular mortality: the Framingham study. *Am Heart J* 1987; 113: 1489-94.
  9. Palatini P, Casiglia E, Julius S, Pessina AC. Heart rate: a risk factor for cardiovascular mortality in elderly men. *Arch Intern Med* 1999; 159: 585-92.
  10. Arakawa K. Antihypertensive mechanism of exercise. *J Hypertens* 1993; 11: 223-9.
  11. Staessen J, Bulpitt CJ, Thijs L, et al. Sympathetic tone and relation between sodium intake and blood pressure in the general population. *BMJ* 1989; 299: 1502-3.
  12. Palatini P, Penzo M, Racioppa A, et al. Clinical relevance of nighttime blood pressure and of daytime blood pressure variability. *Arch Intern Med* 1992; 152: 1855-60.
  13. Van Saase JL, Noteboom WM, Vandenbroucke JP. Longevity of men capable of prolonged vigorous physical exercise: a 32 year follow up of 2259 participants in the Dutch eleven