

## OBSERVATIONS

## Beneficial Effects of a 4-Week Exercise Program on Plasma Concentrations of Adhesion Molecules

Plasma concentrations of adhesion molecules are elevated in patients with endothelial dysfunction and atherosclerosis (1), as well as in patients with impaired glucose tolerance (IGT) or type 2 diabetes—even those without angiographic evidence for atherosclerosis (2). Physical activity is associated with reduced risk of cardiovascular disease and total mortality in men with type 2 diabetes (3). The beneficial effects of physical activity could be mediated by improved markers of endothelial dysfunction, including adhesion molecules. We therefore tested the hypothesis that an intensive 4-week physical training program leads to improved plasma concentrations of intracellular adhesion molecule (ICAM)-1, vascular cell adhesion molecule (VCAM)-1, and E-selectin.

In this study, 60 individuals with normal glucose tolerance ( $n = 20$ ), IGT ( $n = 20$ ), and type 2 diabetes ( $n = 20$ ) were enrolled in a previously described (4) supervised physical training program. At baseline and after 4 weeks of training, fasted blood samples were taken, oral glucose tolerance test and euglycemic hyperinsulinemic clamps were performed, in addition to maximal exercise tests and dual X-ray absorptiometry. Serum samples for adhesion molecules were mea-

sured as previously described (2). For statistical data analysis, random-intercept models have been calculated as previously described (4).

In all groups, 4 weeks of physical training resulted in significant decreases in BMI, waist-to-hip ratio, and percent body fat. In patients with IGT and type 2 diabetes, insulin sensitivity and  $VO_{2max}$  significantly improved, whereas elevated baseline plasma ICAM-1, VCAM-1, and E-selectin concentrations significantly decreased after 4 weeks of exercise. However, in subjects with normal glucose tolerance, circulating ICAM-1, VCAM-1, and E-selectin did not significantly change after the training program. Circulating ICAM-1 was significantly correlated with percent body fat ( $r^2 = 0.2$ ,  $P < 0.001$ ), BMI ( $r^2 = 0.1$ ,  $P < 0.001$ ), fasting plasma glucose ( $r^2 = 0.07$ ,  $P < 0.001$ ), and insulin concentrations ( $r^2 = 0.12$ ,  $P < 0.001$ ). There was a significantly negative correlation between ICAM-1 concentrations,  $VO_{2max}$  ( $r^2 = 0.1$ ,  $P < 0.001$ ), and glucose infusion rate during the clamp ( $r^2 = 0.23$ ,  $P < 0.001$ ). Parallel significant correlations were observed for VCAM-1, E-selectin, and these parameters. Random-intercept models revealed that the significant decreases in circulating ICAM-1, VCAM-1, and E-selectin after 4 weeks of intensive training were higher than the expected effects from the improvement of insulin sensitivity, reduced percent body fat, and increased fitness level.

In conclusion, in patients with IGT and type 2 diabetes, physical training led to a near normalization of increased ICAM-1, VCAM-1, and E-selectin plasma concentrations after only 4 weeks. The improvement in adhesion molecules goes beyond the expected effects from the improvement in percent body fat,  $VO_{2max}$ , and insulin sensitivity after training.

ANKE TÖNJES, MD<sup>1</sup>  
 MARKUS SCHOLZ, PHD<sup>2</sup>  
 MATHIAS FASSHAUER, MD<sup>1</sup>  
 JÜRGEN KRATZSCH, PHD<sup>3</sup>  
 FAUCI RASSOUL, PHD<sup>3</sup>  
 MICHAEL STUMVOLL, MD<sup>1</sup>  
 MATTHIAS BLÜHER, MD<sup>1</sup>

From the <sup>1</sup>Department of Internal Medicine III, University of Leipzig, Leipzig, Germany; the <sup>2</sup>Institute for Medical Informatics, Statistics, and Epidemiology, University of Leipzig, Leipzig, Germany; the <sup>3</sup>Institute of Clinical Chemistry and Pathobiochemistry, University of Leipzig, Leipzig, Germany.

Address correspondence to Prof. Dr. M. Blüher, Medical Department III, University of Leipzig, Ph.-Rosenthal-Str. 27, D-04103 Leipzig. E-mail: bluma@medizin.uni-leipzig.de.

DOI: 10.2337/dc06-1760

© 2007 by the American Diabetes Association.

**Acknowledgments**—This study was supported by a grant from Deutsche Forschungsgemeinschaft (DFG), BL 580/3-1 (to M.B.).

### References

1. van der Wal AC, Das PK, Tigges AJ, Becker AE: Adhesion molecules on the endothelium and mononuclear cells in human atherosclerotic lesions. *Am J Pathol* 141:1427–1433, 1992
2. Blüher M, Unger R, Rassoul F, Richter V, Paschke R: Relation between glycaemic control, hyperinsulinaemia and plasma concentrations of soluble adhesion molecules in patients with impaired glucose tolerance or type II diabetes. *Diabetologia* 45:210–216, 2002
3. Tanasescu M, Leitzmann MF, Rimm EB, Hu FB: Physical activity in relation to cardiovascular disease and total mortality among men with type 2 diabetes. *Circulation* 107:2435–2439, 2003
4. Oberbach A, Tönjes A, Klötting N, Fasshauer M, Kratzsch J, Busse MW, Paschke R, Stumvoll M, Blüher M: Effect of a 4 week physical training program on plasma concentrations of inflammatory markers in patients with abnormal glucose tolerance. *Eur J Endocrinol* 154:577–585, 2006