

# Wechselwirkung Sport und Atheroskleroserisiko

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John Singleton Copley, *The Copley Family*, 1776-1777, American.

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## ORIGINAL CONTRIBUTIONS

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# Mögliche Mechanismen für die cardiovasculäre Risikoreduktion durch regelmässige sportliche Betätigung

## Kardiovasculäre Einflüsse:

- Absenkung der Ruhe- und Belastungsherzfrequenz
- Abnahme des Ruhe- und Belastungsblutdrucks
- Abnahme des myocardialen Sauerstoffbedarfs
- gesteigerter Parasympaticotonus
- Zunahme der myocardialen Kontraktilität
- Zunahme des coronaren Blutflusses
- Bildung von coronaren Kollateralen
- Zunahme des peripheren Venentonus
- positive Effekte auf das Gerinnungssystem
- Expansion des Plasmavolumens
- Zunahme der endothelvermittelten Vasodilatation
- vermehrte Genexpression von NO-Synthase

# Mögliche Mechanismen für die cardiovasculäre Risikoreduktion durch regelmässige sportliche Betätigung

## Metabolische Einflüsse:

Verbessertes Lipidprofil  
günstige Effekte auf den Glukosestoffwechsel  
Gewichtsreduktion

## Einflüsse auf den Lebensstil:

Geringere Wahrscheinlichkeit des Nikotinkonsums  
Bessere Stressbewältigung  
verminderter Appetit / günstigere Ernährung

# Long-term Exercise and Atherogenic Activity of Blood Mononuclear Cells in Persons at Risk of Developing Ischemic Heart Disease

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**Context** Increasing evidence demonstrates that atherosclerosis is an immunologically mediated disease in which the secretion of atherogenic and atheroprotective cytokines, by infiltrating blood mononuclear cells, plays an important role. It is not known whether long-term exercise alters this atherogenic and atheroprotective activity directly.

**Objective** To determine the effect of long-term exercise on the atherogenic activity of blood mononuclear cells in persons at risk of developing ischemic heart disease.

## Long-term Exercise and Atherogenic Activity

### Zelluläre Bestandteile einer frischen atherosklerotischen Läsion:

aktivierte Immunzellen ( CD4+ / CD8+ T-Zellen )

Monozyten, Macrophagen, Endothelzellen

## Long-term Exercise and Atherogenic Activity

Lokale Produktion von :

Interleukin 1,2,4,6,10

Tumornekrosefaktor alpha

Interferon gamma

Transformierender

Wachstumsfaktor beta

primär Überwiegen der proinflammatorischen Effekte

## Long-term Exercise and Atherogenic Activity

----- reaktive Produktion  
atheroprotectiver Faktoren :

Interleukin 4

Interleukin 10

transformierender

Wachstumsfaktor beta

## Long-term Exercise and Atherogenic Activity

- Studienaufbau:** Verlaufsstudie bei freiwilligen Studienteilnehmern
- Probanden :** erhöhtes CV-Risiko ( CRP,C3,Fibrinogen )  
unauffälliger Belastungstest
- Ziel:** Auswirkungen des Trainings auf atherogene / atheroprotective Faktoren
- Technik:** Messung verschiedener Faktoren (Cytokine, Lymphozytenphänotypen, Lymphozyten-Reaktion auf Mitogene,CRP) im Blut bzw. in Blutmonozyten-Kulturen

**Table 1.** Risk Factors for Cardiovascular Disease\*

Characteristics	Men (n = 18)	Women† (n = 25)	Overall (N = 43)
Age, mean (SD), y	48.1 (8.0)	49.7 (7.2)	49.0 (7.5)
Hypertension‡	61.1	12	32.6
Elevated total cholesterol-HDL ratio§	83.3	52	65.1
Family history of coronary heart disease	66.7	60	62.8
Diabetes mellitus	5.6	4	4.7
Smoker	5.6	16	11.6
Obesity	27.8	24	25.6
Inactivity¶	55.6	64	60.5

\*All data are presented as percentages except for age. All subjects had blood levels of C3 and/or C-reactive protein that placed them at greater risk of future heart attack (risk ratio  $\geq 1.7$ ); 6.9% of subjects had no other risk factors; 18.6% had 1 other risk factor; 18.6% had 2 other risk factors; 23.3% had 3 other risk factors; 27.9% had 4 other risk factors; and 4.7% had 5 other risk factors.

†Of the women, 68% were amenorrheic (44%, postmenopausal; 24%, posthysterectomy and oophorectomy). Of the amenorrheic women, 71% were taking estrogen replacement medication.

‡Subjects younger than 50 years were considered to have hypertension if they had a systolic blood pressure of at least 140 mm Hg, those older than 50 years if their systolic blood pressure was at least 150 mm Hg, or if at any age they had a diastolic blood pressure of at least 90 mm Hg on 3 or more occasions.

§The total cholesterol-high-density lipoprotein (HDL) ratio was greater than 4.96.

||Body mass index was greater than 30 kg/m<sup>2</sup>.

¶No physical activity for more than 1 year.

## Long-term Exercise and Atherogenic Activity

Durchschnittliches zeitliches Engagement :  
2.5 Stunden / Woche

( 0,3-7,4 Stunden/Woche )

mittlere Trainingsdauer : 70 min ( 36-103 min )

Verteilung der Aktivitäten:

Gewichtheben	35 %	Aerobics	3 %
Laufen	32 %	Rudern	3 %
Fahrradfahren	16 %	Bergsteigen	2 %
Stretching	8 %	Skifahren	1 %

**Table 2.** Effect of Exercise on Cytokine Production by Blood Mononuclear Cells\*

	Before Exercise, pg/mL	After Exercise, pg/mL	% Change	<i>P</i> Value†
<b>Phytohemagglutinin Negative Cultures</b>				
IL-1 $\alpha$	95 (15)	92 (16)	-3	>.05
TNF- $\alpha$	364 (50)	262 (43)	-28	.003
IFN- $\gamma$	23 (4)	13 (1)	-44	.007
IL-4	13 (2)	13 (2)	0	>.05
IL-10	5 (4)	52 (14)	+940	.003
TGF- $\beta$ 1	2347 (168)	3350 (139)	+43	<.001
<b>Phytohemagglutinin Positive Cultures</b>				
IL-1 $\alpha$	1194 (101)	1041 (87)	-13	.047
TNF- $\alpha$	3340 (293)	1621 (180)	-51	<.001
IFN- $\gamma$	7270 (1087)	2101 (495)	-71	<.001
IL-4	123 (27)	239 (31)	+94	.001
IL-10	1136 (70)	1242 (75)	+9	>.05
TGF- $\beta$ 1	2495 (156)	3422 (137)	+37	<.001

\*Sources of cytokines in blood mononuclear cell preparations include monocytes (interleukin [IL] 1, tumor necrosis factor [TNF]  $\alpha$ , IL-10, and transforming growth factor [TGF]  $\beta$ 1); T lymphocytes (IL-1, TNF- $\alpha$ , interferon [IFN]  $\gamma$ , IL-4, and IL-10); natural killer (NK) cells (IFN- $\gamma$  and TNF- $\alpha$ ); and B cells (IL-1 and IL-10). Mononuclear cell sources in atherosclerotic lesions are similar except that NK and B cells are usually rare or absent. Data are presented as mean (SEM).

†Before exercise vs after exercise (2-sided *t* test). Cytokines IL-1 $\alpha$ , TNF- $\alpha$ , and IFN- $\gamma$  are atherogenic, whereas IL-4, IL-10, and TGF- $\beta$ 1 are atheroprotective cytokines.

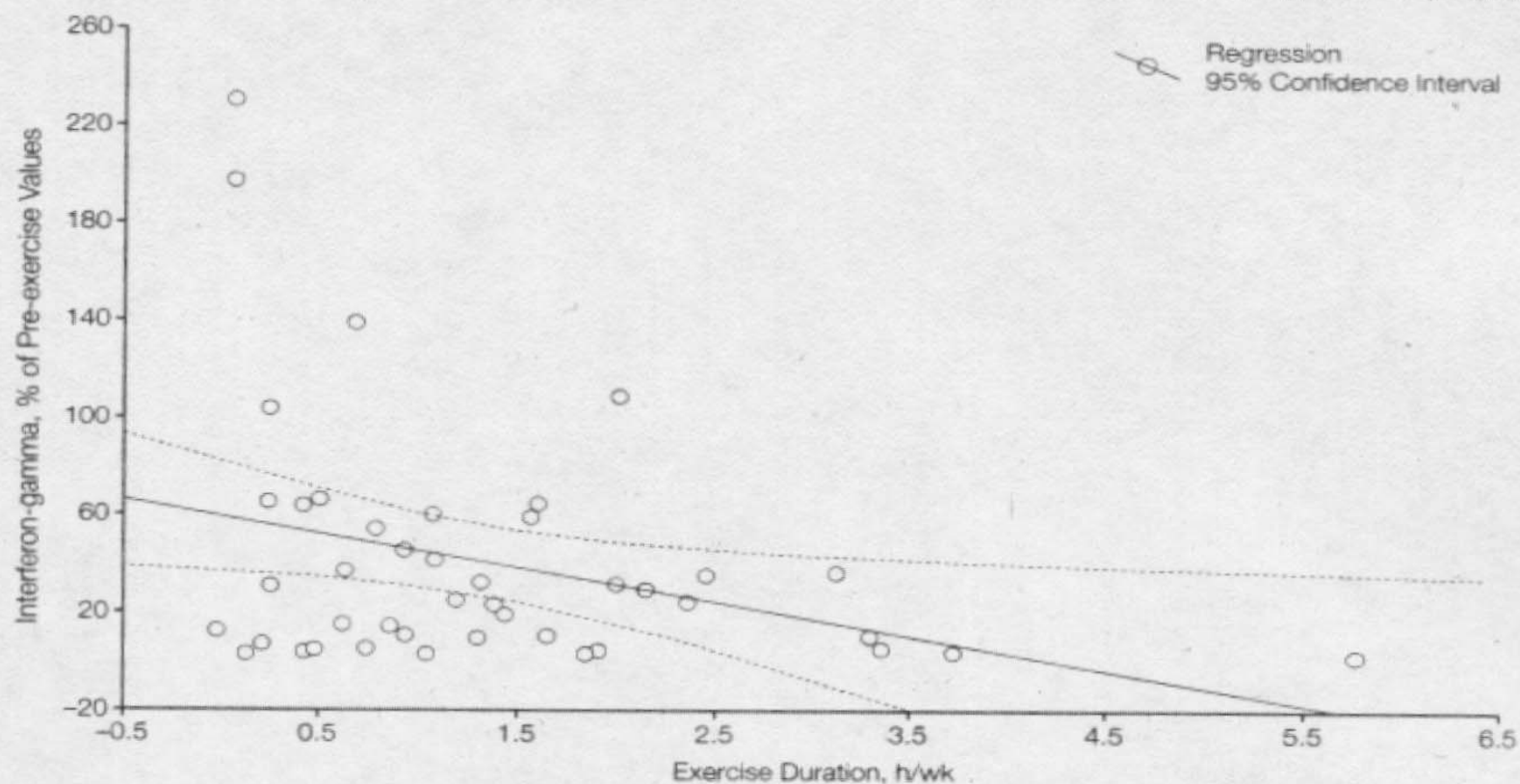
## Long-term Exercise and Atherogenic Activity

Veränderungen nach 6 Monaten Training :

Abnahme der atherogenen Cytokine - 58.3 % (p < 0.001)

Zunahme der atheroprotectiven Cytokine + 35.9 % (p < 0.001)

**Figure.** Effect of Exercise Duration on the Production of Interferon Gamma (IFN- $\gamma$ ) by Phytohemagglutinin-Stimulated Mononuclear Cells



The average number of hours per week each subject spent doing repetitive lower-body motion exercises (walking, running, cycling, rowing, climbing, aerobics, and skiing) is plotted against the change in IFN- $\gamma$  production that occurred following these exercises ( $r = 0.3$ ,  $P = .03$ ). The production of IFN- $\gamma$  decreased in proportion to the duration of exercise.

## Long-term Exercise and Atherogenic Activity

Veränderungen nach 6 Monaten Training :

proliferative

Antwort der Lymphozyten auf PHA - 76 % (p < 0.001)

C-Reaktives Protein - 35 %

Keine Veränderung in den Lymphozyten-Phänotypen

## Long-term Exercise and Atherogenic Activity

Hypertoniker zeigten signifikant höhere

IL1 alpha und TNF alpha - Spiegel als Normotoniker

---- erhöhte Atherosklerose-Prädisposition

## Long-term Exercise and Atherogenic Activity

Positive Effekte umso deutlicher je höher die Beinaktivität

---- Besonders günstig: Walking, Laufen, Fahrradfahren,  
Rudern, Bergsteigen, Aerobics, Skifahren

---- Sport ist Prophylaxe und Therapie der Atherosklerose



