FREE COMMUNICATION

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OXIDATIVE BURST ACTIVITY OF NEUTROPHILS FOLLOWING CYCLE ERGOMETER EXERCISE AT 80, 100 AND 110% OF THE INDIVIDUAL ANAEROBIC THRESHOLD

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Moderate exercise (Ex) is supposed to enhance, intensive (strenuous) Ex to impair neutrophil function, but evidence by controlled studies using identical lab methods is lacking.

The goal of this project was to test moderate endurance exercise to prime neutrophils and intensive aerobic exercise to impair their functions. In randomized order 13 healthy endurance athletes performed three separate endurance Ex sessions on the same cycle ergometer: 1) 80% of the individual anaerobic threshold (IAT) for 60 min [="moderate" (M-Ex); maximal lactate concentration (la_{max}): mean $2.2 \pm$ SD 0.6 mmol$\cdot$l^{-1}]; 2) 100% IAT [="intensive" (I-Ex); la_{max}: 4.5 ± 0.9 mmol$\cdot$l^{-1}]; 3) 110% IAT until subjective exhaustion [mean time: 28 ± 7min; ="highly intensive" (HI-Ex); la_{max}: 7.9 ± 2.0 mmol$\cdot$l^{-1}]; 4) control day (CO) without Ex. Each Ex or CO was accompanied by 6 venous blood samples up to 1 day after the end of Ex for measurement of fMLP-stimulated intracellular oxidative burst acitivity of neutrophils on a single cell basis flowcytometrically.

The fMLP-stimulated oxidative burst activity peaked at 2h post Ex for M-Ex (+29% of the CO´s value), whereas both I-Ex and HI-Ex dropped by -28% (p<0.01 for M-Ex vs I-Ex) and -30% (p<0.01 for M-Ex vs HI-Ex; p>0.1 for I-Ex vs HI-Ex), resp.

These data suggest: 1) Moderate endurance exercise primes neutrophils, whereas intensive/strenuous aerobic exercise does not. 2) Impaired oxidative burst activity suggests a suppression of an essential neutrophil function following intensive endurance exercise at or above the maximum lactate-steady-state.

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SALIVARY IGA MONITORING PREDICTS INFECTION RISK IN ELITE SWIMMERS

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The aim of this study was to characterize the relationship between salivary IgA concentrations and the incidence of upper respiratory tract infection in athletes.

A cohort of 26 elite swimmers (14 male, 12 female) and 12 moderately exercising control subjects (7 male, 5 female) were assessed over a 7 month training program for changes in salivary IgA, intensity and volume of training, psychological stress and infection rates.

Salivary IgA levels (in-house ELISA) measured in the swimmers before training sessions (pretraining) showed significant correlations with infection rate (p=0.017), month of training (p=0.026) and gender (p=0.048). The pre-training IgA levels were 4.1% lower for each additional month of training and 5.8% lower for each additional infection. The post-training salivary IgA levels were significantly correlated with month of training (p=0.005), gender (p=0.012) and session volume (p=0.013). The post-training IgA level was not significantly correlated with infection rate but was 7% lower for each additional month of training. The same variables were also significantly associated with mean pre- and post-training salivary IgA levels in control subjects. The number of infections observed in the swimmers was predicted by the pre-season (p=0.05) and the mean pre-training (p=0.006) salivary IgA levels. The trends in pre-training IgA levels over the 7 month season, calculated as individual slopes of pre-training IgA levels over time, were also predictive of the number of infections (p=0.03) in athletes. The Spielberger anxiety score showed little variation over the season for individual athletes or controls and showed no association with changes in salivary IgA levels or infection rates.

The results indicate that measurement of salivary IgA levels over a training season may be predictive for athletes at risk of infection. Monitoring may allow intervention strategies to be implemented to avoid illness.

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INFLUENCE OF AN INTENSIVE WORK-OUT PROGRAM ON ANTIBODY RESPONSES TO A HEPATITIS A-VACCINE IN MODERATELY TRAINED, FITNESS-ORIENTED ATHLETES

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To assess the influence of a two-week intensive training program on the antibody response to a hepatitis A-vaccine, 28 fitness-oriented athletes (age 27.8±4.9 yrs, usual work-out 4.6±2.1 hours a week) were investigated. All subjects were healthy by history, physical examination and routine laboratory examinations, seronegative for hepatitis A and signed a written consent before participating in the study. The athletes were randomly assigned to either of the following four groups: (I) vaccination before the work-out program, (II) vaccination after one week of the work-out, (III) vaccination after the end of the training period and (IV) controls. The training program consisted of continuous bicycle exercise, five times a week at 110% of the individual anaerobic threshold (IAT) to exhaustion. IAT was determined as lactate threshold by an incremental exercise test on a cycle ergometer. Venous blood samples for the measurement of the antibody response, immunglobulin isotypes and IgG subclasses were drawn before, two and four weeks after the vaccination and six month later.

Two weeks after the vaccination, participants of groups I, II and III developed significant lower antibody titer than controls (I=26 IU/l, II=32 IU/l, III=23 IU/l, IV=68 IU/l; $p < 0.03$). Four weeks after, the antibody response still exhibited a non significant tendency to lower levels in the training groups, especially in group III, followed by II and I. Six month later, antibody titers of all groups showed almost equal levels.

The data indicates that intensive work-out may have a suppressive effect on the antibody response to a hepatitis A-vaccine that may last up to two weeks after cessation of the training.

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IN VITRO CYTOKINE SYNTHESIS BEFORE AND AFTER MODERATE ENDURANCE TRAINING

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Epidemiologic studies point to a lower rate of upper respiratory tract infections in subjects who participate in moderate endurance training programs. The reason for this observation is not clear, only some studies could show no significant changes of immunologic parameters after moderate endurance training.

We determined the in vitro cytokine synthesis in eight subjects before and after a moderate endurance training program. As controls served seven healthy students who participated moderately in leisuretime sports and did not change their activity during this time. The blood samples were cultured in a whole blood assay. For the induction of IL-1β and IL-6 LPS was added. IL-2 and INF-γ were induced with PHA. Cytokine concentrations in the supernatants were determined by standard ELISA technique. Additionally, sIL-2-R and IL-1-RA and Cortisol were determined by ELISA technique. The significance of the data was validated by the t-test. The level of significance $p \leq 0.05$ was described as being of low significance. The intensity of the

training was determined by the levels of lactic acid (running speed during the training below 2.5 mmol/l lactic acid).

After 9 weeks of training (45 minutes running three times per week) the 4mmol/l lactic acid threshold increased significantly from 2.97 to 3.20 m/s. In the control group the synthesis of IL-1β, IL-6, IL-2 and INF-γ did not change. In the training group the IL-1β (p$\leq$0.008) and IL-6 (p$\leq$0.061, trend) production was higher after training.

These results indicate that regular physical exercise influences the production of monocyte derived cytokines while the production of cytokines mainly synthesized by T-cells is not influenced.

Shephard RJ, Shore S

IMMUNE RESPONSES TO EXERCISE AND TRAINING IN CHILDREN TREATED WITH CHEMOTHERAPY

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Cancer treatments leaves physical problems (muscle wasting and low aerobic power), anxiety and depression. Regular graded exercise may help, but will the immune system withstand vigorous exercise?

A preliminary trial monitored immune responses in 6 children treated for acute lymphoblastic leukaemia and other tumours. Three children were trained [T] at 70-85% HRmax (3 times/wk for 12 wk) and 3 children served as controls [C]. Initial VO$_2$max was low [33.7 [T], 38.8 [C] ml/{kg*min}], with large Σ_5 skinfolds [94 mm T, 91 mm C] relative to 11 normal students.

VO$_2$max increased 6% in T, but decreased 6% in C. In students currently receiving chemotherapy, resting data showed low CD3+, CD4+, CD8+, CD19+ and CD25+ counts and impaired PHA-induced lymphocyte proliferation. Further impairment of immune responses resulted from acute exercise [30 min of exercise at the anaerobic threshold) or training; the CD4+/CD8+ ratio dropped below unity, the CD56+ count was much lower than normal, and both spontaneous and IL-2 stimulated cytolytic activity were impaired, although no clinical manifestations of immunosuppression were seen.

The data suggest exercise and training can exacerbate immunosuppression when children are receiving chemotherapy. Although such individuals derive physiological and psychological benefit from regular exercise, treatment must be individually prescribed, with careful monitoring of immune function.

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THE MAJORITY OF CD4+, BUT NOT CD8HI, T-CELLS MOBILIZED TO THE PERIPHERAL BLOOD DURING EXERCISE EXPRESS A CD45RO+ MEMORY PHENOTYP

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Under normal resting conditions, naive and memory T cells follow distinct pathways of recirculation. During periods of heavy physical exercise, T cells with a high-density expression of the α chain of LFA-1 (i.e., CD11a^{hi}) are preferentially mobilized to the blood. Since memory T cells display high levels of CD11a expression and are the predominate phenotype within the marginal lymphocyte pool, we anticipated that the majority of T cells mobilized to the blood during heavy physical exercise would be of a memory phenotype.

To test this hypothesis, venous blood samples were (i) obtained from 12 active males (27.1 $\pm$ 5.3 yr, 76.9 $\pm$ 12.0 kg, VO$_2$peak = 3.37 $\pm$ 0.7 L•min^{-1}, mean $\pm$ SD) before, during and after 40 min of cycle ergometry (65% VO$_2$peak), and (ii) analysed by two-colour flow cytometry (PerCP and PE, respectively) to enumerate total CD4+ and CD8^{hi} T cells and their respective populations of CD45RO- (naive) and CD45RO+ (memory) cells. Changes in cell concentrations relative to baseline were determined by one-way repeated measures ANOVA; all concentrations are expressed as means. The baseline concentration of 0.74 x 10^9 peripheral blood CD4+ T cells L^{-1}, increased by 23% in response to the test exercise (p>0.05). Of the 0.16 x 10^9 CD4+ T cells L^{-1} that were mobilized to the circulation, the majority (~80%) were of a memory (CD45RO+) phenotype. Conversely, the 44% increase (0.50 to 0.72 x 10^9 cells L^{-1}) in CD8^{hi} T cells (p<0.01) was attributable to almost equal proportions of naive and memory cell populations (43% and 57%, respectively).

Therefore the results suggest that the exercise-induced mobilization of CD4+, but not CD8^{hi}, T cells is linked in some way to memory phenotype.

Rhind S, Shore S, Shinkai S, Shephard RJ

IMMUNE RESPONSE TO EXERCISE AND TRAINING: IS THERE A TRAINING VOLUME EFFECT?

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If training volume is sufficient to induce a negative energy balance, then the anticipated benefits of an enhanced immune response may be lost.

We examined this question in sedentary men aged 19-29 yr. A 60 min exercise challenge at 60% VO$_2$max was performed before and after 12 wk of either light training (L, 18 M, 70-85% HRmax 3 times/wk), moderate training (M, 9 subjects, similar programme 4-5 times/wk) or control observation (6 subjects).

Training increased VO$_2$max (8%, light, 21% moderate). Body mass increased in L, but training led to an 8.2% loss of body mass and 18.1% loss of fat in M. Controls showed no changes. Training increased resting CD16+ counts by 27% (L) and CD16+CD56+ counts by 21% (M), with less post-exercise suppression of cytolytic cell counts than at recruitment. Light training also decreased CD3+ and CD4+ counts without changing CD4+/CD8+ ratio. Moderate training gave less increase of non-MHC-restricted cytolytic cells than light training, and also decreased resting CD19+ count.

We conclude that from the viewpoint of immune function, the optimum training regimen is of low volume. Training that induces a negative energy balance can have negative consequences for the immune response.

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INFLUENCE OF MODE AND CARBOHYDRATE ON THE CYTOKINE RESPONSE TO HEAVY EXERTION

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This randomized, double-blind, placebo-controlled study was designed to determine the influence of exercise mode, and 6% carbohydrate (C) versus placebo (P) beverage ingestion, on blood cell counts, plasma glucose, hormone, and inflammatory cytokine responses (5 total samples over 9 hours) to 2.5 h of high intensity running and cycling (~75% VO$_{2max}$) by 10 triathlets who acted as their own controls. C relative to P ingestion (but not exercise mode) was associated with higher plasma levels of glucose and insulin, lower plasma cortisol and growth hormone, and diminished perturbation in blood immune cell counts.

The pattern of change over time for interleukin (IL)-6 was significantly different between C and P conditions (P=0.021) and between running and cycling modes (P<0.001), with the lowest post-exercise values seen in the C-cycling sessions (10.7 ± 1.8 pg/ml), and the highest in the P-running sessions (51.6 ± 14.2 pg/ml). The pattern of change over time between C and P conditions (but not modes) was significantly different for IL-1 receptor antagonist (P=0.003), with values once again lowest for the C-cycling sessions (1.5-h post exercise, 301 ± 114 pg/ml) and highest for the P-running sessions (1171 ± 439 pg/ml).

These data indicate that carbohydrate ingestion is associated with higher plasma glucose levels, an attenuated cortisol response, and a diminished pro- and anti-inflammatory cytokine response.

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IMMUNE RESPONSE TO EXERCISE TRAINING AND/OR ENERGY RESTRICTION IN OBESE WOMEN

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The effect of exercise training (five 45 minute walking sessions/wk at 60-75% maximum heart rate) and/or moderate energy restriction (4.19-5.44 MJ or 1,200-1,300 kcal per day) on innate and adaptive immunity (including mitogen-stimulated lymphocyte proliferation (MSLP), natural killer cell activity (NKCA), and monocyte and granulocyte phagocytosis and oxidative burst (MGPOB) was studied in obese women (N=91, age 45.6±1.1 y, body mass index 33.1±0.6 kg/m^2) randomized to one of four groups: control (C), exercise (E), diet (D), exercise and diet (ED). Aerobic power, body composition, and immune function were measured in all subjects before and after a 12-week diet intervention period, with data analyzed using a 4 x 2 repeated measures design. All subjects self-reported symptoms of sickness in health logs using a precoded checklist.

Data from this study indicate that allthough exercise training was unrelated to any significant changes in resting immune function, the number of days with symptoms of upper respiratory tract infection (URTI) was reduced relative to subjects in the nonexercise groups (5.6±0.9 and 9.4±1.1 sickness days, respectively, P<0.05). Energy restriction and weight loss (7.9±0.7 kg) was associated with a significant decrease in MSLP, but no change in NKCA, MGPOB, or URTI. The data are consistent with the viewpoint that weight loss, even at moderate rate, is associated with a decrease in adaptive, but not innate, immunity.

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HIGH ALTITUDE AND INTENSIVE TRAINING AFFECT IMMUNOLOGICAL PARAMETERS OF ELITE SWIMMERS

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Elite endurance athletes in a number of sports have trained at high altitude of benefit subsequent athletic performance. The aim of the current study was to determine if high altitude training by members of the 1996 Australian Olympic Swim Team elicited changes in a variety of immunological parameters.

Blood samples were taken from 10 swimmers (5 males and 5 females, average age 21 years) and 8 controls non-training but high altitude-exposed Team staff (all male, average age 37 years). Samples were obtained before and after a 21 day altitude training camp (mean training volume 200 km) in Flagstaff, AZ (elevation 2.102 meters). Blood values were determined for leukocytes, hemoglobin, platelets, and leukocyte subsets. The blastogenic responses of peripheral blood leukocytes to concanavalin-A (con-A) or lipopolysaccharide (LPS) were also determined.

Leukocyte concentration decreased significantly after high altitude exposure, however, the decrease was more pronounced in the swim group (~3% for controls vs. ~38% for swimmers) ($p < 0.05$). Only hemoglobin levels of the control group increased significantly after high altitude exposure ($p < 0.05$). No changes were observed in platelet levels over time in any group. Con-A-induced blastogenesis decreased significantly after high altitude exposure in both swim and control groups, however, the level of decrease was less in the swim group (~56% for controls vs. ~32% for swimmers) ($p < 0.05$). LPS-induced blastogenesis increased in the swimmers only (~33%, $p < 0.05$). For the leukocyte surface markers tested, a decrease in the % of cells expression HLA-DR (33% for swimmers and 20% for controls) and an increase in CD4 expression (16% in swimmers only) ($p < 0.05$) were observed after high altitude exposure.

These results suggest that swim training at high altitude can alter discreet immunological parameters; however, some training induced changes may be secondary to those induced by high altitude exposure alone.

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CYTOKINE PRODUCTION AND HEAD-DOWN TILT BED REST

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Head-down tilt bed rest (HDT) is used as an analogue to study physiological effects mimicking those occurring in weightlessness during space flight. An unusual high frequency of infectious diseases during long duration HDT has been described along with a decreased natural killer cell activity.

In the present study, 8 volunteers were subjected to a strict HDT of -6° for 42 days. Blood samples were obtained 12 days before, at day 14, 35, and 42 during and 14 and 35 after HDT. Facscan analysis was used to determine cell subpopulations. Plasma was used to quantify various plasma hormone levels. Whole blood and reconstituted blood was triggered with various activators such as PHA, PHA combined wit PMA, anti-CD2, anti-CD3, and LPS. Supernatants were collected and analysed for IL-1, 2, 6, and 10, and for IFN-alpha and IFN-gamma, and TNF-alpha.

No significant changes in the percentage and total number of T-cells (CD2, CD3, CD4, and CD8) were observed. The percentage and total number of natural killer cells (CD2+/CD3-/CD56+) decreased in all subjects after 14 days of HDT. Cytokine analysis are underway, but preliminary results show no changes in IL-2, 6, 10 and TNF-alpha. The level of the hormones cortisol, prolactin, TSH and growth hormone remained unchanged while the level of 1,25-dihydroxyvitamin D3 and parathormone decreased significantly during HDT. The observed decrease in natural killer cell activity during and after HDT by other investigators might be due to a decrease in their absolute number.

In fact, this decrease is probably neither due to an increase in stress hormone levels such as cortisol, nor to a decrease in cytokine production.

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HUMAN NEUTROPHIL ACTIVITY AT DIFFERENT EXERCISE INTENSITIES

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Neutrophils together with macrophages, ingest invading organism by phagocytosis. In samples from burns patients, neutrophil bactericidal ability was restored by adding glutamine to culture medium (Ogle et al., 1995). A marked neutrophilia mostly accounts for the increase in circulating total leucocytes observed after a marathon. In runners given glutamine or placebo after a marathon, circulating neutrophil numbers were decreased in the glutamine group (Castell & Newsholme, 1997). The degranulation response/cell of bacterially stimulated neutrophils was attenuated during recovery from submaximal cycling (Blannin et al., 1996).

Ethical permission was obtained for the present investigation on the effects of diffe-rent exercise intensities upon neutrophil activity and plasma glutamine levels ([pGln]). Fasting, healthy subjects (male, 24-41 yrs) cycled (A) at 55% for 3 hrs (n=3); or (B) at 80% VO_{2max} to exhaustion (mean 40 min; n=6); blood samples were taken pre-exercise, immediately, 1 hr and 2.5 hrs post-exercise, and from five fasting, healthy controls at 0.2 and 4 hrs. Neutrophil activity measured by oxidative burst was expressed as mean fluorescence intensity (MFI)/cell; [pGln] was measured enzymatically. MFI gradually decreased and reached statistical significance at 1 and 2.5 hrs after exercise (Table). [pGln] was decreased by 23% at 1 hr after (A), similar to the decrease observed after running a marathon (Castell & Newsholme, 1997) but not after (B).

Table: Mean fluorescence intensity (MFI)/cell before and after exercise, $\pm$ SEM. Sta-tistical significance (Students t-test) compared with pre-exercise values is denoted as follows: *p<0.05; **p<0.02.

	Pre-ex	Immediatly post-ex	1 hr post-ex	2.5 hrs post-ex
(A)	241 ± 25	191 ± 23	159 ± 10**	58 ± 8*
(B)	161 ± 35	112 ± 37	88 ± 6	162 ± 18*

	O hr	2 hrs	4 hrs
Controls	120 ± 17	98 ± 25	147 ± 24

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PROLONGED ENHANCEMENT OF MURINE PERITONEAL MACRO-PHAGE FUNCTION AFTER CESSATION OF 3WEEK TREADMILL-TRAINING

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We have recently found that phagocytosis-associated oxygen radical production of murine peritoneal and spleen macrophages was enhanced after more than 3 weeks of treadmill exercise. The aim of this study was to clarify the detraining effect on the enhanced function of peritoneal macrophages.

Thirty-six male C3H/HeN mice aged 8 weeks were randomly assigned to either sedentary control (SC), trained (T), or detrained (D) group. Group SC was just caged throughout the 6-week experimental period, while group D were trained for the first 3 weeks on a rodent treadmill at 15m/min, 30min/day, 5 times/week and kept sedentary in their cage for the last 3 weeks. Group T was kept sedentary for the first 3 weeks, and underwent the treadmill exercise for the last 3 weeks at the same intensity as for group D. All 3 groups of mice were sacrificed at the end of the 6-week

experimental period, 24 hr after the final exercise session of group T. Resident peritoneal macrophages were collected by peritoneal lavage and were further purified by seeding into a plastic vial and the following removal of non-adherent cells. More than 90% of adherent cells were positive for non-specific esterase. Purified macrophages were primed by recombinant Interferon (IFN)-gamma for 12hr. The amount of oxygen radical produced after the stimulation of the cells with immune-complex particles was measured by luminol-enhanced chemiluminescence method.

There was no difference in the number of cells obtained by peritoneal lavage. The amount of chemiluminescence was as follows: SC 2.23 ± 0.14 x 10^4cpm/10^5cells; T 6.68 ± 0.11 x 10^4cpm/10^5cells; D 4.72 ± 0.91 x 10^4cpm/10^5cells.

The enhancement in the production of oxygen radicals is prolonged even after the cessation of exercise. The result suggests that the functional enhancement of macrophages induced by exercise is not transient and that the enhancement is dependent upon the cell turnover of peritoneal cavity.

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THE ROLE OF ENDOGENOUS OPIOIDS IN MODERATE EXERCISE-TRAINING INDUCED ENHANCEMENT OF SECONDARY ANTIBODY RESPONSE

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Studies have shown that moderate exercise-training enhances the secondary antibody response. The mechanism underlying this enhancement has not been elucidated. Endogenous opioids like enkephalins, in moderate doses, enhance antibody response. Furthermore, serum concentrations of endogenous opioids increase in response to exercise and training augments this effect. Therefore, we hypothesized that moderate exercise-training induced enhancement of secondary antibody response may be mediated, in part, by endogenous opioids.

To test this hypothesis, C57BL/6 mice immunized to human serum albumin (HSA) were randomly assigned to receive naltrexone, placebo, or no pellet implantation. Groups were randomly subdivided into exercising (treadmill running at 15m/min, 0° slope, 5 days/week for 8 weeks) or sedentary conditions.
At the end of 8 weeks, booster immunization was given and the exercising mice continued their exercise protocol. Ten days later, at the peak of secondary antibody response, serum anti-HSA antibodies were measured by ELISA.

Our results show that naltrexone pellet implanted exercising mice showed a depression of secondary antibody response when compared to placebo or no pellet implanted exercising mice. This suggests that endogenous opioids may be playing a role in moderate exercise-training induced enhancement of secondary antibody response.

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ROLE OF CENTRAL OPIOID RECEPTORS IN THE ENHANCEMENT OF IN VIVO CYTOTOXICITY SEEN AFTER CHRONIC VOLUNTARY EXERCISE IN RATS

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Chronic voluntary exercise in wheels for 5 weeks in spontaneously hypertensive rats (SIR) augments in vivo natural killer (NK) cell cytotoxicity. Endogenous β-endorphin is increased in cerobrospinal fluid after voluntary exercise in rats and we have recently shown that β-endorphin administered i.c.v. augments NK cell mediated cytotoxicity in vivo in a similar way as chronic voluntary exercise. We have now further investigated the involvement of central opioids systems in the exercise-induced augmentation in natural immunity.

Exercise consisted of voluntary running in wheels for 5 weeks and the mean running distance was 6.0 km/24 h. In vivo cytotoxicity was measured as clearance of injected ^{51}Cr-labeled YAC-1 lymphoma cells from the lungs.

The clearance of YAC-1 cells in vivo was significantly increased in runners as compared to sedentary controls ($p<0.001$). Selective δ, κ, or µ-opioid receptor antagonists were administered i.c.v. with osmotic minipumps during the last week of the 5 weeks of running. The δ-receptor antagonist Naltrindole (40-50 µg/day) significantly but not completely inhibited the enhanced NK-cell cytotoxicity seen after 5 weeks of exercise. Neither the κ-receptor antagonist NorBNI or the µ-receptor antagonist β-FNA influenced the augmentation in NK cell cytotoxicity. Furthermore, Naltrindole and NorBNI per se significantly augment in vivo cytotoxicity, indicating some agonist opioid-mediated effect on natural immunity.

Our data suggest the involvement of central δ-opioid receptors in the enhancement of natural cytotoxicity seen after chronic voluntary exercise. Further studies are needed to elucidate the involvement of central opioid systems in exercise-induced changes in immune function.

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CHANGES IN LYMPHOCYTE 5' NUCLEOTIDASE WITH EXERCISE

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This study was undertaken to extend the characterization of influxing lymphocytes associated with exercise. B and to a lesser extent T lymphocytes have the

membrane bound enzyme 5' nucleotidase (also designated CD73). This enzyme catalyses the dephosphorylation of purine and pyrimidine nucleotides to their corresponding nucleic acid metabolites for transport across the cell membrane. Decreased lymphocyte levels of 5' NT have been reported in clinical immunodeficiency states and with cell immaturity. In addition, lowered activity has been reported with psychological stress (thesis writing), which prompted us to investigate lymphocyte 5'nucleotidase levels using an exercise stress model.

Subjects performed 30 min of stationary cycling [VO_2 max range 65%] and had venous blood samples drawn before, immediately after the exercise and one hour post exercise. Blood cell counts (Coulter) and lymphocyte enzyme activity (change in absorbance Hitachi) were assessed on either total peripheral blood mononuclear cells (PBMC) or on sub-set depleted cell suspensions. Additionally, flow cytometry was done to enumerate $CD16^+$ and $CD73^+$ lymphocyte populations.

As expected, this form of exercise caused an absolute leukocytosis and lymphocytosis. This elevation in cell number however was accompanied by a decreased total level of lymphocyte 5' NT enzyme activity (nmol/hr/mg protein) when compared to baseline resting values ($p < 0.05$). When enriched for influxing B cells, initially there were higher $CD73^+$ counts but these decreased after cessation of exercise.

Overall, lymphocyte 5' NT levels decreased with exercise. This could be associated with the influx of less mature or different sub-sets of cells and might contribute to the decreased immune status and increased susceptibility to illness often reported with repeated intense exercise.

Gotovtseva EP, Uchakin PN, Sams C, Marshall GD

TH1/TH2 AND INFLAMMATORY CYTOKINE RESPONSE TO HIGH-MILEAGE TRAINING FOR THE FIRST MARATHON RUN IN MIDDLE-AGED WOMEN

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The study was addressed to evaluate the Th1/Th2 and inflammatory immune response and clinical outcomes of high mileage training in first-time female trainees.

Six middle-aged (35.5±4.5 yr.) moderately trained women were followed during a 4-month training for a first marathon run. Six healthy sedentary age/sex -matched individuals served as controls. A weekly running mileage varied between 26.0-40.4 km during the study. Running intensity was about 76-82% of the individual HRmax. Mitogen- (PHA/ PMA) and specific antigen/*allergen (Tetanus toxoid, Candida albicans*, and Der p1) -induced IFN-γ, IL-10, and IL-4 production by primary PBMC and specific T cell lines, as well as plasma level and endotoxin (LPS)-induced IL-1β, IL-6, TNF-α, IL-10 synthesis by PBMC were evaluated by commercial ELISA. Cytokine production was assessed on week 10, 14, and 22 of training, five days

before and next day following 20K, 25K, and 42K runs. A 1.6-2.5-fold increase in running mileage resulted in 66% incidence of muscle/join injury. Two runners dropped out of the study before a 42K run due to severe injury and chronic fatigue.

Mild menstrual dysregulations were reported in 50% cases. Rest high production of both PHA/PMA and specific antigen-induced IL-10 and IL-4 was found in runners, while low or no production of these cytokines was observed in controls. IFN-γ synthesis corresponded to normal high values in all subjects. No significant changes were observed 24h following the runs. Rest plasma IL-6 level was elevated in five out of six runners throughout the study, while no plasma IL-1β and TNF-α activity was detected either in runners, or in controls. LPS-induced IL-1β, IL-6, and IL-10 production was significantly higher in runners, than in controls before and after 20K and 25K runs.

These data indicate that chronic high-mileage running induced a shift in the Th1/Th2 cytokine balance toward Th2 predominance, and activated host inflammatory mechanisms.

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THE SEQUENTIAL RELEASE OF CYTOKINES IN STRENUOUS EXERCISE.

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It has been suggested that the cytokine response to strenuous exercise can be used as a model of the cytokine response to sepsis and trauma. Two studies were performed to reveal in detail the changes over time of cytokine concentrations.

In one study athletes (n=10) performed 2.5 hours treadmill running at 75% of VO_2-max. Blood samples were collected before, during (30 min intervals) and post exercise (1 hour intervals for 6 hours). In the second study athletes (n=20) participated in the Copenhagen marathon 97. Blood samples were drawn prior to, immediately after and subsequently every 30 min until 4 hours after the marathon. The concentrations of cytokines in plasma were measured using commercially available ELISA-kits (R&D Systems): IL(interleukin)-1ra, IL-6, IL-1β, and TNFα.

The peak concentration of IL-6 was found immediately after exercise in both the treadmill and the marathon study (respectively 25 fold and 100 fold increase as compared to pre-exercise value). The peak concentration of IL-1ra followed 1 to 2 hours after exercise (18 fold and 78 fold increase). The concentrations of TNFα, IL-1β, TNF-R1 and TNF-R2 increased only slightly in both studies (less than 2.5 fold). An increase in the concentration of the chemokines MIP-1β and IL-8 could be found after the marathon race (3- 4 fold).

The magnitude of the increase in cytokine concentrations has previously been shown to be related to muscle damage, but these studies suggest that also the duration of the exercise has an effect. Furthermore, the results support the idea that in relation to strenuous exercise TNFα, IL-1β, IL-6 and IL-1ra are released in a sequential manner comparable to that observed in sepsis.

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KINETICS OF PHA-STIMULATED IL-6 PRODUCTION AFTER RESISTANCE EXERCISE

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Increases in plasma IL-6, but not in peripheral blood mononuclear cell (PBMC) mRNA for IL-6, have been measured after strenuous exercise.

The purpose of this investigation was to examine whether brief, intense resistance exercise enhanced the production of IL-6 by stimulated PBMC. The kinetics of IL-6 production was examined in PBMC collected from 15 females before and immediately after a 6 x 10 repetition maximum squat resistance exercise. PBMC (2×10^6) in 1 ml medium were stimulated with 10 μg of PHA for 1, 3, 5, and 20 h, and IL-6 in the supernatants was quantitated using an ELISA.

Pre- and post-exercise PBMC produced similar concentrations of IL-6 after 1, 3, and 5 h of stimulation. After 20 h of stimulation, IL-6 ($pg.ml^{-1}$) post-exercise (mean±SD, 7034±2631) was greater than ($P<0.05$) pre-exercise (5263±3237). Monocytes, and T and B cells are the primary PBMC populations to produce IL-6. When corrected on a per cell basis to exclude NK cells, IL-6 at 20 h ($pg.cell^{-1} \times 10^{-3}$) was 45% higher ($P<0.001$) post-exercise (4.2±1.6) than pre-exercise (2.9±1.8). Having measured enhanced IL-6 production by PHA stimulated PBMC following exercise, it was of interest to determine whether PHA stimulated lymphocyte proliferation also was increased. Incorporation of 3H-TdR per T cell was similar pre- and post-exercise at optimal (5 μg/ml) but 17% greater post-exercise ($P<0.05$) at suboptimal (2 μg/ml) PHA concentrations. Thus, while the early kinetics were not changed following the exercise, there was a delayed increase in IL-6 production by PBMC. IL-6, and/or the exercise-related factors that stimulated production of IL-6 in PBMC, may have played a role in enhancing T cell proliferation.

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EVIDENCE THAT IL-6 IS PRODUCED IN SKELETAL MUSCLE DURING INTENSE LONG-TERM MUSCLE ACTIVITY

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This study was performed to test the hypothesis that inflammatory cytokines are produced in skeletal muscle in response to long-term intense exercise.

Muscle biopsies and blood samples were collected from runners before, immediately and 2 h after a marathon race. The concentration of interleukin (IL)-6 protein in plasma increased from 1.5 ± 0.7 ml^{-1} to 94.4 ± 12.6 immediately post-exercise and to 22.1 ± 3.8 two hours post. IL-1 receptor antagonist (IL-1ra) protein in plasma increased from 123 ± 23 pg ml^{-1} to 2795 ± 551 and increased further 2 hours post to 4119 ± 527. Comparative PCR technique was used to evaluate mRNA for IL-6, IL-1ra, IL-1β and TNF-α in skeletal muscle and blood mononuclear cells (BMNC) (n=8). Before exercise, mRNA for IL-6 could not be detected in neither muscle nor BMNC, and was only detectable in muscle biopsies (5 out of 8) after exercise. Increased amounts of mRNA for IL-1ra was found in 2 muscle biopsies and 5 BMNC samples, and increased amounts of IL-1β mRNA was found in 1 muscle and 4 BMNC samples after exercise. TNF-α mRNA was not detected in any samples.

This study indicates that exercise-induced destruction of muscle fibres in skeletal muscles may trigger local production of IL-6 that stimulates the production of IL-1ra from circulating BMNC.

Furian TC, Sallinger B, Ritthaler, F

RATES OF INFECTIOUS DISEASES IN YOUNG ATHLETES AND SEDENTARY CONTROLS

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The rates of infectious diseases in adult athletes is thought to behave similar to a „j-curve", suggesting that the incidence increases with training volume, intensity of the work-out etc.

To investigate wether this susceptability to infections is also true for young athletes, a retrospective survey was done by questionnaires. 800 athletes of various disciplines, mean age 14.3 years±3.6 were questioned about the incidence and duration of different symptoms over the last twelve months. Parents of 50 of these athletes were also questioned to evaluate the recall ability of adolescents. 300 sedentary and moderately active pupils from different schools served as controls. Signs of infectious diseases were considered to be usual symptomes of upper respiratory tract infections of non-allergic orgin (URI) and urinary tract infections, fever, diarrhea and clinical signs of defined illness e.g. angina. Of the athletes, 76.2% remembered any sign in the last 12 months, whereas 94.6% of the sedentary controls did so. The athletes were grouped according to the total work-out time (TWT) (5 h or less hours a week [AI], 5 to 10 h [AII], 10 to 15 h [AIII] and more than 15 hours [AIV] or sports

discipline cohorts (endurance, ball-games, compository, strength). Controls were grouped by the time (no physical activities [PI], up to 3 hours a week [PII], 3 to 5 hours [PIII], more than 5 h [PIV] and type of physical activities (endurance, ball-games).

The mean cummulative prevalence (MCP) of URI rose significantly with higher TWT in the athletes (AI = 16.8 days/year; AIV = 22.4 days/year, p<0.05) whereas the controls exhibited significant lower MCP with rising TWT (PI = 18.5 days/years; PIV = 12.7 days/years, p<0.05). Comparing PIV to AIV the difference was highly significant (p<0.01). In the discipline cohorts, endurance athletes had the highest MCP (24.9 days/year, whereas pupils, engaged in leisure time endurance activities showed the lowest rate (8.7 days/year), p<0.05.

These data indicate, that physical activities may also have an effect on the incidence of infections in the adolescents, similar to that observed in adults.

Townsend EL, Catlin PA, Joyner DR, Lewis ML, Schwartz AL, Kapasi ZF

THE EFFECTS OF INTENSE PHYSICAL EXERCISE ON SECONDARY ANTIBODY RESPONSE IN YOUNG AND AGED MICE

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Based largely on data from young subjects, intense physical exercise is believed to suppress immune function. Also, immune function, including antibody response, declines with advancing age. Therefore, we hypothesized that intense exercise in aged subjects would further suppress the immune response.

Thus the object of this in vivo study was to investigate the effects of intense physical exercise on secondary antibody response in young (6-8 weeks) and old (22-24 month) C57BL/6 mice immunized to human serum albumin (HSA). One group of young and old mice were exposed to a single bout of intense exercise to exhaustion and immediately boosted with injection of HSA. Ten days later, at the peak of secondary antibody response, serum anti-HSA antibodies were measured by ELISA. To evaluate the impact of intense exercise during both the initiation and evolution phase of the secondary antibody response, a second group of young and old mice continued their daily bouts of intense exercise to exhaustion over the next 10 days.

A control group of young and old mice showed a trend toward suppression of secondary antibody response following intense exercise, old mice exposed to a single bout of intense exercise, showed enhancement of the response to levels seen in the young control mice.

While the widely accepted hypothesis that „intense exercise suppresses the immune system" may be true for young mice, the same may not be assumed for old mice.

Kapasi ZF, Catlin PA, Geis C, Crater G, Guadanino D, Pohnert T

EFFECTS OF MODERATE EXERCISE TRAINING ON ANTI-TETANUS ANTIBODY RESPONSES IN YOUNG SEDENTARY INDIVIDUALS

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Moderate exercise training is believed to enhance immune function including anti-body response to specific antigens. However, the effects of moderate exercise training on antibody response has not been examined in humans. The purpose of this study was to examine effects of moderate exercise training on anti-tetanus antibody response in young, sedentary individuals.

Fifteen, sedentary subjects engaged in moderate exercise training (72% max H.R.) (Age±SD; 25.4±2.8 yrs.) or maintained sedentary levels (25.4±3.7 yrs.) for a period of eight weeks. Subjects received booster immunization with tetanus toxoid at six weeks. The ELISA measured serum anti-tetanus antibodies in blood taken at zero, six and eight weeks.

Our results indicate that the mean anti-tetanus antibody response following booster immunization with tetanus toxoid was 40% greater in exercising subjects when compared to nonexercising subjects. Furthermore, Brief Symptom Inventory (BSI) administered to the subjects to provide an independent assessment of the relative degree of distress associated with exercise during the study showed no significant differences between the sedentary and exercising subjects, suggesting that physiological distress may not have played a role in causing the changes in anti-tetanus antibody levels.

We conclude that our results support the hypothesis that moderate exercise training enhances immune function.

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SALMONELLA TYPHI VACCINE RESPONSE IN ELITE SWIMMERS

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The aim of this study was to assess the ability of elite swimmers to respond to an oral vaccine during a period of significant physical and psychological stress.

A cohort of 16 elite swimmers (10 male, 6 female) were orally immunized against salmonella typhi (Thyphvax, CSL, Australia) on completion of an intensive 3 week high altitude training camp after returning to Australia on a 14 hour international

flight. Eight age matched local university students (2 male, 6 female) were immunized, during a non-stressful mid-semester period, as a control group for comparison of th mucosal vaccine between response. IgA, IgG and IgM specific antibodies to S.typhi were measured in saliva from day 0 (pre-immunisation) to day 26 post immunization.

There were no significant differences in the mucosal response to the vaccine between swimmers or control subjects. Peak median IgA antibody responses occured in saliva of both swimmers and controls at 10 days post immunization. An IgG response occured in 46% of subjects and an IgM response in 75% of subjects, with similar distributions in swimmers and control subjects. The peak antibody values were not significantly different between swimmers and controls. The results indicate that this cohort of swimmers was able to respond to an oral vaccine in a manner equivalent to that of a control group.

The results are consistent with the systemic immune responses observed to a pneumococcal vaccine* (Pneumovax, CSF, Australia) and indicate adequate B-cell immune responses to novel antigens in swimmers training at an elite level.

* Ref: Gleeson M et al. Clin. Exp. Immunol. 1996; 105: 238-244.

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OCCUPATIONAL PHYSICAL ACTIVITY AND NON-HODGKIN'S LYMPHOMA

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Clinical evidence suggests that immune dysregulation may contribute to the risk of non-Hodgkin's Lymphoma (NHL). Intense physical exercise has been shown to profoundly, but transiently, suppress immune function. The purpose of this study was to evaluate the role of occupational physical activity in the development of NHL.

Cases (n=1.165) of NHL were ascertained from 4 states between 1976 and 1986 through state cancer registries and surveillance of area hospitals. Population-based controls (n=3.545) without hematopoietic or lymphatic cancer were randomly selected by RRD and by a sample of HCFA files. Assessment of physical activity was based on occupational job titles (1977 SOC system) and included 2 measures: energy expenditure (EE) and sitting timing (ST). Odds ratios (Ors), adjusted for age, state, and hair dye exposure, were calculated according to Gart's method and linearity of trends using Mantel's one tailed test.

For men, the risk associated with moderate (OR=1.1, 95% CI=0.89, 1.24) and high (OR=1.0, 95% CI=0.71, 1.29) EE were not statistically significant. For women, the risk associated with moderate (OR=0.9, 95% CI=0.57, 1.48) and high (OR=1.7, 95%

CI=0.21, 11.73) EE were not statistically significant. Risk of NHL was not significantly associated with ST in men or women.

From these data using occupational codes, physical activity either has no effect on NHL or a small effect below that observed for colon and other cancers.

Woods JA, Wolters BW, Ceddia MA, Germann C

EFFECTS OF CHRONIC EXERCISE TRAINING ON THE GENERATION OF ANTI-EL-4 CYTOTOXIC T LYMPHOCYTES

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No studies have examined the effects of exercise on specific anti-tumor immunity, such as demonstrated by cytotoxic T lymphocytes (CTL's). The purpose of this study was to determine the effects of exercise on the ability to mount a CTL response to injected allogeneic tumor cells.

Female Balb/c ($H-2^k$) mice were randomized into 3 groups: one group (n=25) was moderately exercise trained (T-) for 13 wks (45 min/day at 15-21m/min, 5% grade), another group (n=8, stress-control, SC) was exposed to the treadmill environment for 13 wks, and the last group (n=11) was kept in their home cages (HCC). At the end of the training period, all mice were inoculated (i.p.) with 50 x 10^6 allogeneic EL-4 lymphoma cells ($H-2^b$). The trained mice were further randomized into 3 groups: continuation of moderate exercise (T-MOD, n=8), exhaustive exercise (T-EXH; 2-3 hrs/day at 15-31 m/min, 5%, n=9), or cessation of exercise (T-CON, n=8). This paradigm was completed over an 11 day period designed to generate anti-EL-4 CTL's. Mice were sacrificed 24 hr after the last exercise session. Peritoneal exudate and spleen cells were obtained and passaged through nylon woll columns to enrich for T lymphocytes. Cells were adjusted to appropriate effector:target (E:T) and CTL killing was assessed using a 4 hr ^{51}Cr release assay using ^{51}Cr-labled HL-4 targets. Percentages af $CD8^+$ cells were determined by immunofluorescence and flow cytometry.

In the peritoneum, trained groups manifested significantly ($p<0.05$) lower % cytotoxicities (T-MOD 16$\pm$1.7; T-EXH 18$\pm$3.2; T-CON 22.4$\pm$2.1) when compared to HCC (31.6$\pm$1.5) or SC (29$\pm$2.6) at 20:1. The percentage of $CD8^+$ cells was lower in the chronical trained groups (T-MOD 20$\pm$13; T-EXH 44$\pm$18; T-CON 32$\pm$13) when compared to HCC (71$\pm$5) or SC (55$\pm$11). Splenocytes also showed significantly ($p<0.05$) lower cytotoxicities in the T-MOD (21$\pm$3.7) and T-EXH (17$\pm$2.6) groups when compared to T-CON (33.7$\pm$2.3), HCC (35$\pm$2.5), or SC (39$\pm$2.6) at 80:1. However, there were no significant differences in the percentage of $CD8^+$ cells between groups.

These results indicate that chronic training may suppress the generation of tumor specific CTL's and cessation of exercise during the tumor rejection period may improve this response.

Rätz M, Gabriel HHW, Kindermann W

EFFECTS OF AN INTENSIVE CONCENTRIC INTERVAL TRAINING SESSION ON LYMPHOCYTE IMMUNOPHENOTYPES

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Intensive concentric exercise (EX) leads to postexercise suppression of lymphocyte and natural killer (NK) cell concentrations. One primary item of the present study was to examine, if an intensive concentric interval training session augments this decrease more than a single intensive 60 sec-test. Secondly we tested the hypothesis that the removal of lymphocytes with high expression of CD18 out of the circulation is increased in relation to cells with low expression.

12 healthy male athletes performed in random order three separate EX sessions on the same cycle ergometer: a) CO: nonexercise control day b) SMT: a single maximal (all-out) test for 60 sec; c) INT: SMT, 10 min at rest followed by 8 x 10 sec all-out tests with 5 min at rest per interval. Venous blood samples were taken before,15 min, 2hrs (2h p) and 24hrs after exercise, (CO: same time points). Total cell concentrations were measured by triple color flow cytometry, concentrations of serum cortisol were determined radioimmunologically and values were analysed by ANOVA (3×4, $p<0.05$).

T cells (decline SMT: 25%; Int: 33%, related to CO), B cells (SMT: 12.5%, INT: 19%) and NK cells (SMT: 36.5%, INT: 25%) were significantly decreased after both SMT and INT at 2h p (except for B-cells after SMT) but no significant differences between SMT and INT were observed. $CD18^{high+}$ T cells decreased significantly after both SMT and INT at 2h p ($p<0.01$) (SMT: 33%, INT: 40%), $CD18^{+low}$ T cells after INT ($p<0.01$) (SMT: 17.5%, INT: 33%). The higher declines of $CD18^{+high}$ in relation to $CD18^{+low}$ T cells after both SMT and INT at 2h p are not significant. Cortisol after INT was significantly increased at 2h p in comparison to SMT ($p<0.01$) (SMT: 200%, INT: 350%, related to CO), cortisol concentration did not correlate to the decrease of the above mentioned cell populations. As the suppression of T, B and NK cells following a single maximal EX cannot be enhanced by the superimposition of 8 maximal 10sec-tests, the extent of cortisol secretion is not strongly related to postexercise lymphocytopenia. Removal of $CD18^{+high}$ lymphocytes out of the circulation is tendentially stronger, but further investigations including CD11a and CD11b must provide more decisive results.

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INCREASED C-REACTIVE PROTEIN LEVELS INDICATE AN ACUTE-PHASE-RESPONSE FOLLOWING AN INTENSIVE CONCENTRIC INTERVAL TRAINING SESSION

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Eccentric exericse is capable to induce an acute-phase-response (APR). One focus of the present study was to find out, if a concentric intensive interval training session may induce an APR.

In random order 12 healthy athletes underwent the following three conditions: a) CO: control day without physical exercise; b) SMT: a single maximal (all-out) cycle ergometer test for 1 min; c) INT: an intensive interval training session on the same cycle ergometer (1min all-out exercise followed by 10 min at rest, subsequently 8 repetitions of 10s all-out tests interrupted by 5 min at rest). CO, SMT and INT were accompanied by 4 venous blood samples before and up to 1 day after the end of exercise and - among more parameters - surface receptors CD14 and CD16 of monocytes were measured by flow cytometry; lactate, blood-pH, C-reactive protein, ACTH and cortisol were also determined.

Following SMT the lactate concentration increased to 14.6 (mean)±2.0 (SD) mmol·l^{-1} and blood pH decreased to 7.16±0.08 (3x4 ANOVA, post hoc Scheffé test; significance level: $p<0.05$). During INT lactate concentrations ranged from 13.0 to 14.5 mmol·l^{-1} at a blood pH of 7.17±0,07. In comparison to the correspondent CO value ACTH increased 2.5fold and 8.5fold after SMT and INT, respectively. Cortisol was slightly higher following SMT and showed a 3.5fold increase following INT. 2 hours post INT monocyte counts increased by 70%. CD14^{+}CD16^{+} monocytes increased more than CD14^{+}CD16^{-} monocytes. 1 day after INT CRP was higher in comparison to CO but no increase following SMT was seen. 2 hours post INT monocyte counts correlated to CRP 1 day post INT (r=0.86; $p<0.001$).

It is concluded that concentric intensive interval training sessions but not single maximal anaerobic exercise is capable to induce the APR moderately.

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MODERATLY ACTIVATED T-CELLS IN ENDURANCE ATHLETES DURING A REGENERATIVE TRAINING PERIOD - A CROSS SECTIONAL STUDY

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Long endurance exercise is capable to increase CD45RA$^+$CD45RO$^+$ T-cells. The goal for this study was to test the hypothesis, if individual endurance athletes have increased cell concentrations of CD45RO$^+$ T-cells compared with sendentary individuals.

Under standardized experimental and laboratory conditions lymphocyte subpopulations and distribution of CD45RO$^+$ within T-cells of 55 males (22 sendentary controls [CO], individual threshold [IAT]: 2.2±0.3W·kg^{-1}, VO$_{2max}$: 47±3ml·min^{-1}·kg^{-1}; 13 endurance athletes [ET1], training for 3-10 hours weekly, IAT: 3.0±0.3W·kg^{-1}, VO$_{2max}$: 57±2 ml·min^{-1}·kg^{-1}; 20 endurance athletes [ET2], training for >10 hours weekly, IAT: 3.7±0.3W·kg^{-1}, VO$_{2max}$: 64±1 ml·min^{-1}·kg^{-1}) were measured (direct immunofluorescence, flow cytometry).

In both ET1 and ET2 percentages of CD3$^+$ T-lymphocytes were significantly (ANOVA: P<0.05) higher for CD45RA$^-$CD45RO$^+$, but not CD45RA$^+$CD45RO$^+$ cells. Correspondingly CD3$^+$CD45RA$^+$CD45RO$^-$ cells were reduced in ET1 and ET2. Both CD3$^+$CD4$^+$ and CD3$^+$CD8$^+$ T-cells were responsible for the increase of CD45RA$^-$CD45RO$^+$ T-cells. Furthermore, interleukin-2 receptor positive T-cells (CD3$^+$CD25$^+$) were significantly higher for ET1 and ET2 than CO.

These data suggest for endurance athletes in regenerative training periods that 1) endurance training leads to increased CD45RO$^+$ T-cell concentrations indicating moderately increase activity of the cells, 2) compared to severe infections this increase is small and 3) an enhanced resistance to recall antigens is possible.

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EFFECTS OF TRAINING STATUS AND SUPRAMAXIMAL EXERCISE ON LYMPHOCYTE SUBSETS ABSOLUTE COUNTS

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Conflicting results exist in the literature concerning the effects of training status on resting lymphocyte subsets counts and the cross effects of physical training and acute exercise on lymphocyte subsets changes. A new technique, using fluorescent microspheres (Coulter Flow-Count fluorospheres, Coulter, Hialeah, FL, USA) prior to flow cytometric analysis has been developed in order to provide greater count accuracy without referring to complete blood count. We used this technique to investigate whether significant lymphocyte subsets differences between trained and untrained subjects could be objected at resting level and following an acute supramaximal exercise.

Eight trained (TR; age 30.5±SEM 1.5 yrs) and seven untrained (UN; 32.4±2.5 yrs) male subjects underwent a 30 s Wingate test and blood samples were collected before and 3 min following exercise. Whole blood CD19+, CD3+/CD45+,

CD3+/CD4+, CD3+/CD8+, CD56+, CD3-/CD56+/CD16+ absolute counts were measured with flow cytometry Coulter systems, Coulter clones, Immunoprep EPICS leucocyte preparation, Multi-Q-Prep EPICS immunology work station, Flow-count fluorospheres, EPICS MCL-XL.

TR subjects demonstrated higher ($p<0.01$) average power mean (9.13 ± 0.02 vs 7.13 ± 0.18 W.kg^{-1}) than their UN peers. At baseline level no differences were found in lymphocyte subsets except for CD19+ cells, absolute counts that were ($p<0.05$) lower in TR than in UN (0.14 ± 0.02 vs 0.32 ± 0.06 $10^9.1^{-1}$ respectively). Supramaximal anaerobic exercise did not induced different profiles in subsets variation except for CD3+CD45+ cell count that showed a greater increase ($p<0.05$) in TR compared to UN subjects (+62.5% vs +29.6% respectively).

These results suggest a lower resting B cell count and a greater T cells count increase after exercise in trained young men than in untrained young men. Suppressor T and NK cell counts variations occuring after supramaximal exercise do not seem affected by training status or total amount of work performed.

Gleeson M[a], McDonald WA[b], Pyne DB[b], Hall ST[a], Clancy RL[a], Cripps AW[c], Collins MF[d], Francis JL[a], Perry C[b], Fricker PA[b]

SALIVARY IGM SUPPRESSION IS ASSOCIATED WITH INFECTION RISK IN ATHLETES

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The aim of this study was to determine the relationship between mucosal immunosuppression and the risk of infection in a cohort of elite swimmers.

22 elite swimmers (12 males, 10 females) were monitored during a full 12-week training program in preparation for national championships. Salivary immunoglobulins (inhouse ELISA) and albumin (rate nephelometry) levels were measured at two-weekly intervals, before and after a scheduled training session.

Salivary IgA ($p=0.005$) and salivary IgM ($p=0.001$) levels decreased after individual training sessions. There was a significant linear fall in the concentrations of salivary IgA ($p=0.03$) and salivary IgM ($p=0.04$) after exercise over the study period. No significant changes after exercise or trends over time were observed in salivary IgG or albumin concentrations over the study period. The fall in the salivary IgM concentration after exercise was significantly greater in swimmers with upper respiratory tract infections (URTI) compared with swimmers who had no episodes of infection ($p=0.01$). A physiological assessment, Profile of Mood State (POMS) questionnaire, showed no correlation with any measure of mucosal immunity. The POMS scores for

anger, tension, depression, confusion and total mood disturbance were significantly higher in swimmers with URTI compared with swimmers without infections.

Athletes who compensated for the mucosal suppression of IgA with adequate levels of IgM appeared to be protected from URTI. The data indicates that supression of salivary IgM after intensive training may provide a marker for identifying athletes at risk of URTI, particulary in the pre-competition training period.

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SERUM PARAMETERS AND IN VITRO CYTOKINE SYNTHESIS AFTER TAPERING

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To elucidate the question whether intensive training has longlasting effects on the immune system we measured cytokine synthesis and other parameters in 9 swimmers of the national top class after a short period of tapering. As control group serverd 9 moderate active subjects.The leucocyte counts were measured with a Digitana counter (Sysmex). The differential blood picture was determined from the cells physical characteristics (lymphocytes, granulocytes) and the expression of the CD14 antigen (monocytes).The following lymphocyte subpopulations were identified by flow cytometry CD 14 + / CD 45 + (leucogate), CD4+, CD8+, CD16 +. Within 3 hours after collection the blood samples were cultured in a whole blood assay. For the induction of IL-1β, IL-6 and TNF-α LPS was added. IL-2 and INF-γ was induced with PHA. Cytokine concentrations in the supernatants were determined by standard ELISA technique. Additionally sIL2-R, IL1-RA and Cortisol in the blood were determined. The significance of the data was validated by the Mann Withney U test.

Lymphocyte and monocyte counts were lower in the athletes group, but no level of signifcance was reached. Lymphocyte subpopulations and cytokine synthesis did not differ significantly, too. Cortisol, s-IL2-R and IL1-RA were not elevated.

The results show that after a short period of tapering the function of the immune system in top athletes is unimpaired.

Henneicke-von Zepelin HH[a], Hentschel C[b], Köhler G[a], Kohnen R[c], Wüstenberg P[a]

CLINICAL EFFICACY AND SAFETY OF ESBERITOX® N IN COMMON COLD-RESULTS OF A DOUBLE-BLIND PALCEBO-CONTROLLED MULTICENTER STUDY

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[c]IMEREM GmbH, Nürnberg

Clinical efficacy of Esberitox® N (radix echinacea, radix baptisiae, herba thujae) in the treatment of the common cold, which is one of the most frequent diseases in man worldwide[1], has been shown in recent studies[2,3]. The objective of this study was to verify these results under (i) GCP-quality assurance and (ii) common situations at family doctors.

Patients attending one of 15 study centres because of an acute common cold were included and treated with Esberitox® N or placebo for 7 to 9 days in a double-blind manner. Patients daily documented the intensity of 17 cold symptoms and the cold overall by the use of 10-point scales. Safety parameters such as adverse events, vital signs and laboratory parameters were documented, overall tolerability was estimated by patient and investigator.

262 patients were included, 242 patients were evaluable (62% female, 41±13 years). Stratification with regard to the initial severity of indicator symptoms and their development during the first three days after baseline (stable/progredients vs. remittent) resulted in four subgroups. In patients with a minimum extend of symptoms stable or worsening during the first three days after baseline Esberitox® N had a superior efficacy as compared to placebo (p<0.05) four days after baseline until end of treatment in total score of symptoms and in patients overall rating of the cold intensity. In 24 patients (18%) receiving Esberitox® N and 21 patients (16%) receiving placebo adverse events were reported but not due to any specific effects. Serious adverse events did not occur.

This study shows that Esberitox® N is most effective, if the therapy starts as early as possible after occurance of initial cold symptoms when the maximum of the cold has not yet been reached. However, when treatment decisions have to be made at time of doctor's visit the course of a clinical signs cannot be foreseen. Therefore and because of the very good efficacy and safety data the use of Esberitox® N in all patients attending their family doctor for a common cold is reasonable.

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[2] Vorberg, G.: Bei Erkältung unspezifische Immunabwehr stimulieren. Ärztl. Praxis 36 (1984), 97-98
[3] Reitz H.-D., Hergarten H.: Immunmodulatoren mit pflanzlichen Wirkstoffen, notabene medici 20 (1990), 181-185, 249-252 and 362-366.

Klöpping-Menke K, Baum M, Liesen H.

EFFECTS OF A TEN DAY INTENSIVE TRAINING CAMP ON THE PERIPHERAL BLOOD PICTURE AND ITS FUNCTIONAL PARAMETERS.

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Many studies have shown that a single bout of exercise is followed by changes in immunological parameters. However, not much is known about the immune system under conditions of rest before and after repeated intensive exercise. In some studies a decrease of leukocyte and lymphocyte counts is described, whereas other studies report an elevation in percentages of NK-cells in top athletes.

We, therefore, investigated the women C-cadre of the national field hockey team (n=20, age 19.75±1.16, height 1.67±0.05, weight 62.72±4.92) before and after a ten day intensive training camp with up to five hours per day training including mainly technical/tactical elements, strength training and sprint training. We measured the following parameters: leukocyte, lymphocyte, granulocyte and monocyte counts, CD4+, CD25+, CD45 RO+ and CD16+ cells. Soluble interleukin-2-receptor (sIL-2-R), IL-1-RA were measured with ELISA's.

Significant changes were observed for the following parameters. The granulocyte count decreased significantly from 3850±732 to 3342±729 (p<0.023). The NK cell count was elevated highly significant from 7± 4 to 13± 3 (p<0.000) and sIL-2-R increased significantly from a mean value of 518±165 to a mean value of 573±137 (p<0.008).

We conclude that repeated intensive exercise mainly influences the NK cell system. Furthermore, the increase of the sIL-2-R might indicate a slight activation of the specific immune system. However, there is no indication that the high training load may cause an impairment of the athletes health.

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BODY MASS INDEX PREDICTS THE CHANGE IN CD4+ CELL COUNT FOLLOWING EXERCISE TRAINING IN EARLY SYMPTOMATIC HIV INFECTION

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Published studies on the effects of exercise training in HIV infected persons often show positive changes on CD4+ cell count (CD4), but sometimes negative CD4 changes are found. This raises the important question when CD4 improves and when it deteriorates following exercise.

The purpose of the present analysis was to examine the relationship between pre-training body mass index (BMI) and pre-post CD4 changes in early symptomatic HIV infected men (n=11) and women (n=6), who were the experiments in a randomized controlled trial on the effects of exercise training. Subjects were 35.0 years old (range 26 to 48), had a mean pre-training CD4 of 467/mm^3 (240 to 772), and a BMI of 25.8 kg/m^2 (19.5 to 47.6). The exercise training consisted of 45 minutes of supervised interval cycle ergometry, 3 d/wk, for 12 weeks, at an intensity of 70 to 80% of maximal heart rate.

On average, these subjects showed a small pre-post increase in CD4 (10±95). A significant correlation was found between pre-training BMI and CD4 change (r_S=-0.58; p=0.02). This correlation was stronger than that between CD4 change and initial CD4 (r_S=-0.10), initial VO$_2$max (0.04), initial tension-anxiety (-0.14), or initial depression-dejection (-0.32). Of all the parameters that were investigated, initial BMI best predicted CD4 change. Subjects with a high initial BMI (>25, n=7) had an average decrease in CD4 (-42±65), those with a normal initial BMI (>25, n=10), showed an average increase (47±95). This difference is borderline significant (p≈0.05). It should be noted, however, that also among those with a high initial BMI, CD4 sometimes increased, while it sometimes decreased in subjects with a normal initial BMI. In conclusion, initial BMI appears to be a reasonable but far from perfect predictor of CD4 change when early symptomatic HIV infected persons engage in aerobic exercise training.

Ronsen O, Rasmussen T, Haugen O, Pedersen BK, Bahr R

LEUKOCYTE RESPONSE TO REPEATED BOUTS OF INTENSIVE ENDURANCE EXERCISE SEPARATED BY 3 AND 6 HOURS OF REST

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Rikshospitalet, Copenhagen

The objective of this study was to compare the leukocyte response of a short versus long period of rest between two bouts of endurance exercise on the same day.

Nine elite national team athletes in triathlon (n=4) and speedskating (n=5), age (21-27 yrs, weight: 70-83 kg, VO$_2$max: 65.1-76.8 ml kg^{-1} min^{-1}, mean 69.1 participated in three trials of 24 h duration: 1) complete bedrest (REST), 2) two bouts of exercise separated by 3 h of rest (SHORT) and 3) two bouts of exercise seperated by 6 h rest period (LONG). All exercise bouts consisted of a 10 min warm-up at 50% of VO$_2$max followed by 65 min at 75% of VO$_2$max on a cycle ergometer. The subjects rested in bed at all hours except when exercising. The exercise bouts were performed at 8:00-9:15 (Short), 11:00 AM-12:15 PM (LONG) and 3:15-4:30 PM (SHORT and LONG). Blood was drawn from a venous catheter at least every hour at identical timepoints starting at 3:00 PM until 8:30 PM, and a final sample was obtained 7:30 AM the next day (15 h recovery). An ANOVA procedure for repeated measures was used to compare the experiments and paired t-tests were used where main effects were found.

During REST there was no change in neutrocyte or lymphocyte counts throughout the 24 h experimental period. Neutrocyte count was higher at the start of the second exercise in SHORT (6.6±0.5) compared to LONG (4.7±0.3) (p=0.008), and in both compared to REST (3.1±0.2) (p<0.001). There was a significant increase in neutrocyte count during exercise, but there was no difference in the magnitude of this increase between SHORT (δ:1.5±0.3) and LONG (δ:1.3±0.2,n.s.). During recovery, there was no difference in neutrocyte response between SHORT and LONG. There was a difference in lymphocyte count at the start of the second exercise bout (SHORT: 1.6±0.1 vs LONG: 2.0±0.1). However, there was no difference in the increase of lymphocyte count between SHORT (δ: 2.7±0.2) and LONG (δ: 2.5±0.2) during exercise. During recovery, there was no effect of trial ($F_{1,8}$-4.54, p=0.066), nor of trial by time on lymphocyte counts.

We observed an effect of 3 h vs 6 h of rest between two bouts of exercise on lymphocyte and neutrocyte counts at the start of and during the second bout of exercise, but no effect of previous rest during recovery.

MALM, C

EFFECTS OF ECCENTRIC EXERCISE ON LEUKOCYTE SUBCLASSES AND THE EXPRESSION OF CD ANTIGENS

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The purpose of this study was to investigate the effects of eccentric exercise on leukocyte subclasses, and the expression of CD antigens on leulocytes in blood, in relation to muscle damage, muscle soreness and physical performance. Blood was drawn before and 6, 24 and 48 h after eccentric leg exercise.

There was a significant increase in: plasma CK activity, delayed onset of muscle soreness (DOMS), the number of leukocytes, monocytes and the density of cell adhesion molecules. There was a decrease in lymphocytes, eosinophils, basophils, NK-cells, T-cells with NK-cell function, CD57+, CD20+CD5+, CD8+CD3- and CD4+CD45RO+ cells.

The results indicate that there is a migration of leukocytes to tissues after exercise. Eccentric exercise affects leukocyte subpopulations for at least 48 h. Leukocyte numbers and changes may depend on physical fitness. Muscle soreness correlated with monocytes, basophils and NK-cells. CK correlated with neutrophils and physical perfomance correlated with monocytes. It is hypothesized that other factors than decreased leukocyte numbers may influence the increased risk for infections after exercise and that DOMS is due to leukocyte infiltration and the muscle repair process.

Klöpping-Menke K, Baum M, Schmid A, Liesen H

IMMUNOLOGICAL PARAMETERS AND INTAKE OF ESSENTIAL NUTRIENTS DETERMINED BY FOOD FREQUENCY ANALYSIS

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The immune system plays a key role in the body's ability to fight infection and reduce the risk of developing tumors, autoimmune and degenerative diseases. Nutritional deficiencies influence various components of the immune system.

We determined the average food consumption with the help of food frequency analysis in 13 leisure time or non-athletes before a 12 week moderate endurance training program with a mean age of weight of and height of. With respect to the parameters investigated the recommendations of the German Federation of Nutrition were reached, namely for carotene, Vitamin B6, B12.

Only folate acid did not reach the recommended level in all participants. These data were correlated to the resting values of leukocytes, granulocytes, monocytes, lymphocytes, NK cells, synthesis of IL-1ß, IL-6, IL1-receptor, and soluble interleukin-2-receptor (sIL-2-R). The correlation coeffecient was validated by the Pearson-test, the level of significance $p \leq 0.05$ was described as being of low significance. Significant correlations were found between carotene intake and monocytes, leukocytes, IL-6-production, IL-1ß-production, IL-1-receptor as well as between Vitamin B6 intake and IL-6-production, IL-1ß-production, sIL-2-R, between Vitamin B12 intake and IL-1ß-production and folic acid and IL-6-production, IL-1ß-production.

Further research with respect to the combined determination of nutrient concentration and immunological parameters may give evidence for the importance of the nutritional status.

Hough HJ[a], Failla ML[b]

DAILY VARIABILITY OF IN VITRO ACTIVITIES OF IMMUNE CELLS IN SEDENTARY AND FIT POSTMENOPAUSAL WOMEN

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Previous research suggests that the phenotypic profile and in vitro effector functions of immune cells exhibit daily cyclic and rhythmic fluctuations. Consequently, Smith (1995) has recommended that the same subject must be tested on several occasions to offset intra-individual variability when assessing the impact of exercise on immunocompetence.

The purpose of this study was to examine the daily variability of selected in vitro immune cellular activities in fourty postmenopausal women 45-70 years of age. Subjects were tested on three separate occasions over the course of one week, and blood was collected in the resting state at the same time each day.

Neutrophil respiratory burst activity (RBA), natural killer cell activity (NKCA), and mitogen-induced proliferation of T cells were assessed as indicators of immune function. Marked daily variation was observed in RBA using PMA ($p < 0.05$), but not opsonized zymosan, as a stimulator. A significant daily difference was also found in NKCA ($p < 0.05$). No significant difference was found between days for whole blood cultures stimulated with PHA or ConA. In conclusion, a single blood sample is insufficient for accurately assessing resting baseline values.

Data are also being evaluated to determine any additional impact that fitness and hormone replacement therapy may have on the variability of these immune assays.

Shephard RJ, Shore S

IMMUNE RESPONSES TO EXERCISE AND TRAINING: A COMPARISON OF CHILDREN AND YOUNG ADULTS

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Because of differences in the relative size of the thymus, immune responses to exercise and training might differ between children and adults.

Accordingly, findings in 11 children (9M, 2F, age 10.3 ± 0.6 yr) are compared with data for young adults. Immune responses at rest and after 30 min exercise at anaerobic threshold have been examined before and after 12 wk of training (30 min at 70-85% HRmax, 3 times/wk), sampling at rest, post-exercise, and after 30 min recovery. Data included leukocyte and subset counts (Coulter counter), FACScan CD markers, cytolytic activity (tritiated thymidine) and lymphocyte proliferation (PHA and PWM-stimulated).

At rest, total lymphocyte, CD3+ and CD8+ counts were larger, and CD4+/CD8+ ratio and CD25+ count lower than in adults. Acute exercise induced increases in CD4+, CD8+ and CD56+ cells, with a decrease in CD4+/CD8+ ratio, but unlike adults, there was little decrease in CD56+ count during recovery. After training which increased lean mass and absolute aerobic power by 6%, resting data showed decreases in total leukocytes, CD3+ and CD25+ counts, and acute exercise also induced lesser increases in leukocyte and subset counts, but the post-exercise decrease in CD4+/CD8+ ratio was diminished. Two control children showed no changes other than a decrease of CD25+ count over the same 12 week interval.

We conclude that responses to exercise and training are similar in children and

young adults.

Miles MP, Leach SK, Dohi K, Bush JA, Kraemer WJ, Mastro AM

LYMPHOCYTE RESPONSE TO TETANUS TOXOID STIMULATION AFTER RESISTANCE EXERCISE

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The lymphocyte proliferative response to tetanus toxoid (TT) stimulation reflects the status of the antigen specific, secondary immune response in vaccinated individuals. The aim of this investigation was to determine whether heavy resistance exercise affects the lymphocyte proliferation response to TT. Isolated peripheral blood mononuclear cells from 30 females were cultured with TT over 24 serial dilutions from 0.5 µg/ml to 0.003 pg/ml before and immediately after a 6 x 10 repetition maximum squat resistance exercise. Proliferation was quantitated through the incorporation of tritiated thymidine.

The proliferation response pre-exercise was maximal over the highest 6 dilutions, dropped to near or below background over the next 4 dilutions, increased to about one third of maximum with the next 2 dilutions, and gave a linear dose-response decrease to background over the next 6 dilutions. After exercise, proliferation decreased ($p < 0.05$) in the maximal response range but increased ($p < 0.05$) over the dose-responsive range. When corrected on a per memory lymphocyte basis (CD45RO+, determined using flow cytometry), the response at maximum was no longer decreased, but proliferation over the dose-response range was increased ($p < 0.05$). The mean relative increase over the dose-response dilutions was 23% for the uncorrected response and 40% when corrected per memory lymphocyte. The specific dilutions yielding maximum and dose-responses did not change after the exercise.

Thus, there was an enhancement of lymphocyte proliferation for lower doses of tetanus toxoid, suggesting an enhancement of the secondary immune response immediately following heavy resistance exercise.

Bermon S[a], Ferrari P[b], Candito M[b], Dolisi C[a], Philip P[c]

EFFECTS OF EXERCISE AND TRAINING ON NK CELLS COUNTS IN THE ELDERLY

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Aging has been linked to impairments in strength reserve and in some aspects of immune function, including changes in NK cell count. This study investigated the effects of strength training and exercise on NK cell count in the elderly.

Eighteen healthy and sedentary elderly men (70.4±1.2 yrs) and nine healthy young men (29.4±1.4) gave their informed consent and were referred to our laboratory for a standardized strength test before (all subjects, n=27), and after a 8-wk strength training program (trained elderly (TR), n=9) or a 8-wk period of habitual physical activity (untrained elderly (UN), n=9), For TR, the training program consisted of three sets of leg press, knee extension and bench press exercises, three days a week at 80% of RM1 for eight repetitions. The standardized strength test consisted of five sets of the same exercise at 80% of RM1 for eight repetitions. Prior, immediately and 6h after the test, blood samples were drawn and whole blood CD56+/CD16+ absolute counts were measured by flow cytometry.

TR improved ($p<0.001$) their strength performance with training. Although relative workloads were the same during the strength test, TR showed, after training, a different ($p<0.02$) CD56+CD16+ cells profile.

		CD56+CD16+cells absolute counts			
		Baseline $(10^6.L^{-1})$	Post Exercise $(10^6.L^{1})$	Recovery $(10^6.L^{-1})$	Lifted Load (daN)
Untrained Elderly	Before	165 ± 19	122 ± 11	136 ± 16	5841.3 ± 501.1
	After	166 ± 42	132 ± 24	155 ± 33	6001.6 ± 524.5
Trained Elderly	Before	165 ± 26	111 ± 19	133 ± 12	5980.3 ± 549.0
	After	165 ± 29	167 ± 31	137 ± 24	7122.2 ± 616.3
Young Controls		158 ± 32	250 ± 44	160 ± 32	9755.8 ± 221.3

Our data show that in elderly sedentary men, short-term strength training modifies the exercise-induced NK response towards the one observed in younger men. These results evidence a strong relationship between aging, physical activity and immunological status.

Jonsdottir IH, Hoffmann P

VOLUNTARY CHRONIC EXERCISE AND IN VIVO NATURAL IMMUNITY IN RATS. THE SIGNIFICANCE OF DURATION OF EXERCISE TRAINING AND RUNNING DISTANCE

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The relationship between the duration of exercise training and the beneficial effects of natural immune function was studied in spontaneously hypertensive rats (SHR).

Exercise consisted of voluntary running in wheels for 5 or 11 weeks. In vivo cytotoxicity was measured as clearance of injected ^{51}Cr-labeledd YAC-1 lymphoma cells from the lungs. Compared to sedentary controls, increase in vivo cytotoxicity was seen after 5 weeks of exercise (p<0.001) but not after voluntary exercise for 11 weeks. Interestingly, 11 weeks of voluntary training with resting periods (the wheels were locked 3 days a week during the last 6 weeks of running) significantly augments in vivo cytotoxicity. When compared to the sedentary controls, all runners exercising for 5 weeks, regardless of running activity exhibit significantly higher in vivo clearance of tumour cells from the lungs then the controls. Further analysis, with the animals divided into four groups according to running distance (0-4, 5-8, 9-12 and over 12 km/day) showed that the runners with lowest running activity (<4km/day) exhibit significantly lower in vivo clearance of tumour cells from the lungs when compared to animals running more than 4km/day. No other differences were seen between the groups.

We conclude that the duration of exercise training has significant effects on the training-induced effects on natural immune function and that the resting periods for the 11 weeks group seem to be of great importance. This could be of interest, giving the possibility to study overtraining effects in animals.

Ogawa K, Nagatomi R, Yoshida Y, Tamagawa A, Ohmori H

MODULATION OF HUMAN BLOOD MONOCYTE FUNCTION AFTER A SINGLE BOUT OF EXERCISE

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Several investigators have reported modified function and phenotype of monocyte/macrophage lineage after exercise. We have also found out that mild endurance training enhances the immune-complex induced production of oxygen radicals from gamma-IFN activated monocytes or macrophages in human and mice. In mice studies, we found that at least 3 weeks of repeated exercise was necessary to obtain a significant level of enhancement in peritoneal macrophages. Considering that peripheral blood monocyte is a direct precursor of macropahges, we postulated that exercise-modulated monocytes accumulate and differentiate into macropahges in various organs such as liver, spleen, lung or peritoneal cavity maintaining the functional enhancement. In this study we tried to find out whether a single bout of

exercise could induce functionally enhanced monocytes in the blood stream, which would eventually be distributed to various organs.

6 healthy subjects (3 males and 3 females aged 24±1 years) participated in the study. They were told not to exercise from 1 week before the study until the end of the 2-week experimental period. Control blood samples were drawn for the first 4 days at 17:00 daily. On the 7th day at 16:30 subjects were told to exercise on a bicycle ergometer at 60-70% HRmax for 30 min. Blood samples were drawn just after the exercise, 24, 48, 72, and 96hr after the exercise. Monocyte population was purified from the blood samples and analyzed for the ability to produce oxygen radicals in response to IgG immune complex stimuli after 12hr of incubation with or without 1000U gamma-IFN by means of luminol-dependent chemiluminescence method.

The number of blood monocytes per volume blood did not show significant change throughout the experiment. The amount of oxygen radicals produced per unit cells from gamma-IFN activated monocytes was significantly increased by 55% at 24hr, 27% at 48hr, 12% at 72hr after exercise and returned to the control level at 96hr after exercise.

It was suggested that a single bout of exercise induces functionally-potentiated monocytes in the blood stream which might eventually be distributed to and accumulated in various organs, considering the fate of blood monocytes.

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IMMUNE STATUS OFTEN IMPROVES BUT SOMETIMES DETERIORATES FOLLOWING EXERCISE TRAINING IN THE HIV-INFECTED: A META-ANALYSIS.

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Following LaPerriere's initiative in the early 1990's a sufficiently large number of randomized controlled trials on exercise training for the HIV-infected have been published to warrant quantitative meta-analysis. In all studies where exercise physiological parameters were used as dependent variables, the experimental groups showed clear advantages over the control groups. A meta-analysis of the effect-sizes reveals that these advantages are significant: Exercise training for the HIV-infected improves body weight, strength and VO2max. On the other hand, the effects on immunological parameters (such as: CD4-count) and psychological parameters (such as: mood) are mixed: In most cases these parameters improve, but in some studies deterioration was observed. In particular, negative effects were found in Schlenzig's PhD-study (1992) which is somewhat inaccessible and has remained relatively unknown; nevertheless, Schlenzig's study is well-designed and

documented with great precision. Meta-analysis of the immunological and physiological effect-sizes in all published studies, points to non-random differences between studies that report improvement and studies that report deterioration. Several hypotheses were formulated to systematically explain these differences. So far, hypotheses that were tested turned out to be insufficiently discriminative. No systematic relationship couls be found between immunological and psychological effects, and there is no systematic relationship between such effects and stage of discase. In HIV-infection, immunological and psychological parameters are of great relevance. Explaining why these parameters often improve but sometimes deteriorate following exercise training offers an important research priority for the coming years.

Philip P[a], Baldid M[a], Bermon S[b]

EXERCISE-INDUCED LYMPHOCYTE SUBSETS CHANGES: ABSOLUTE COUNTS MEASURED WITH A FLUORESCENT MICROSPHERES SYSTEM

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In the field of exercise immunology numerous studies focused on exercise or training-induced lymphocyte subsets variations. These cell absolute number changes are calculated on the basis of routine complete blood counts data which represents a non negligible source of error (Coefficent of Variation sometimes >20%). In our laboratory, we adjunct fluorescent microspheres (Coulter Flow-Count fluorspheres, Coulter, Hialeah, FL, USA) to labled samples prior to flow cytometric analysis in order to provide greater precision to the absolute count determination (CV<2%). The aim of this study was to investigate whether this new measurement method is suitable for exercise immunology studies.

Eight trained male subjects (age 30.5±SEM 1.5 yrs) underwent a 30 s bicycle Wingate test and blood samples were collected before and 3 min following exercise. Whole blood CD19+, CD3+/CD45+, CD3+/CD4+, CD3+/CD8+, CD3-/CD56+/CD16+ absolute counts were simultaneously measured with flow cytometry Coulter systems. Coulter clones, Immunoprep EPICS leucocyte preparation, Multi-Q-Prep Epics immunology work station, Flow-count fluorspheres, EPICS MCL-XL.

Average power mean was 9.13 ± 0.02 W/kg^{-1}. CD19+, CD3+/CD45+, CD3+/CD4+, CD3+/CD8+, CD3-/CD56+/CD16+ cells absolute counts significantly ($p<0.05$) increased after supramaximal exercise (0.14 ± 0.02 to 0.18 ± 0.04, 1.41 ± 0.14 to 2.28 ± 0.26, 0.60 ± 0.09 to 0.73 ± 0.82, 0.72 ± 0.12 to 1.22 ± 0.22, 0.25 ± 0.06 to 0.90 ± 0.22 $10^9.1^{-1}$ respectively).

These lymphocytes subsets change patterns after a brief supramaximal exercise are in accordance with those previously reported under the same conditions (Nieman et

al., 1992). The Flow-count fluorospheres system appears suitable for cell absolute counts determination in exercise immunology studies.

Ronsen O, Rasmussen T, Haugen O, Pedersen BK, Bahr R

LEUKOCYTE RESPONSE TO SINGLE VS. REPEATED BOUTS OF INTENSIVE ENDURANCE EXERCISE

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Norwegian University of Sport and Education, Oslo
Rigshospitalet, Copenhagen

The objective of this study was to compare the leukocyte response of one versus two bouts of endurance exercise on the same day.

Nine elite national team athletes in triathlon (n=4) and speedskating (n=5), age (21-27 yrs, weight: 70-83 kg, VO_2max: 65.1-76.8 ml kg^{-1} min^{-1}, mean 69.1 participated in three trials of 24 h duration: 1) complete bedrest (REST), 2) one bout of exercise (ONE), 3) two bouts of exercise separated by a 3 h rest period (TWO). All exercise bouts consisted of a 10 min warm-up at 50 % of VO_2max followed by 65 min at 75% of VO_2max on a cycle ergometer. The subjects rested in bed at all hours except when exercising. The exercise bouts were performed 11:00 AM-12:15 PM (only in TWO) and 3:15-4:30 PM (ONE and TWO). Blood was drawn from a venous catheter at least every hour at identical timepoints starting at 3:00 PM until 8:30 PM, and a final sample was obtained 7:30 AM the next day (15 h recovery). An ANOVA procedure for repeated measures was used to compare the experiments and paired t-tests were used where main effects were found.

During rest there was no change in neutrocyte or lymphocyte concentration throughout the 24 h experimental period. Neutrocyte count was elevated at the start of the afternoon exercise bout when the subjects had exercised previously (TWO: 6.6±0.5 vs. ONE: 3.1±0.2;p<0.001). There was a significant increase in neutrocyte count during exercise, but there was no difference in the magnitude of this increase between TWO (δ: 1.5±0.3) and ONE (δ: 2.0±0.3, n.s.). During recovery, there was an effect of trial ($F_{1,8}$=5.20, p=0.052) and trial by time ($F_{7,56}$=5.04, p<0.001) on neutrocyte count. Neutrocyte counts was increased in TWO compared with ONE at 15 min post-exercise, but not at 30 min and beyond. There was no difference in lymphocyte count at the start of the afternoon exercise bouts (TWO: 1.6±0.1; ONE: 1.6±0.1). However there was a greater increase in lymphocyte count during exercise in TWO (δ: 2.7±0.2) vs. ONE: (δ: 1.8±0.2) (p<0.003). During recovery, there was no effect of trial ($F_{1,8}$= 3.68, p=0.091), but an interaction effect of trial by time ($F_{7,56}$=8.29, p<0.001) on lymphocyte count.

We observed an effect of previous exercise on lymphocyte and neutrocyte counts during exercise, but only minor effects of previous exercise during early recovery.

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THE EFFECT OF ACTIVE RECOVERY UPON LEUKOCYTES AND MYOCELLULAR ENZYMES AFTER MODERATE- AND HIGH INTENSITY RUNNING IN TRAINED SUBJECTS

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Extensive research are currently being carried out in the area of exercise immunology based on the J-formed relationship between physical fitness and the prevalence of upper respiratory tract infections (URTI). In short, the population of well-trained endurance athletes seem to be more susceptible to infections than any other group investigated. The recreational exercisers seem to have the lowest incidence of URTI. After the immediate leucocytosis triggered by physical and mental stress, there is seen a decrease even below resting levels in the number of white blood cells (WBC) in blood 15-60-min post exercise. This has often been referred to as „the open window", reflecting an opportunity for possible immunosuppression, before a second leukocytosis is detected 2-4h following exercise.

The purpose was to investigate how active recovery (AR, of 50% of VO_2max) influenced the number of WBC in blood in „the open window"-period, after moderate- (60 min at 70% of VO_2max, MI) or high-intensity (30 min at 80% of VO_2max, HI) running compared rest recovery (RR). Supporting variables are creatine kinase, lactate dehydrogenase, thrombocytes, hemoglobin. hematocrit and total protein. 14 endurance trained males (19-36 years, mean VO_2max = 69mL/kg*min)participated in the randomized, cross-over, descriptive study. They performed either AR or RR for 15-min after MI- or HI-exercise. Wilcoxon signed rank test of difference scores was used, and there was a significant difference of WBC after HI exercise between RR and AR 15-min post-exercise.

The drop when performing RR was 36% while the reduction was minimized to 6% after AR (p=0.018). There were no significant findings after MI exercise, although the trends followed the significant findings after HI exercise. The plasma volume changes were statistically equal after AR and RR for both MI- and HI-exercise. The reduced decrease in WBC count might be explained ba a maintained epinephrine level while continuing exercising even if the intensita is low. The subgroups of WBC that responds the most to training are known to be ones with the highest density of β-adrenergic receptors. It also seems that AR may be more beneficary after more exercise, although there were no major accumulation of lactate at neither intensity in this study.

Our findings may contribute in the attempts to minimize the drop in WBC and possibly decrease the vulnerability to infections after intense exercise.