

Age-Related Changes in Immune System Function

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Immune Function: Effect of Aging and Exercise

Why study this?

- **INCREASED RISK for infectious diseases, tumorigenesis, autoimmune disorders associated with aging**
- Exercise may alter immune function: positive and/or negative effects?
- Does exercise pose a risk or a benefit for immune function for the elderly?

Immunity: Types of Immunity

- **Innate, Non-specific Immunity**
 - Physical (body temperature)
 - Body biochemistry (pH)
 - Cellular phagocytosis
 - Macrophages
 - Neutrophils
 - Monocytes
- **Adaptive Immunity**
 - Immune system acquires “memory” for the antigen
 - Second exposure results in a potentiated response proliferating the “memory” cells

Types of Cells/Molecules Involved in the Immune Response

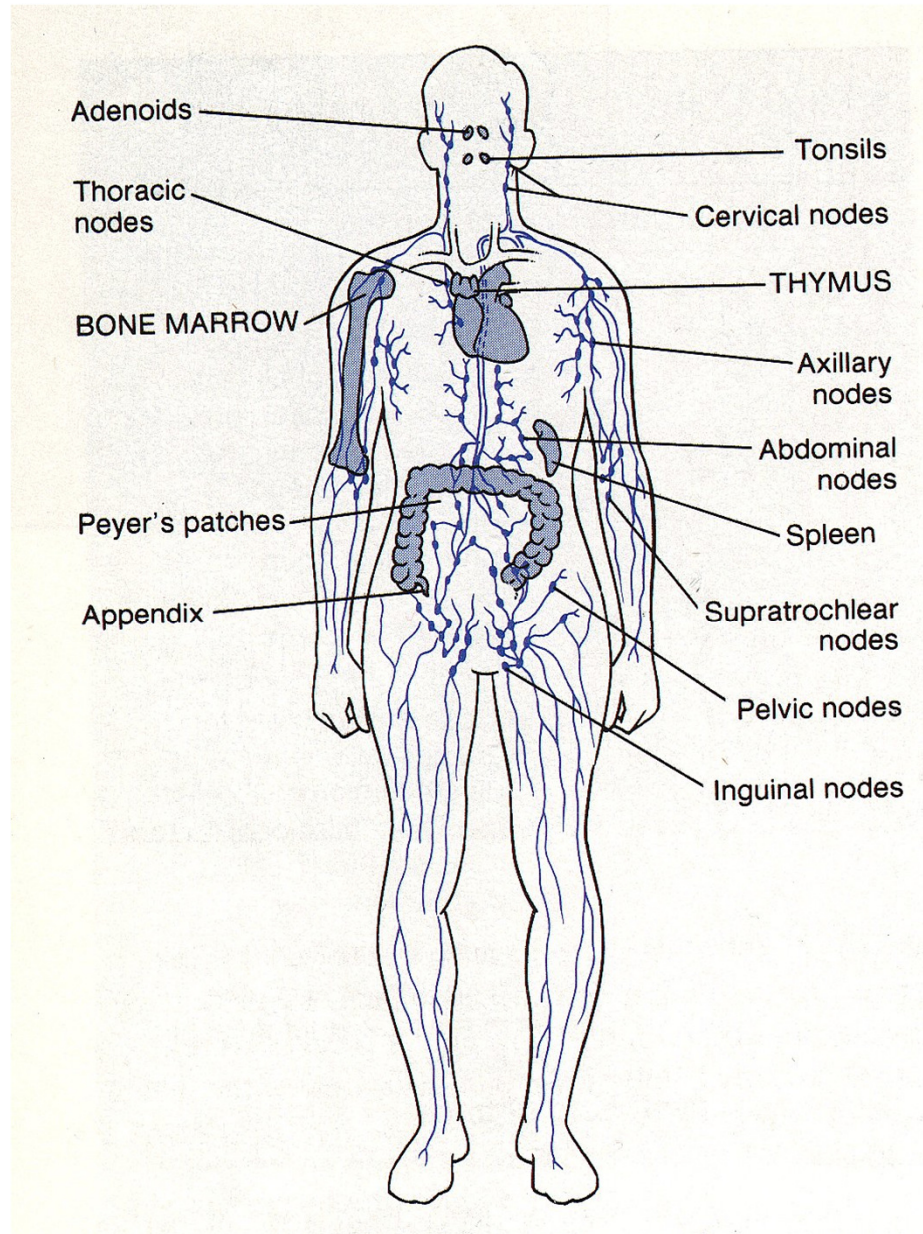
- **Antigen**
 - “Anything that can be bound by an antibody”
- **Antibody**
 - Protein (Immunoglobulin, i.e. IgA) that is *formed in response to an antigen and reacts specifically with that antigen*
- **Antigen Presenting Cells**
 - Macrophages and dendritic cells
 - First cells to encounter and interact with antigen
- **Lymphocytes**
 - *Recognize, bind, and interact with antigens*
 - B Cells will bind antigens and become activated to produce antibodies (sometimes require the help of T Cells to become activated)
 - T Cells will bind antigens and become activated and will kill the target cell or serve to recruit other white blood cells

Types of Cells/Molecules Involved in the Immune Response

- **Phagocytes**
 - Macrophages and neutrophils
- **Natural Killer Cells (NK)**
 - Lymphocytes that are *cytotoxic in the absence of prior “stimulation”*
 - First line of defence against infection, tumor growth
- **Cytokines**
 - Biologically active substances produced by cells that influence other cells

Organs and Tissues of the Immune System

- **Bone Marrow**
 - Major source of all blood cells including LYMPHOCYTES
- **Thymus**
 - Critical organ where T cells mature and differentiate
- **Secondary Lymph Organs**
 - Lymph nodes concentrate or “trap” antigens present in lymph



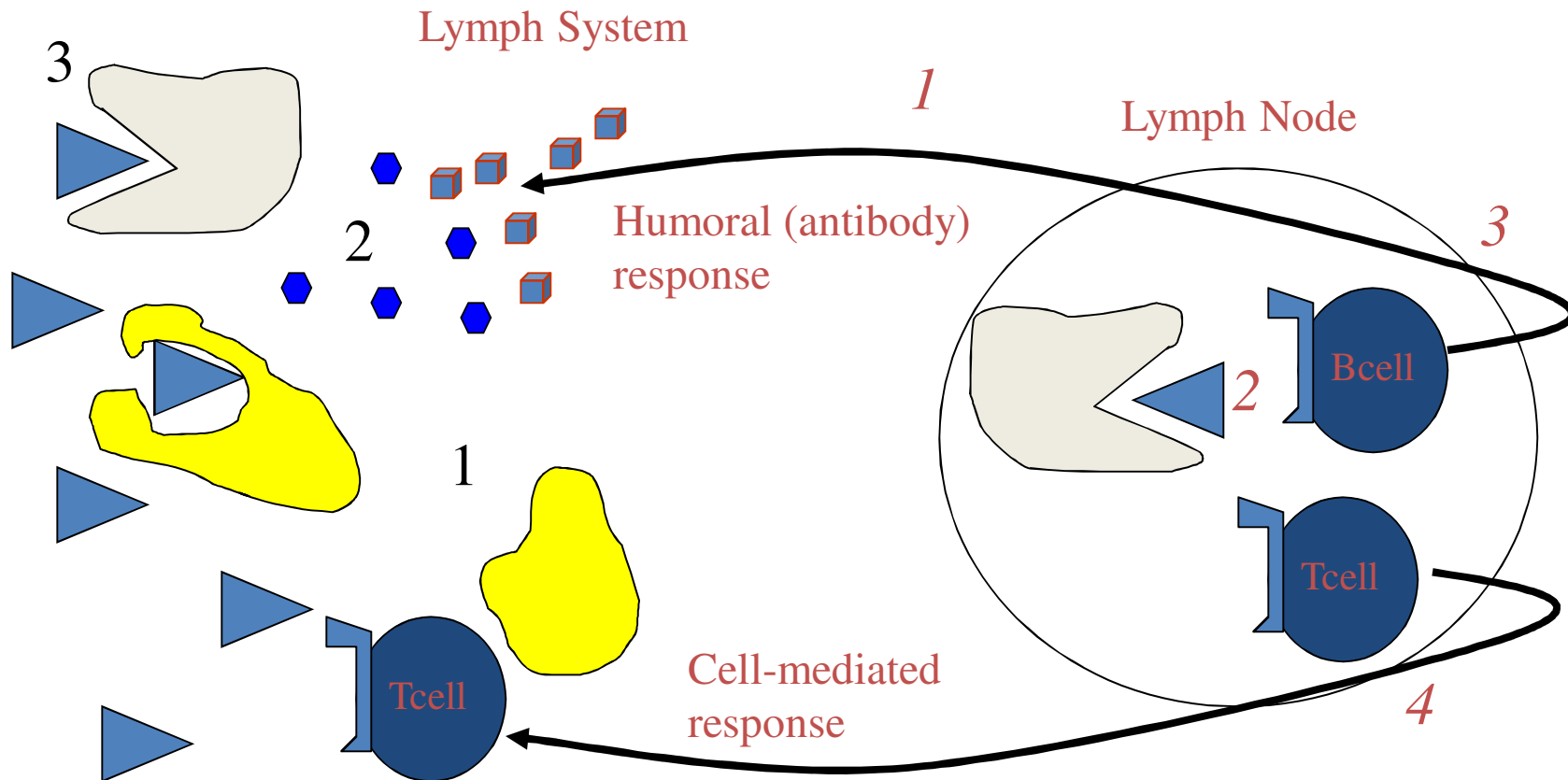
Schematic of Immune Response

First Line of Defence

1. Phagocytosis
2. Cytokine release
3. Antigen-presenting cells bind antigen
4. Presence of antibodies (IgA in saliva)

Second Line of Defence

1. Concentration of antigens in lymph
2. B Cell and T Cell recognition of antigen
3. Activation and proliferation of appropriate antibody producing B cell
4. Activation and proliferation of appropriate T cell



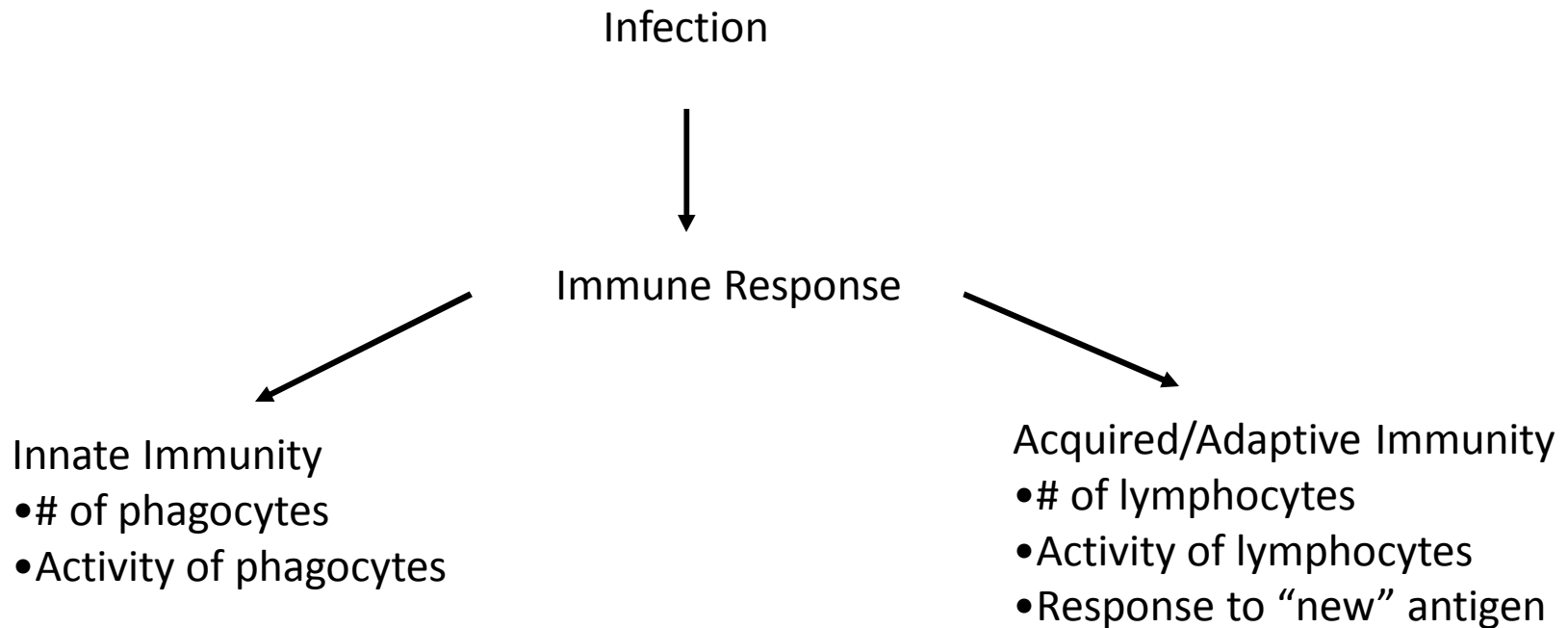
Effect of Aging on Immune Function: Immune Senescence

Functional Decline in several components of the immune system accompanies aging:

1. Substantial shrinking of the THYMUS (largest at puberty, shrinking then begins and is complete by midlife)
2. DECREASED T cell immune response

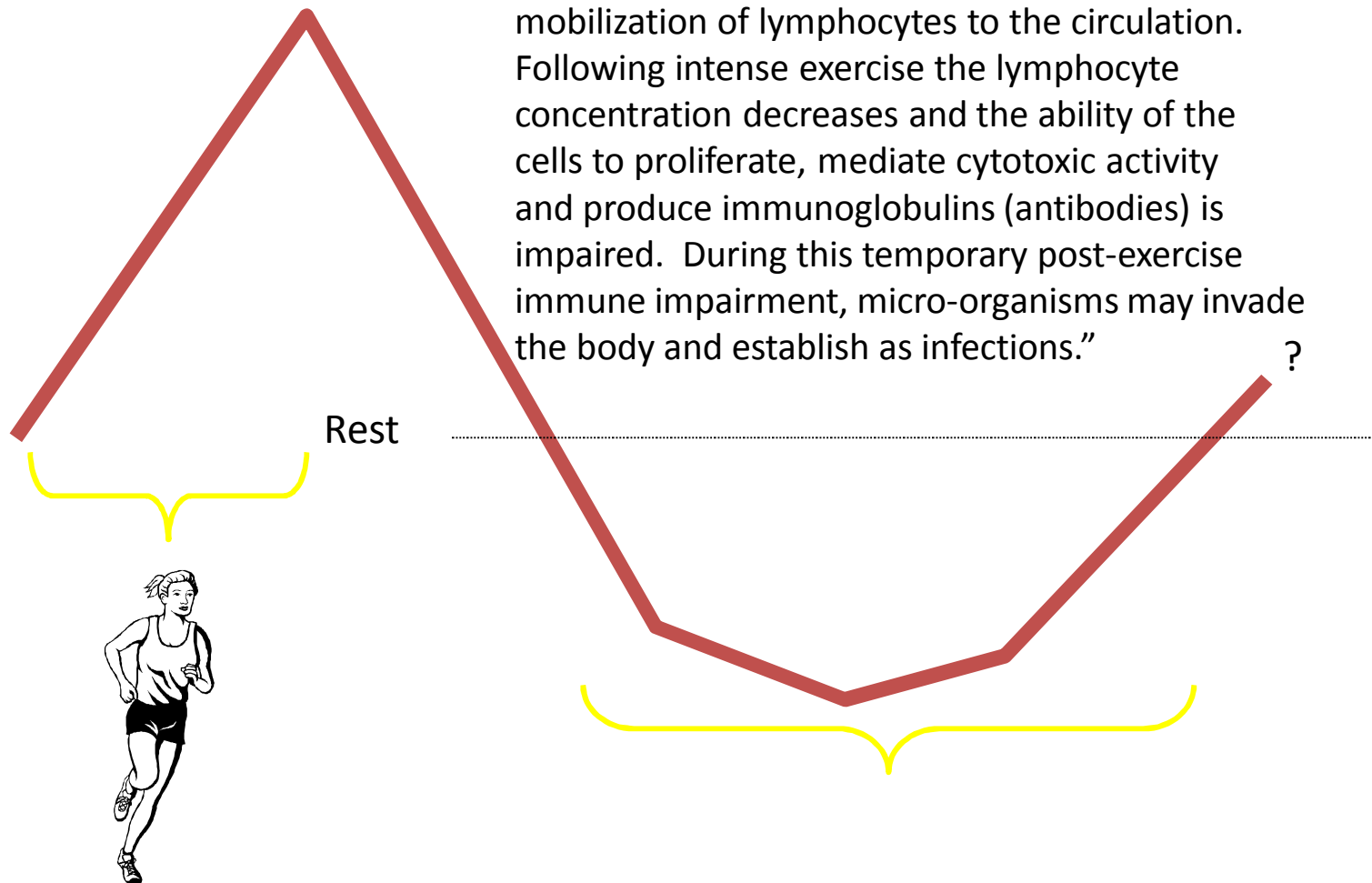
3. Total Bone Marrow is reduced with aging
4. Neutrophil activity declines: “No appetite for killing”
5. Altered cytokine secretion (some increase, some decrease)

Evaluating Immune Function: Quantity vs. Quality of Response



Immune Function: Effect of Exercise

The “Open Window” Theory: “An acute bout of exercise induces mobilization of lymphocytes to the circulation. Following intense exercise the lymphocyte concentration decreases and the ability of the cells to proliferate, mediate cytotoxic activity and produce immunoglobulins (antibodies) is impaired. During this temporary post-exercise immune impairment, micro-organisms may invade the body and establish as infections.”



Single Exercise Bout: Effects on Cells and Molecules of the Immune System

Pedersen, B.K., et al. (2000). "Exercise is a stress that results in an immune system response, similar to other stresses such as trauma, burn, and surgery." *Phys. Rev.*, 80:1055-1081.

Immune Cell/Molecule	Moderate Intensity Exercise (Prolonged)		High Intensity Exercise (Prolonged)	
	<i>During</i>	<i>After</i>	<i>During</i>	<i>After</i>
Neutrophils	↑	↑	↑	↓
Lymphocyte B Cells	↑	↓ back to norm	↑	↓
Lymphocyte T Cells	↑	↓ back to norm	↑	↓
Natural Killer Cells	↑	↔	↑	↓
Cytokines	????	????	????	????
Immunoglobulin (IgA)	↓	↓	↓	↓

Exercise in Older Persons: Effect on Immune Function

Acute Exercise (Limited Data)

- Immune response to exercise in the elderly
 - 23 vs. 69 year old groups: 20 min of 60% peak cycling exercise
 - Immune response prior to exercise was suppressed in elderly vs. young
 - Maximal cycle ergometer test: compared NK cell activity
 - NK activity was not different between young and old before exercise
 - Elderly trained (16 weeks aerobic training) vs. untrained
 - Higher NK activity at rest in trained

Exercise in Older Persons: Effect on Immune Function

Chronic Exercise (Limited Data)

- Immune response to exercise in the elderly
 - 12 weeks walking (5d/week at 60% HR_{max}), 73 year old women
 - Highly trained older women had higher T Cell and NK function than sedentary older women, but still below younger women
 - Habitual male endurance exercisers showed a smaller decline in T Cell function than sedentary counterparts
 - Tai Chi group (mean age 62 years) vs. age matched sedentary controls
 - Higher T Cell activity at rest

Activity Level Determines Immune Response to Vaccine

Kohut, M.L., et al. (2002). "Exercise and psychosocial factors modulate immunity to influenza vaccine in elderly individuals." *J Gerontology: Medical Sciences*, 57A(9): M557-M562.

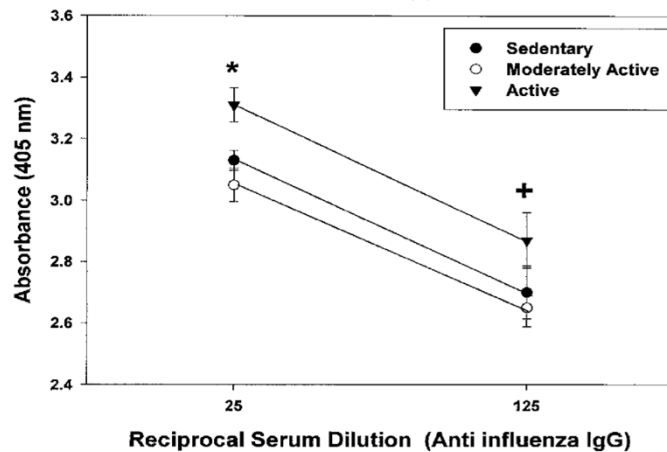


Figure 2. Serum IgG anti-influenza antibody response in sedentary, moderately active, and active at 1:25 and 1:125 dilution. Values are means \pm SEM. Asterisks indicate significant differences ($p < .05$) compared with all other treatment groups. + indicates active significantly greater than moderately active.

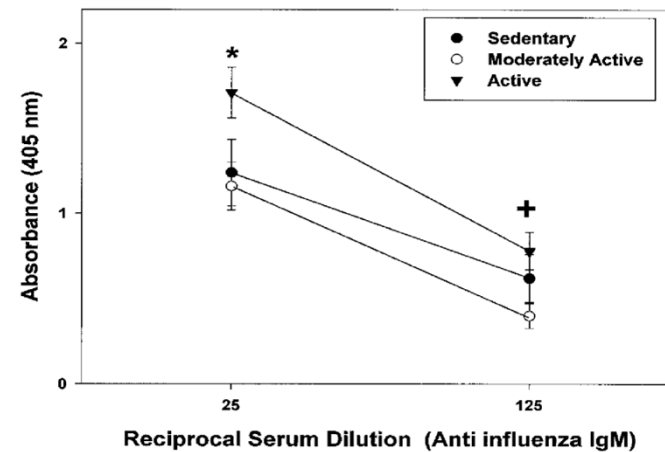
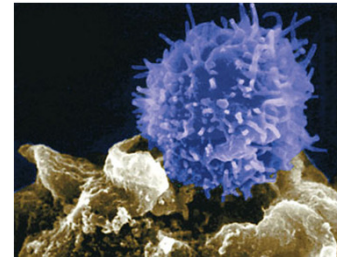
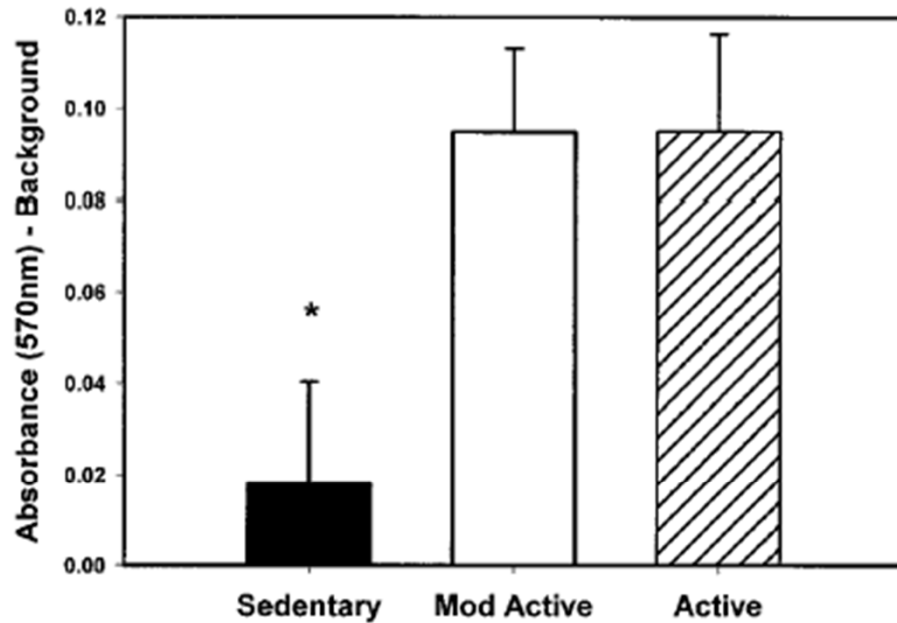


Figure 3. Serum IgM anti-influenza antibody response in sedentary, moderately active, and active at 1:25 and 1:125 dilution. Values are means \pm SEM. Asterisks indicate significant differences ($p < .05$) compared with all other treatment groups. + indicates active significantly greater than moderately active.

- 62+ years old: Active – ≥ 20 min vigorous exercise 3+ times per week
- Moderately Active – regular exercise, less intensity and frequency
- Sedentary – no exercise

Activity Level Determines Immune Response to Vaccine



T-cell

Proliferation of:

- Leukocyte
- Monocyte
- Lymphocyte

Figure 1. Influenza-stimulated proliferation in peripheral blood mononuclear cells (PBMC) from sedentary, moderately active, and active. PBMC were collected 2 weeks postimmunization and were cultured with influenza vaccine for 5 days. Results are expressed as mean \pm SEM. Asterisks indicate significant differences ($p < .05$) compared with all other treatment groups. Background proliferation was determined from the wells containing cells and media without virus. The background was subtracted from the average reading obtained in the wells incubated with virus.

Duration of Training Is A Critical Determinant of Improved Immune T-Cell Function

Woods, J.A., et al. (1999). "Effects of 6 months of moderate aerobic exercise training on immune function in the elderly." *Mechanisms of Ageing and Development*, 109:1-19.

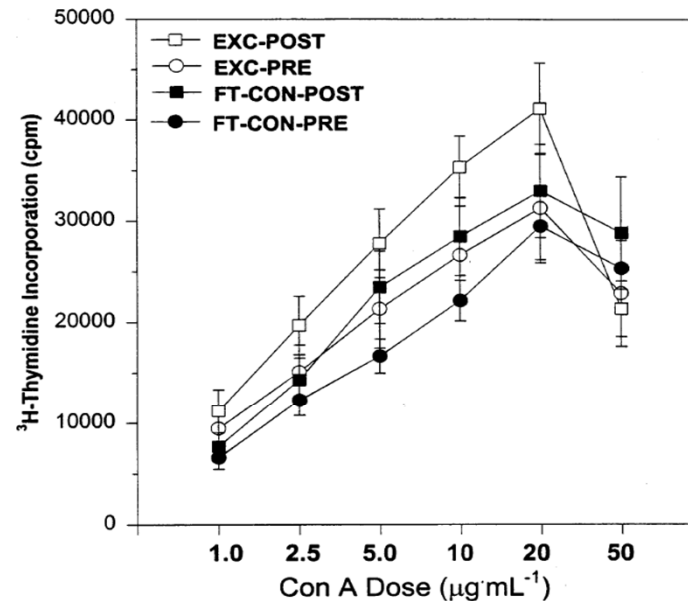


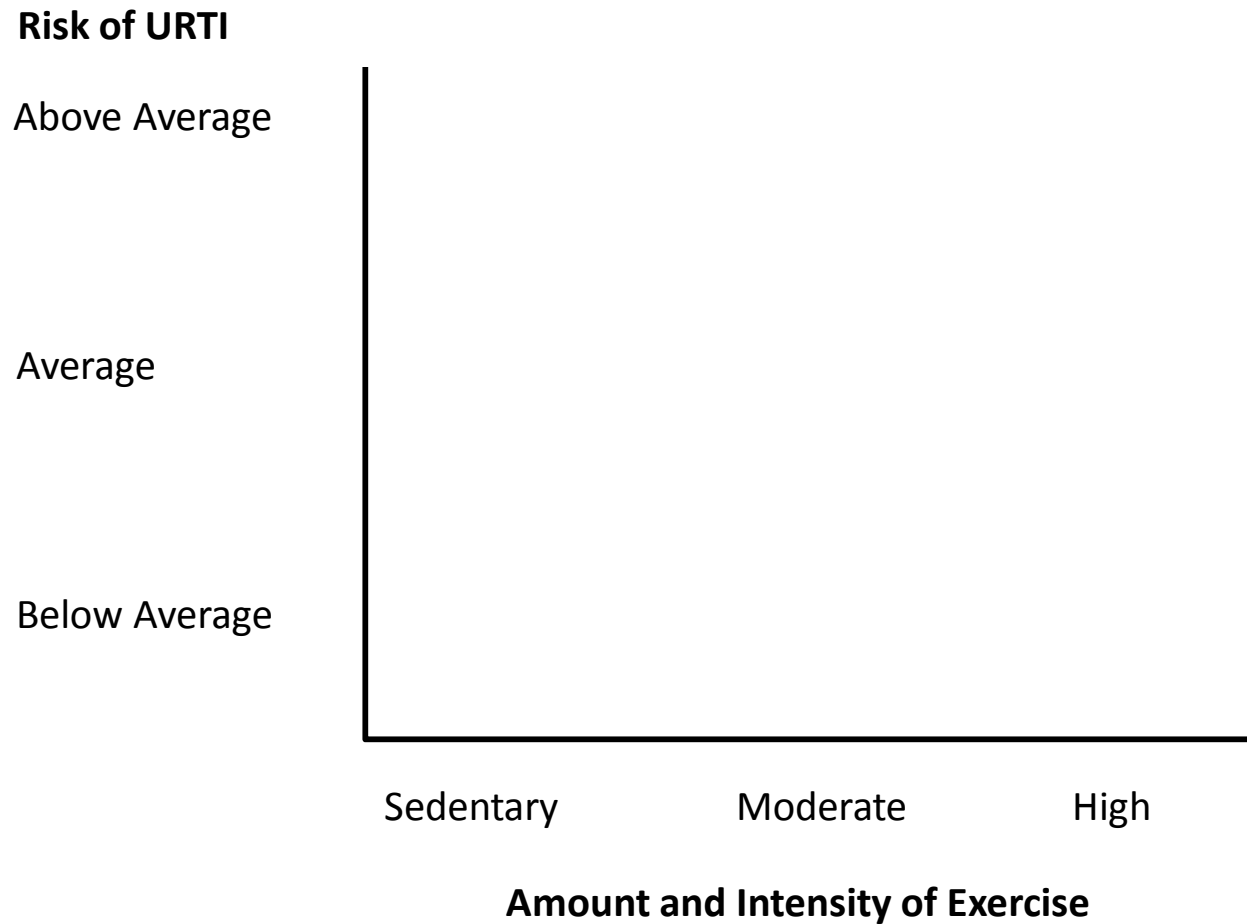
Fig. 1. Effects of 6 months of exercise training on lymphocyte responsiveness to a wide range of Con A concentrations ($n = 12$ and 11 , for FT-CON and EXC, respectively). In the 2-way RM ANOVA model, there were no group or group \times time effects at any of the doses. However, there were significant ($P < 0.05$) time main effects at 2.5, 5, 10, and 20 $\mu\text{g mL}^{-1}$ doses of Con A, such that post-intervention values were greater than pre-intervention values. This effect occurred in both FT-CON and EXC, but was larger in EXC.

FT-CON: Flexibility Toning Control Group

EXC: Aerobic Exercise Training 60% peak VO₂

6 MONTHS OF TRAINING

The “J” Form Curve Hypothesis



URTI: Beneficial Effect of Exercise Training

1,365 women 55-80 years

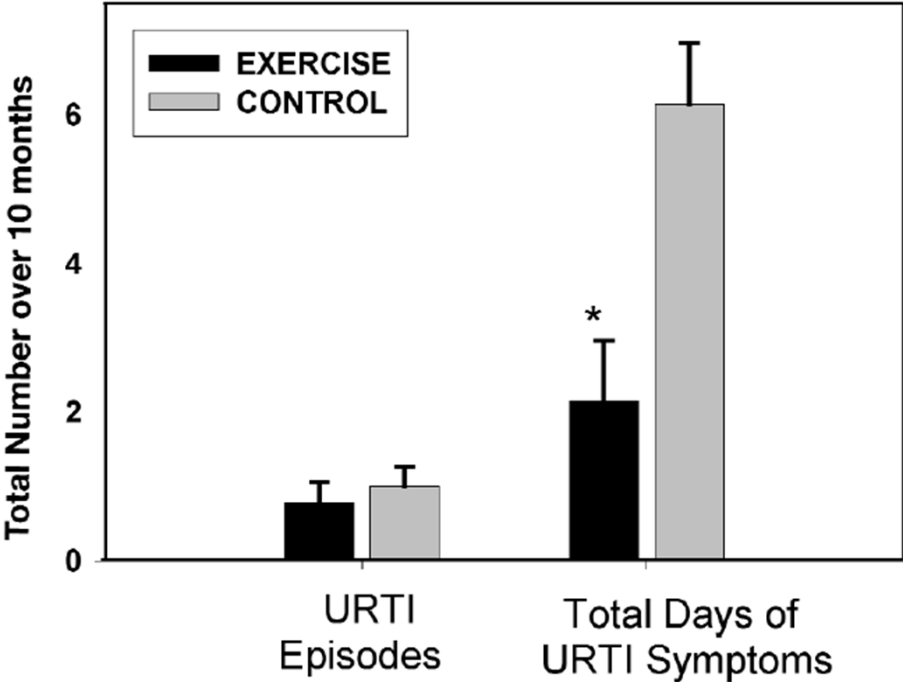
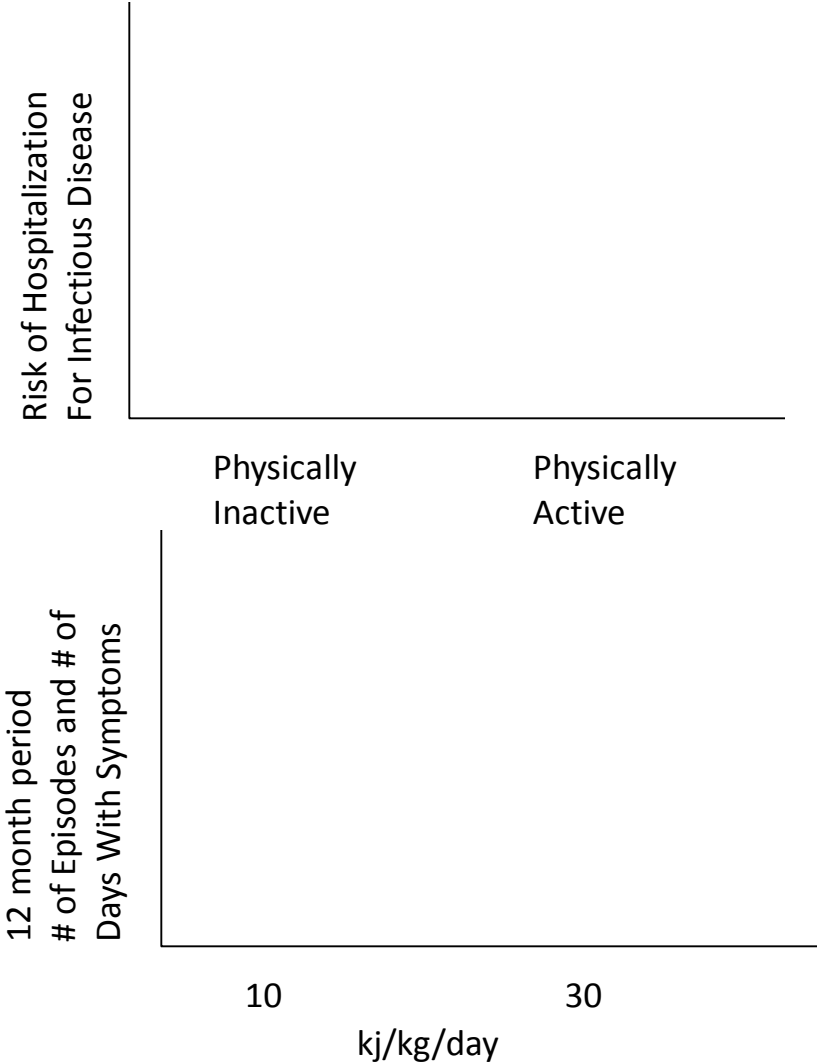


Figure 1. The total number of reported upper respiratory tract infections was compared between aerobic exercise and control subjects over the 10-month intervention period. No difference existed between groups. The total number of days with URTI symptoms was also compared between groups during this same time period. The exercise subjects reported significantly fewer days with symptoms ($p=0.031$). Note, illness were not physician verified and the n was small (n=14 control, n=14 exercise).



Immunosenescence and Exercise

Kohut, M.L. & Senchina, D.S. (2004). "Reversing age-associated immunosenescence with exercise." *Exerc. Immunol. Rev.*, 10:6-41.

Overall, the combined data suggest that exercise may be an efficacious therapy for partially restoring immune function in geriatric populations, particularly when long-term exercise interventions are employed. Currently, there are insufficient data to determine: 1) whether aerobic exercise has different effects than resistance training, 2) an optimal amount of exercise that can be recommended, and 3) if the benefits of exercise are restricted to certain populations.