Exercise Diet & Stress Reduction: What do we tell our patients?

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Outline

- Inflammation and lifestyle
- Inflammation and aging
- Exercise and Immunity
- Stress and Immunity
- Nutrition and Immunity
- Recommendations to patients
Heart Attack

Fatty deposits build up in the lining of arteries over time. As an artery narrows, the risk increases that a clot will form and totally block blood flow.

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Hereditary heart risks

Increased risk of early-onset heart problems for relatives of people who died of cardiovascular disease before age 60, according to a new study:
ROLE OF INFLAMMATION IN PLAQUE RUPTURE

Vulnerable → Rupture → Thrombus → Myocardial Infarction

White blood cells → Platelets and fibrin
CRP and risk of Heart Attack

What do CRP test results mean?

- **BELOW 1 MILLIGRAM PER LITER (MG/L):** Low risk of heart disease.
- **1 TO 3 MG/L:** Average risk. The average American tests between 1 and 2 mg/L.
- **3 MG/L AND ABOVE:** High risk. About 25 percent of Americans fall into this category.
- **10 MG/L:** Experts consider this number abnormally high. It can result from a passing infection (such as the flu). Wait six weeks and retest.
Can we do something about inflammation and CVD?
Aging and Immunosenescence
Aging of the Immune System

- After age 50 the immune system undergoes dramatic changes, loss of protective function; gain in pro-inflammatory functions
- Ubiquitous and dynamic, but not ‘even’ among compartments (innate and adaptive)
- T cells most effected
  - Signaling is “rewired”
  - Acquire ‘senescence associated secretory phenotype’ and induce tissue inflammation
The diagram illustrates the changes in total T cells and specific subpopulations over age. It is divided into three stages:

1. **Memory generation** (blue): This stage shows the increase in memory T cells and pathogen susceptibility with age.
2. **Memory homeostasis** (red): Here, the memory T cell population stabilizes, while circulating memory T cells increase slightly.
3. **Immunosenescence** (green): In this phase, the total T cells decrease, and pathogen susceptibility remains relatively constant.

The y-axis represents the percentage of total T cells, while the x-axis denotes age in years. The right y-axis indicates the infectious disease hospitalization rate per 10,000 individuals.
The Janus Head of Immune Aging

Age-related immunodeficiency
- Shrinking naïve T and B cell compartments
- Contraction in T and B cell receptor diversity
- Decreased T cell receptor sensitivity to respond to stimuli

Age-related inflammatory syndrome
- Preponderance of myeloid over lymphoid lineages
- Excess production of inflammatory cytokines (e.g. IL-6, TNF)
- Failing self-tolerance with production of autoantibodies
Predicted mortality of 85yo> at 2,4,6 yrs
Decreased diversity
Association with CMV
CD4/8 best marker and absent in “successful aging”

- Swedish investigators were the first to identify immunologic predictors of survival and mortality
- OCTO NONA
- “Immune Risk Profile

Immune Risk Profile
- CD4 < CD8
- Low B cells
- Poor proliferative response
- High CD8 + CD28-cells
- Low naïve cells
- CMV seropositivity
- Expansion of CMV-specific clones

Low-grade inflammation
Cognitive impairment
MORTALITY
Aging Inflammation
Immunosenescence

- Changes in lymphocyte subpopulations
  - Changes in lymphocyte subpopulations
  - Thymic involution
  - Immunosenescence
  - CMV, Obesity, Stress

- Inflamming
  - Accumulation of senescent T cells
  - IL-6, TNF-α, PCR, IL-10
  - CD28, KLRG1, CD57

- Telomere shortening and resistance to apoptosis
  - Autoimmune diseases, cardiovascular diseases and cancer
  - Severity of infections
  - Response to vaccines
INFLAMMAGING

- CMV
- ↑ Adiposity
- ↑ ROS
- ↓ Microbiota diversity

- ↑ Memory cell
- ↑ Cytotoxicity
- Activated macrophages
- TLR8
- MyD88
- ROS
- Interaction: microorganisms–enterocytes
  - Mucus, IgA, defensins, antimicrobial peptides
- Activated GALT-DC
- Activation of effector cells

↑ IL-6, TNF-α, CRP, ↓ IL-10

Source: Immunotherapy © 2013 Future Medicine Ltd.
Immune-mediated Inflammatory Diseases

Initiation
Susceptibility
Triggers
Accelerants

Inflammation
(TNF, IL-1, IL-6, IL-17,
IL-23, IL-18, IL-15, Others)

Damage / Destruction / Symptoms
(RA, SLE, PsA, IBD, AS, MS)

DM, CHF, Alzheimer's, Transplant, Sepsis, Allergy, Vasculitis, ASO, HIV
Maintaining a Healthy Immune System: What you can do to help

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Modified from http://nutrigenomics.ucdavis.edu/dietarychemicals.htm
The “J” curve

Risk of URTI

Increased
Normal
Decreased

Sedentary  Moderate  Very high

Training load
EPIDEMIOLOGY OF INFECTIONS AND EXERCISE/TRAINING

- Studies in 80s and 90s (Peters + Bateman, Neiman others) demonstrated increased URI following marathons vs. matched controls (100-500%)
- Not confirmed by all
- Most not clinically confirmed
Exercise effects on mucosal immunity
Maree Gleeson and David B Pyne
Immunology and Cell Biology (2000) 78, 536–544;

Pre-exercise salivary IgA concentrations for each training session over a 2 week period for an elite kayaker and the percentage change from the initial concentration.
Exercise effects on mucosal immunity
Maree Gleeson and David B Pyne
Immunology and Cell Biology (2000) 78, 536–544;

Training volume and upper respiratory tract illness (URTI) episodes during a spring-summer training and competition season for elite swimmers (n = 22). Each shaded block indicates an episode of URTI in a swimmer.
EPIDEMIOLOGY OF INFECTIONS AND EXERCISE/TRAINING

• More recent studies (elite, competitive, untrained) using validated screening instruments and microbial isolation confirmed the “J” curve though pathogens found in only 30%

• Raises the issue of the nature of “URI’ in elite athletes i.e. allergic, vasomotor, other
The “J” curve

Risk of URTI

Increased

Normal

Decreased

Sedentary  Moderate  Very high

Training load

• 1002 adults were followed 12 weeks (winter fall) and monitored for URTI (Wisconsin URSS)
• Subjects reported frequency of aerobic activity and rated their fitness

RESULTS: Number of days with URTI symptoms was reduced 43% in subjects reporting 5 or more days of aerobic training; URTI severity was also reduced

CONCLUSION: Perceived physical fitness and frequency of aerobic training are important correlates of reduced days of URTI and severity in fall/winter

OTHER STUDIES 29% decrease with moderate to vigorous physical activity (Matthews MED SCI SP EX 2002)
Physical activity and immune function in elderly women


- Women 67-85 randomized to walking and calisthenics
- Immune function; Aerobic capacity and URTI were monitored

RESULTS: Incidence of URTI was lowest in the highly conditioned group and highest in the calisthenic control group during the 12-wk study, with the walkers in an intermediate position (chi-square = 6.36, P = 0.042). In conclusion, the highly conditioned elderly women in this study had superior NK and T cell function when compared with their sedentary counterparts.
Anti-inflammatory effects of exercise
### For Important Health Benefits

**Adults need at least:**

- 2 hours and 30 minutes (150 minutes) of **moderate-intensity aerobic activity** (i.e., brisk walking) every week and **muscle-strengthening activities** on 2 or more days a week that work all major muscle groups (legs, hips, back, abdomen, chest, shoulders, and arms).

**OR**

- 1 hour and 15 minutes (75 minutes) of **vigorous-intensity aerobic activity** (i.e., jogging or running) every week and **muscle-strengthening activities** on 2 or more days a week that work all major muscle groups (legs, hips, back, abdomen, chest, shoulders, and arms).

**OR**

- An equivalent mix of moderate- and vigorous-intensity **aerobic activity** and **muscle-strengthening activities** on 2 or more days a week that work all major muscle groups (legs, hips, back, abdomen, chest, shoulders, and arms).

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<table>
<thead>
<tr>
<th><strong>Moderate-intensity Physical Activity</strong></th>
<th><strong>Vigorous-intensity Physical Activity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(Approximately 3-6 METs)</strong></td>
<td><strong>(Approximately &gt;6 METs)</strong></td>
</tr>
<tr>
<td>Requires a moderate amount of effort and noticeably accelerates the heart rate.</td>
<td>Requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate.</td>
</tr>
</tbody>
</table>

**Examples of moderate-intensity exercise include:**

- Brisk walking
- Dancing
- Gardening
- Housework and domestic chores
- Traditional hunting and gathering
- Active involvement in games and sports with children / walking domestic animals
- General building tasks (e.g. roofing, thatching, painting)
- Carrying / moving moderate loads (<20kg)

**Examples of vigorous-intensity exercise include:**

- Running
- Walking / climbing briskly up a hill
- Fast cycling
- Aerobics
- Fast swimming
- Competitive sports and games (e.g. Traditional Games, Football, Volleyball, Hockey, Basketball)
- Heavy shovelling or digging ditches
- Carrying / moving heavy loads (>20kg)
The Basics: Exercise Guidelines

- ACSM minimum guidelines: 150 minutes of moderate to high intensity activity per week
  - Other proposed minimums: 10,000 steps per day
  - Fitbit? Pedometer? IPod/IPhone?
- 2 or more days per week of strength training
## Examples of Moderate and Vigorous Intensity Physical Activities

*(American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention, 2012)*

<table>
<thead>
<tr>
<th>ACTIVITIES</th>
<th>MODERATE INTENSITY</th>
<th>VIGOROUS INTENSITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise and leisure</td>
<td>Walking, dancing, leisurely bicycling, ice and roller skating, horseback riding, canoeing, yoga</td>
<td>Jogging or running, fast bicycling, circuit weight training, swimming, jumping rope, aerobic dance, martial arts</td>
</tr>
<tr>
<td>Sports</td>
<td>Downhill skiing, golfing, volleyball, softball, baseball, badminton, doubles tennis</td>
<td>Cross-country skiing, soccer, field or ice hockey, lacrosse, singles tennis, racquetball, basketball</td>
</tr>
<tr>
<td>Home activities</td>
<td>Mowing the lawn, general yard and garden maintenance</td>
<td>Digging, carrying and hauling, masonry, carpentry</td>
</tr>
<tr>
<td>Occupational activity</td>
<td>Walking and lifting as part of the job (custodial work, farming, auto or machine repair)</td>
<td>Heavy manual labor (forestry, construction, fire fighting)</td>
</tr>
</tbody>
</table>
How Low Can You Go?

Public Health Recommendations

150 minutes per week Mod to High Physical Activity

Well documented that this can be achieved in 10 minute or less sessions!!!!

Yancey A JAMA 309:141,2013
Stress Reduction
Exercise and Stress

- **Fight or flight**
  - Short term beneficial (minutes/hours)
  - Long term deleterious (weeks/months)

- **Mediated by numerous integrated physiologic systems i.e. HPA, immune other**
  - Schedlowskij (J Clin Imm 1993) measured T cells in parachute jumpers pre, post, delayed
    - Increased T NK immediately after (epi); suppressed 2 hrs after (cortisol)
Stress and Inflammation

• Psychological stress may be a trigger of inflammation

• Individuals suffering from chronic inflammatory conditions frequently use stress reduction approaches of the Complementary and Alternative Medicine (CAM) to find the relief
Chronic stress and immunity

- **Dysregulatory**
  - Altered cytokine balance
  - TH1/TH2 skewing
  - Accelerated immunosenescence
  - Decreased numbers, trafficking and function of adaptive immunity

- **Exercise that is prolonged, extreme etc can be deleterious and mimic chronic stress**

- **Exercise that is ‘appropriate’ can be beneficial and serve to de-stress**
Exercise may stimulate the immune system, and thereby prevent or ameliorate cold-n-flu.

http://technorati.com/lifestyle/article/running-to-lose-weight/
Mindfulness meditation may reduce stress, & thereby prevent or ameliorate cold-n-flu.
Research Question:

How can we prevent Acute Respiratory Infection?

(Cold and Flu)
Acute respiratory infection = ARI

• Influenza ARI is associated with ≥ 20,000 deaths and 500,000 hospitalizations in the U.S yearly
• Non-influenza ARI accounts for ≥ 20 million doctor visits and 40 million lost school/work days
• Economic impact of non-influenza ARI ≥ $40 billion, making non-influenza ARI one of the top 10 most expensive illnesses


Q. Can we prevent non-influenza ARI?
A: Maybe, sometimes, don’t know

- Contact avoidance
- Hand-washing
- *Enhance physical health*
- Exercise
- Nutrition
- *Enhance mental health*
- Stress reduction
- Self-care
- Relationships

- Immunization is impractical because too many viruses
- Immune enhancing drugs, herbs (echinacea) and supplements (vitamins) are unproven
MEPARI trial

- Meditation or
- Exercise to
- Prevent
- Acute
- Respiratory
- Infection
MEPARI

• OBJECTIVE

• To evaluate potential preventive effects of mindfulness meditation or sustained moderate intensity exercise on incidence, duration and severity of acute respiratory infection
MEPARI = randomized controlled trial

- Community recruited adults aged 50 years or older were randomized to 1 of 3 conditions:
  - 8-week training in mindfulness meditation
  - matched 8-week training in moderate intensity sustained exercise
  - wait-list observational control
Mindfulness based stress reduction

MBSR

- Standardized 8 week course
- Incorporates aspects of meditation & yoga
- Aims to enhance awareness of body & mind
- Attention to sensation, thought, emotions
- 2.5 hours in class each week
- 45 minutes daily practice

Pioneered by Jon Kabat-Zinn PhD
Center for Mindfulness in Medicine, Health Care
University of Massachusetts Medical School
Exercise

Matched to MBSR by:

- Duration (8 weeks)
- Attention (weekly 2½ hour group sessions)
- Intensity (daily 45 minute at-home practice)
- Location (UW Research Park)

- Aimed at sustained moderate intensity exercise
- Jogging, fast walking, biking, swimming, etc
- Goal of 12 to 16 points on Borg’s Rating of Perceived Exertion

Borg GV, Linderholm H. Perceived exertion and pulse rate during graded exercise in various age groups. *Acta Medica Scandinavica* 1967;472:194-206
Cost benefit analysis

- Economic analysis of ARI-related costs to assess whether mindfulness meditation or exercise add value
- Monte Carlo bootstrap methods evaluated reduced costs of ARI episodes
- Costs per subject were based on cost of generic medications (actually used), missed work days ($126.20 imputed) and clinic visits ($78.70 imputed)

Conclusions:

- Mind-body behavioral trainings such as mindfulness meditation or moderate intensity sustained exercise may reduce incidence, duration and severity of cold/flu illness.

- If these results are confirmed in future studies there may be important implications for both:
  1) health-related policy & practice, and
  2) scientific understanding of mechanisms of health maintenance and disease prevention.
Chronic stress and immunity

• Beneficial effects of exercise on stress are more likely to occur when:
  • Physical and psychosocial aspects of exercise are matched (fitness, capability, temperament, etc) of the individual
  • Highly individual!
Tai Chi Chih

Tai Chi mind-body
Combines physical activity with modest aerobic component with “meditation through movement”
Associated with documented health benefits in multiple domains and the treatment of illnesses such as fibromyalgia
NEJM 2011

Tai Chi Chih
Westernized version
Pathogenesis and Natural History and Latency of VZV

- Can not be cultured
- + S blot and PCR
- neuronal - epineuronal cells
- episomes
- select gene expression
Shingles immunity and health functioning in the elderly: Tai Chi Chih as a behavioral treatment

15 weeks
Randomized
20 movements
45 minutes – 3 times /week
Health education control

After 16 weeks both immunized with VARIVAX

Quantitative measurements of VZV CMI and QOL (SF36)
RESULTS

• Tai Chi group showed higher levels of VZV-CMI than HE controls (2 x)
• Tai Chi alone increased VZV CMI that was comparable to varicella vaccine
• Tai Chi group improved in QOL physical function, pain, vitality, mental

• CONCLUSION Tai Chi Chih improves VZVZ CMI and augments VZV induced CMI from varicella vaccine
The beneficial effects of Tai Chi exercise on endothelial function and arterial stiffness in elderly women with rheumatoid arthritis

Jeong-Hun Shin¹, Yonggu Lee², Soon Gil Kim³, Bo Youl Choi³, Hye-Soon Lee⁴ and So-Young Bang⁵

Abstract

Background: Rheumatoid arthritis (RA) has been known to be associated with increased risk of cardiovascular disease (CVD). The aim of this study was to investigate the effects of Tai Chi exercise on CVD risk in elderly women with RA.

Method: In total, 56 female patients with RA were assigned to either a Tai Chi exercise group (29 patients) receiving a 3-month exercise intervention once a week or a control group (27 patients) receiving general information about the benefits of exercise. All participants were assessed at baseline and at 3 months for RA disease activity (Disease Activity Score 28 and Routine Assessment of Patient Index Data 3), functional disability (Health Assessment Questionnaire), CVD risk factors (blood pressure, lipids profile, body composition, and smoking), and three atherosclerotic measurements: carotid intima-media thickness, flow-mediated dilatation (FMD), and brachial-ankle pulse wave velocity (baPWV).

Results: FMD, representative of endothelial function, significantly increased in the Tai Chi exercise group (initial 5.85 ± 2.05 versus 3 months 7.75 ± 2.53 %) compared with the control group (initial 6.31 ± 2.12 versus 3 months 5.78 ± 2.13 %) ($P = 1.76 \times 10^{-3}$). Moreover, baPWV, representative of arterial stiffness, significantly decreased in the Tai Chi exercise group (initial 1693.7 ± 3483 versus 3 months 1600.1 ± 2910 cm/s) compared with the control group (initial 1740.3 ± 1853 versus 3 months 1792.8 ± 326.1 cm/s) ($P = 1.57 \times 10^{-3}$). In addition, total cholesterol decreased significantly in the Tai Chi exercise group compared with the control group (−7.8 ± 15.5 versus 29 ± 122 mg/dL, $P = 2.72 \times 10^{-3}$); other changes in RA-related characteristics were not significantly different between the two groups. Tai Chi exercise remained significantly associated with improved endothelial function (FMD; $P = 4.32 \times 10^{-3}$) and arterial stiffness (baPWV; $P = 2.22 \times 10^{-3}$) after adjustment for improvement in total cholesterol level.

Conclusion: Tai Chi exercise improved endothelial dysfunction and arterial stiffness in elderly women with RA, suggesting that it can be a useful behavioral strategy for CVD prevention in patients with RA.

Keywords: Rheumatoid arthritis, Tai Chi, Cardiovascular risk
Diet and Immunity

Mediterranean Diet

Mediterranean diet is characterized by:
1. Use of Olive oil instead of butter, lard or any other animal fats.
2. An abundant use of grains, fruits, legumes and vegetables.
3. And moderate use of animal products, instead preferring fish over meat, and reducing use of milk and its derivatives.

www.reduce-weight-digest.com
Some of My Best Friends Are Germs
The Rise of the Microbiome

Pubmed “Microbiome” Hits

NIH HUMAN MICROBIOME PROJECT

Nasal
Oral
Skin
Gastro-intestinal
Urogenital

The New York Times Magazine
The Economist
nature
TED
TRIPLE Probiotic

Germs
Microbes maketh man
OUR OTHER GENOME

NURSE THE BABY
Your Inner Ecosystem

By using this information, you can improve your own microbiome as well as take part in the process of understanding.
Role of the Gut Microbiota in Immunity and Autoinflammatory Diseases

- 100 trillion organisms
  - Digestion/fermentation/vitamin production
  - Development of innate and adaptive immunity
  - Protection from ‘dybiosis’

- When homeostasis is disrupted the microbiota can contribute to disease

Strength of Antiviral Defense Depends on Presence of Commensal Bacteria

- Conventionally housed mice cleared CMV faster than mice treated with broad spectrum ATBs for 2 weeks prior.
- ATB treated mice succumbed to sublethal influenza with increased lung pathology.
- Peritoneal Macrophages from ATB Rx’d mice show down regulation of RIG1 and IFN response genes.
- *Can probiotics influence immunity to viruses?*

What I tell my patients about eating
The Mediterranean Diet is not a diet, as in “go on a diet,” even though it is a great way to lose weight or improve your health. Rather, it is a lifestyle – including foods, activities, meals with friends and family, and wine in moderation with meals.
Mediterranean Diet

• Prospective cohort study - predictors of low mortality
  - MOD Alcohol
  - LOW Meat
  - HIGH Veggies, Fruit, Nuts, Legumes
  - High Olive Oil
Dietary Recommendations

- Abundant plant foods (fruits, vegetables, whole-grain breads, other forms of cereals, beans, nuts, and seeds);
- Minimally processed, seasonally fresh, and locally grown foods;
- Fresh fruits as the typical daily dessert
- Based on nuts, olive oil, and concentrated sugars or honey consumed during feast days;
- Olive oil as the principal source of dietary lipids;
- Dairy products (mainly cheese and yogurt) consumed in low to moderate amounts;
- Fewer than four eggs consumed per week;
- Red meat consumed in low frequency and amounts;
- Wine consumed in low to moderate amounts, generally with meals.
Flexiterean

• “Eat food. Not too much. Mostly plants.” Michael Pollan
What I say

Putting it All Together