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The Center for Vasculitis Care and Research

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


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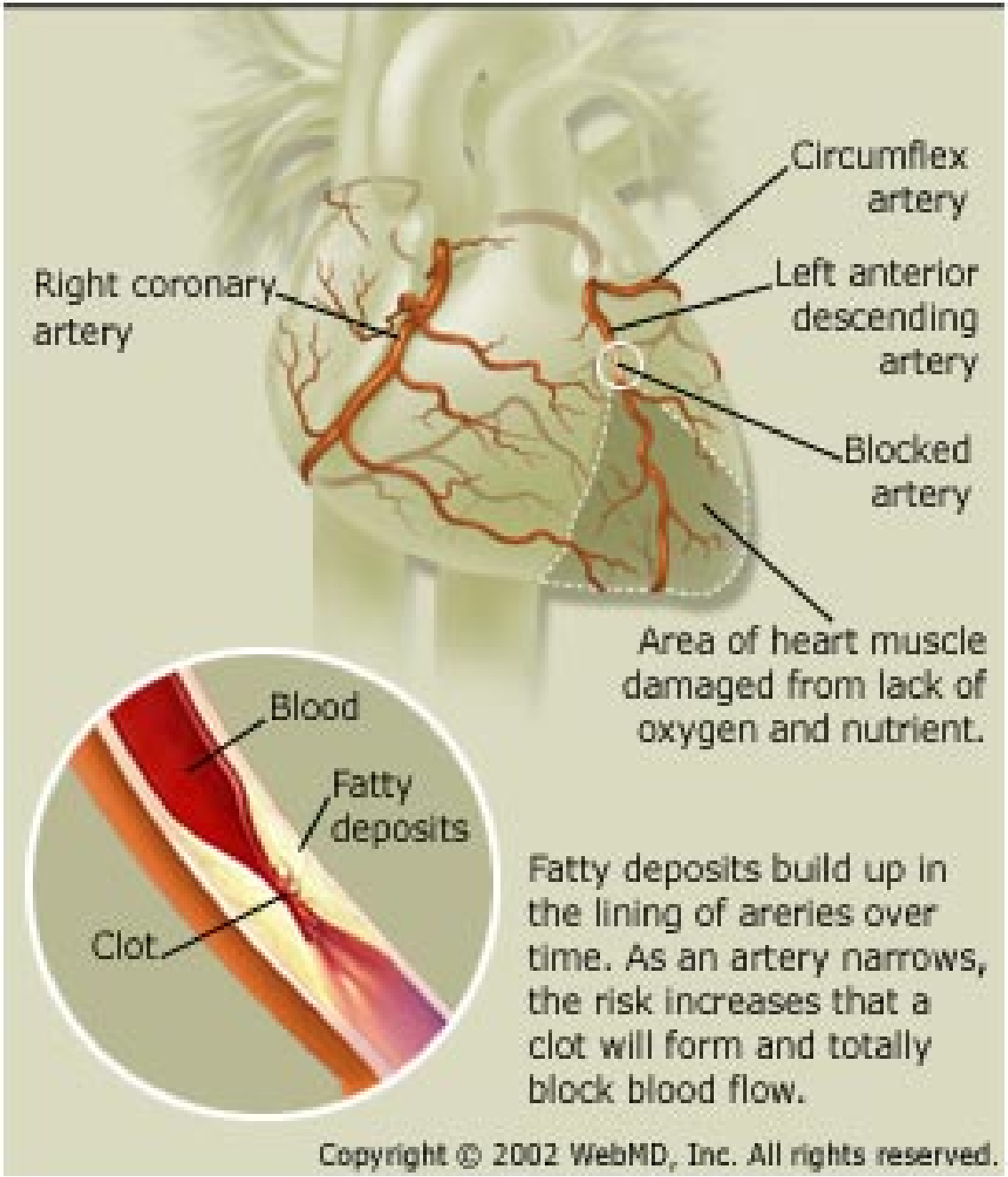
# Outline

- Inflammation and life style
- Inflammation and aging
- Exercise and Immunity
- Stress and Immunity
- Nutrition and Immunity
- Recommendations to patients


TIME
BUSH'S MILITARY RECORDS IS DISNEY MOUSETRAPPED?
THE SECRET KILLER
The surprising link between INFLAMMATION and HEART ATTACKS, CANCER, ALZHEIMER'S and other diseases
What you can do to fight it

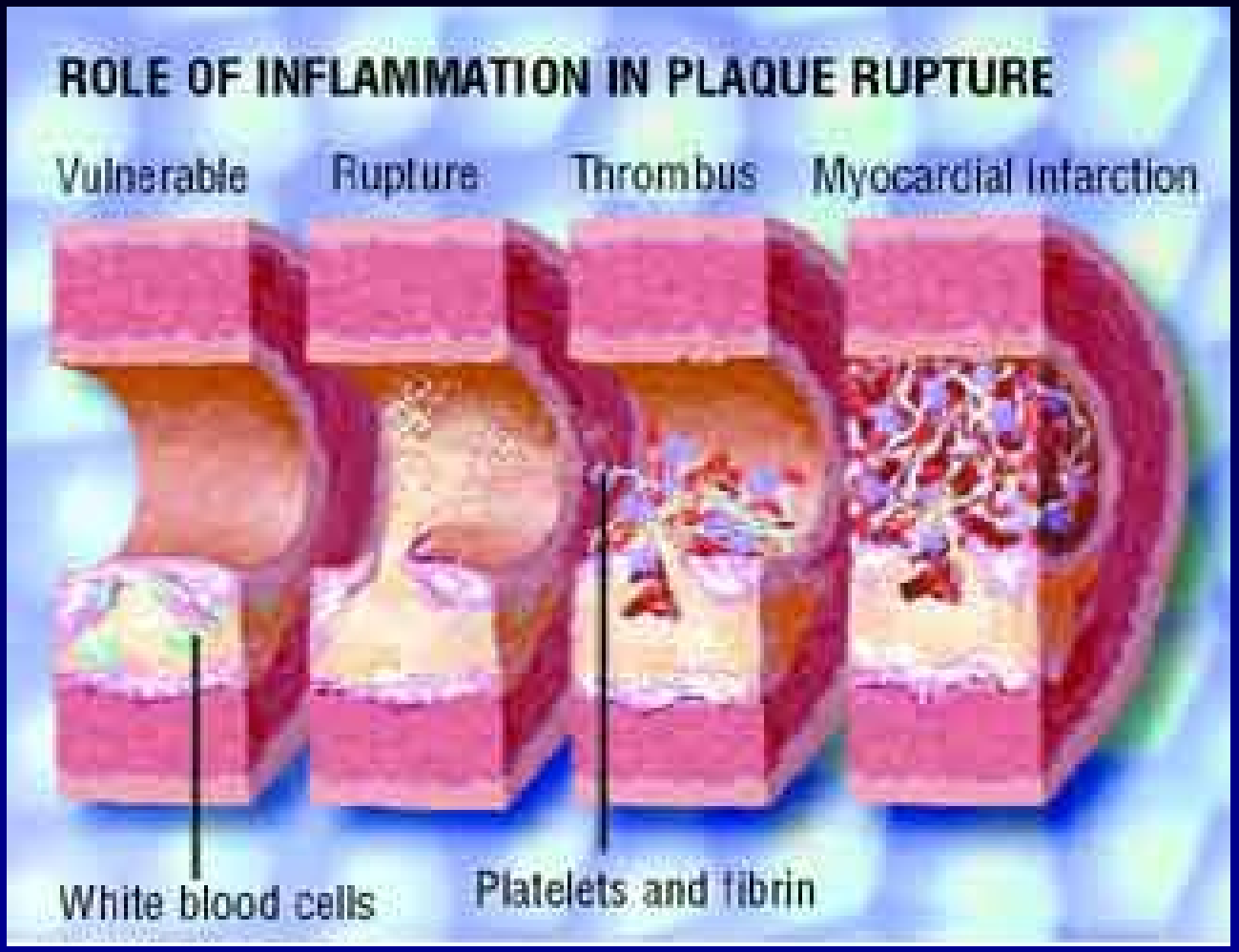
# Heart Attack



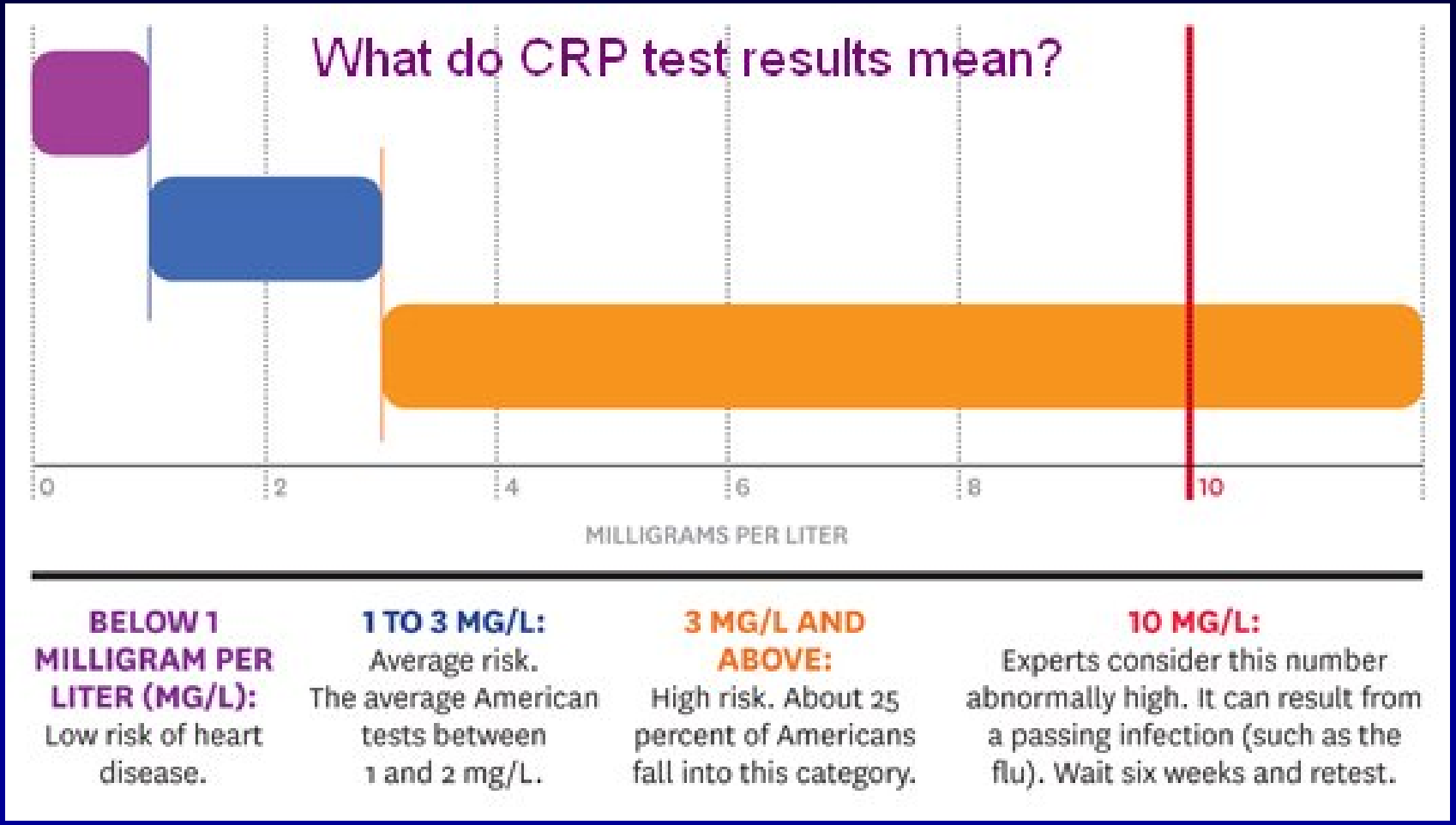
## Hereditary heart risks

Increased risk of early-onset heart problems for relatives of people who died of cardio-vascular disease before age 60, according to a new study:


People
SUMMER'S HOTTEST BACHELORS
91 SEXY AND SINGLE GUYS
MARIO LOPEZ BARES ALL!
EXCLUSIVE COUNTRY STAR SARA EVANS' WEDDING
TIM RUSSERT 1950-2008
A FAMILY'S HEARTBREAK
The newsman's family recalls a life well lived. 'Tim was a happy man,' wife Maureen says. 'He realized all of his dreams.' PLUS Could he have been saved?


ROLE OF INFLAMMATION IN PLAQUE RUPTURE
Vulnerable
Rupture
Thrombus
Myocardial Infarction
White blood cells
Platelets and fibrin

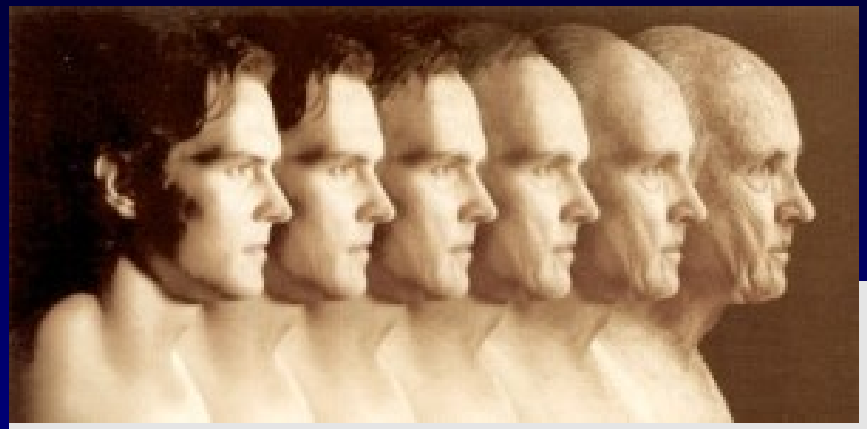
# CRP and risk of Heart Attack



# Can we do something about inflammation and CVD?

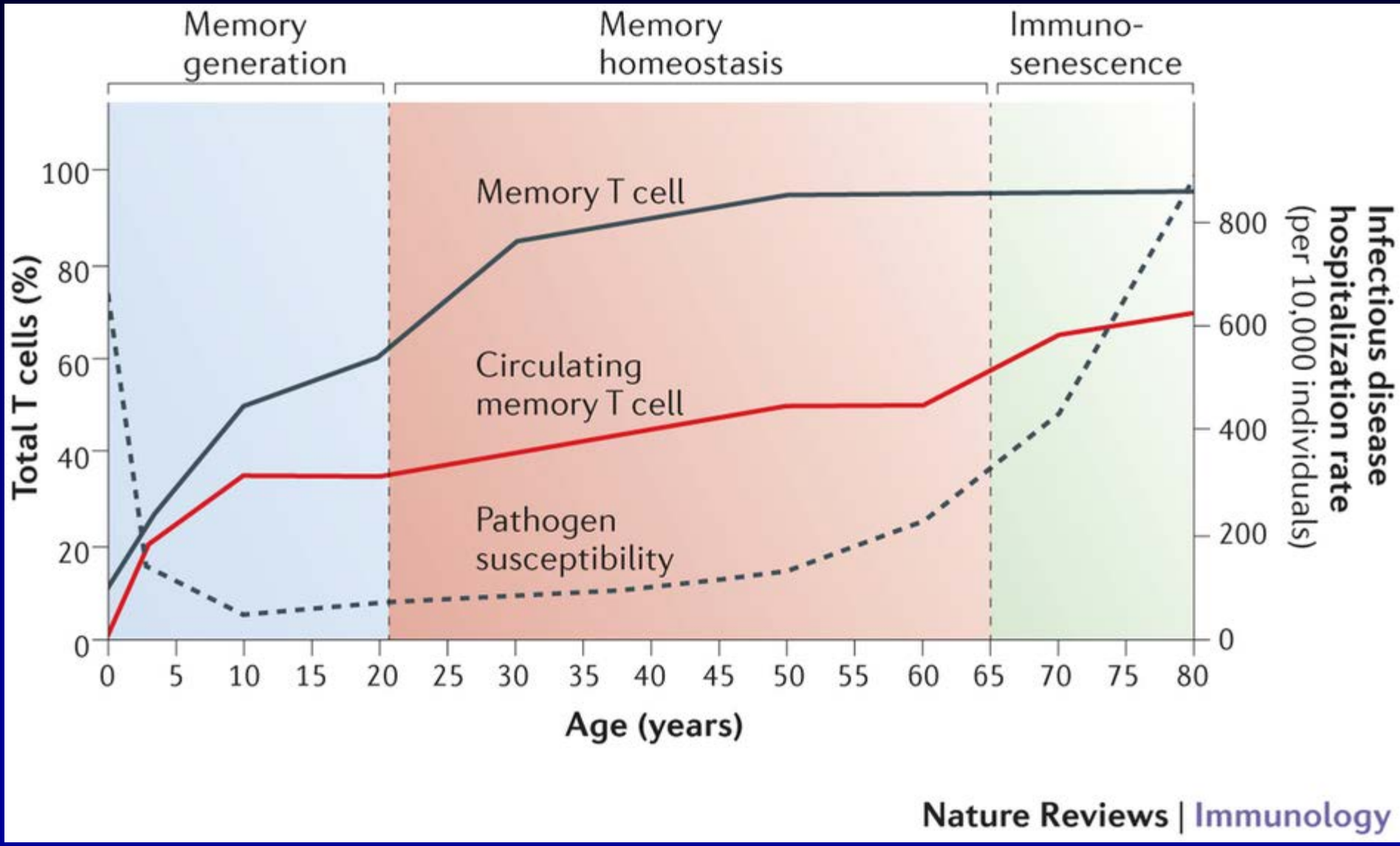
Epidemiology of Increased Cardiovascular Risk in

# Aging and Immunosenescence



# Aging of the Immune Sytem

- After age 50 the immune system undergoes dramatic changes, lo 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


Memory generation
Memory homeostasis
Immuno-senescence
Memory T cell
Circulating memory T cell
Pathogen susceptibility
Total T cells (%)
Infectious disease hospitalization rate (per 10,000 individuals)
Age (years)
0
20
40
60
80
100
0
200
400
600
800
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80
Nature Reviews | Immunology

# The Janus Head of Immune Aging

## Age-related immunodeficiency

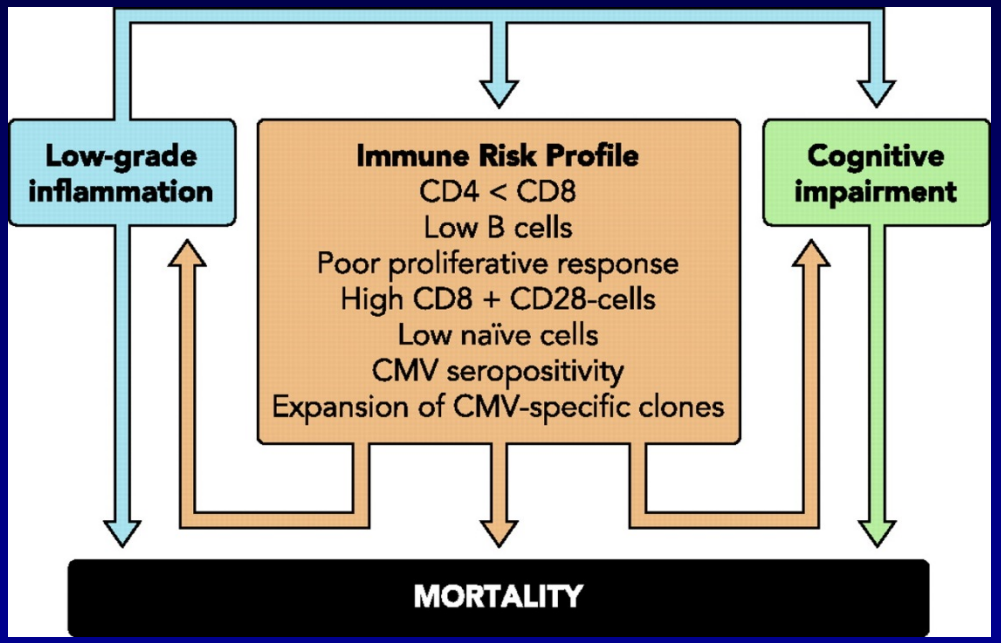
- Shrinking naïve T and B cell compartments
- Contraction in T and B cell receptor diversity
- Decreased T cell receptor sensitivity to respond to stimuli

## 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

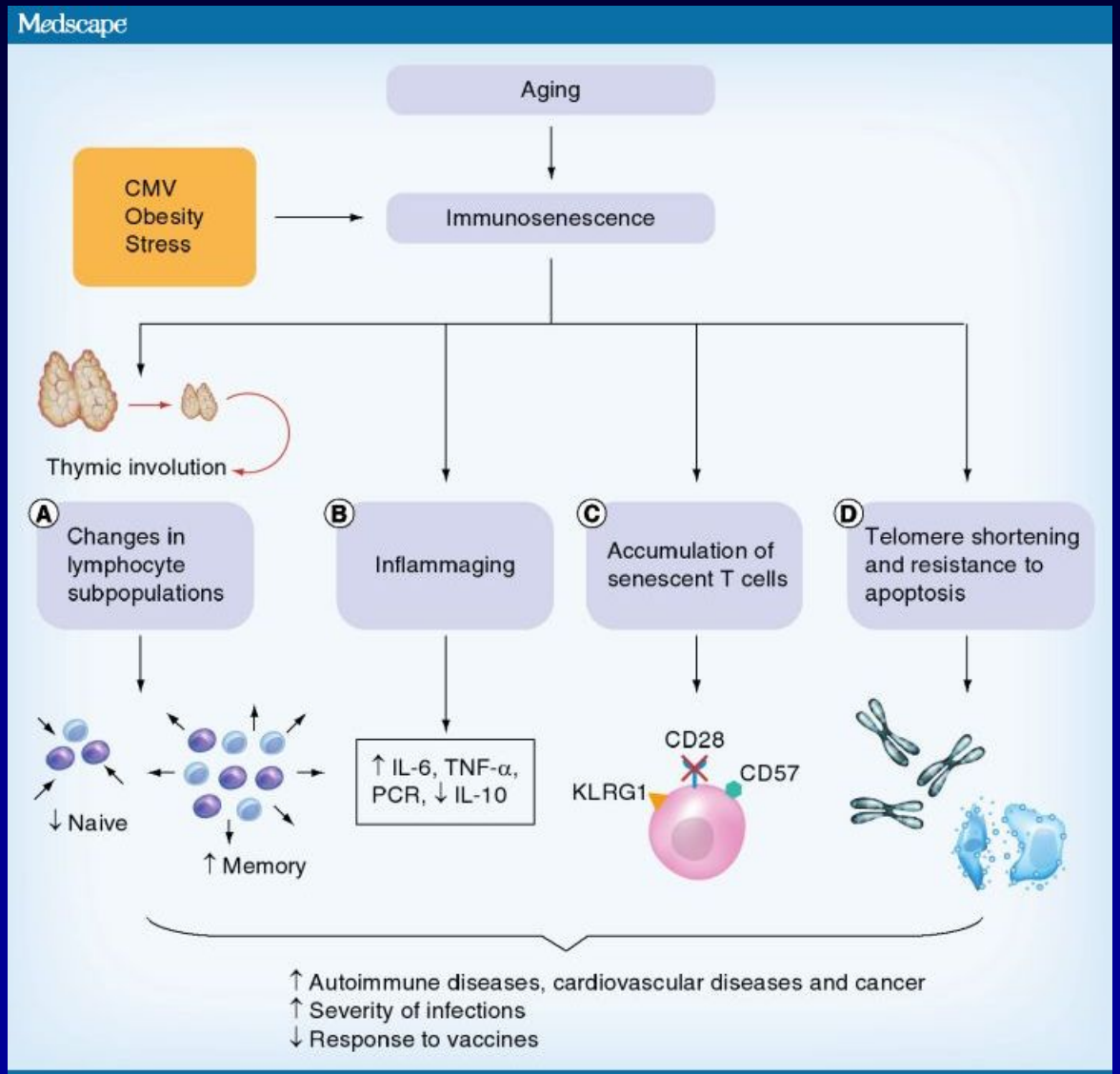
# Immune Risk Profile

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

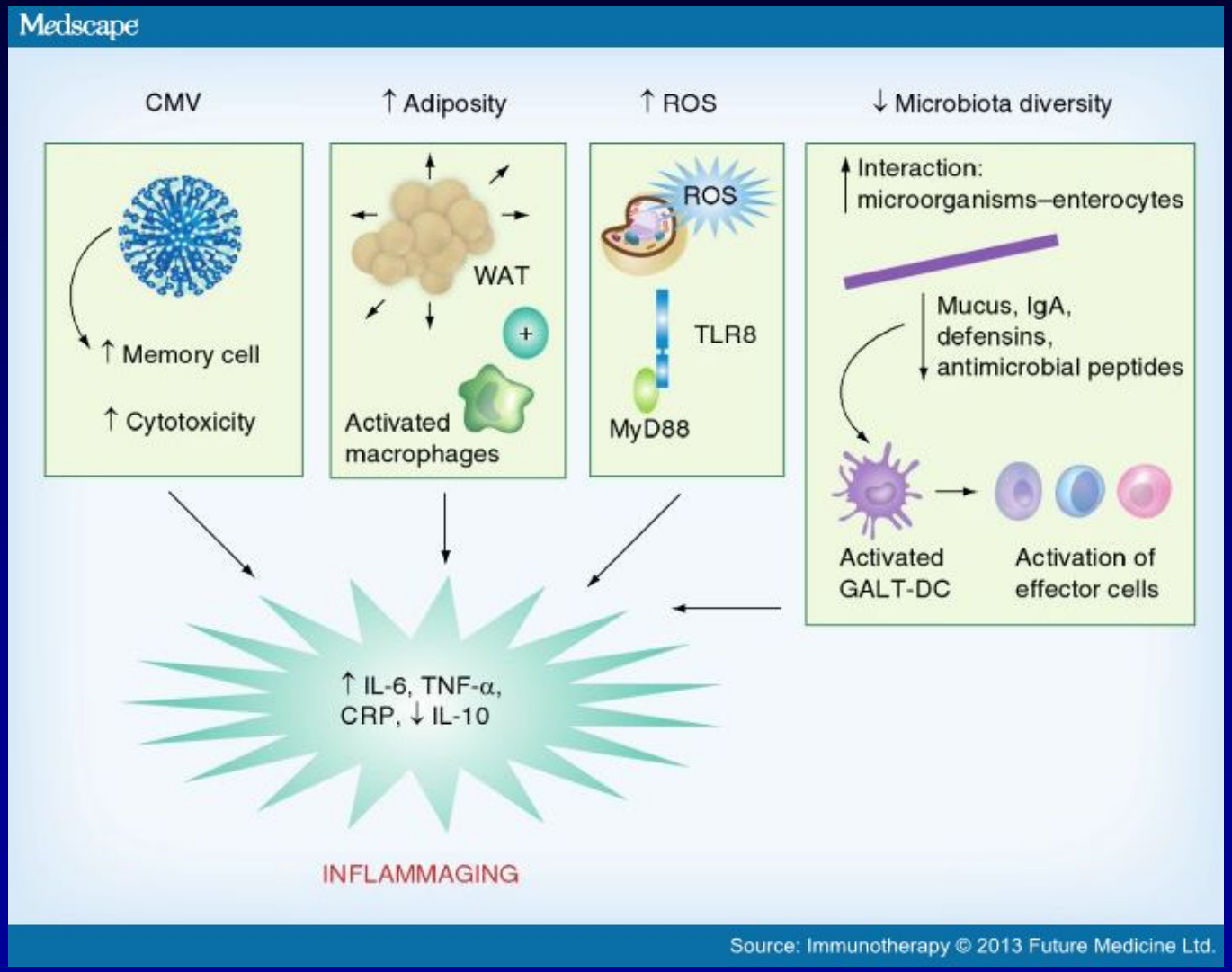



Predicted mortality of 85yo> at 2,4,6 yrs
Decreased diversity
Association with CMV
CD4/8  best marker and absent in “successful aging”

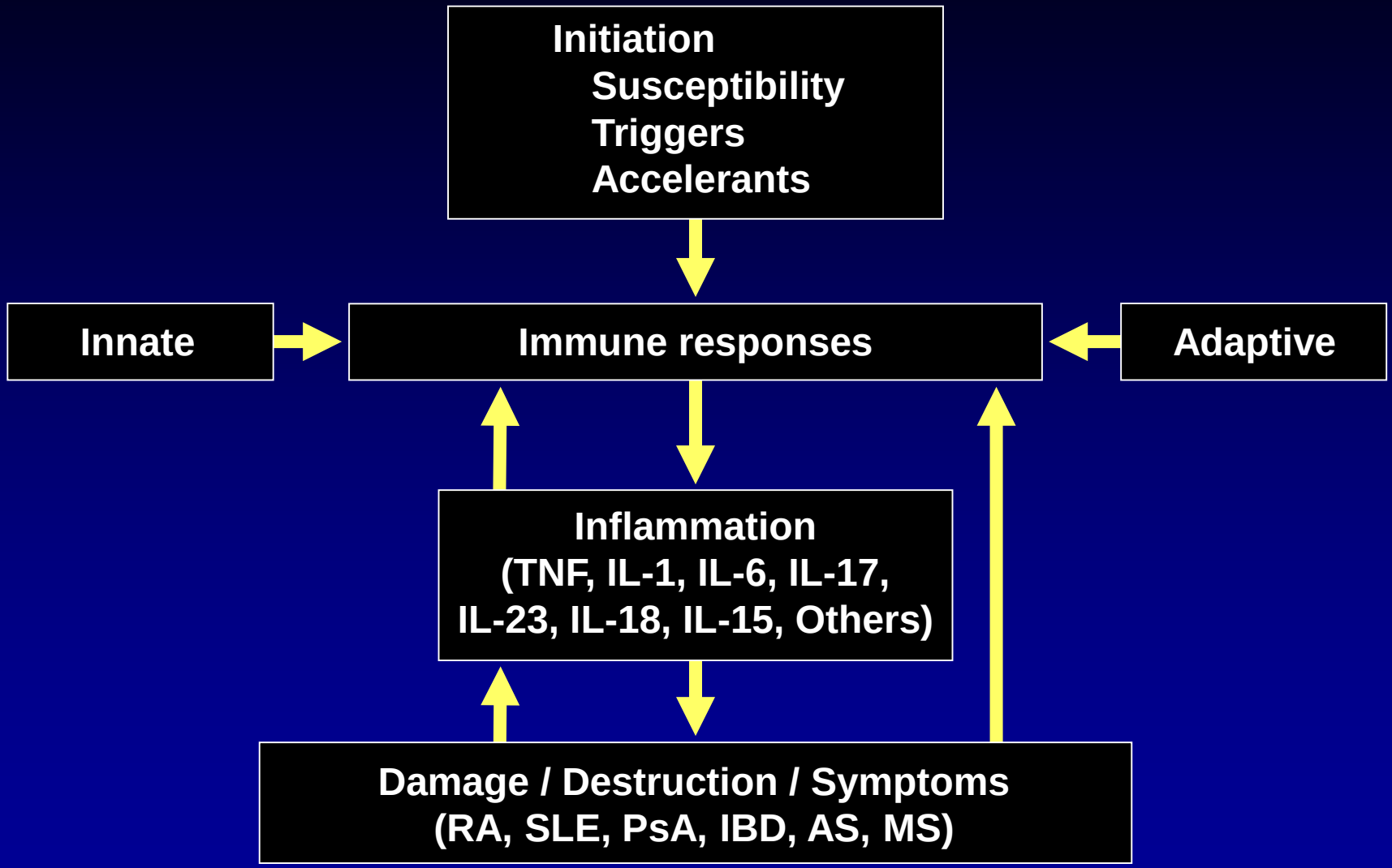
# Aging Inflammation Immunosenescence



# INFLAMMAGING

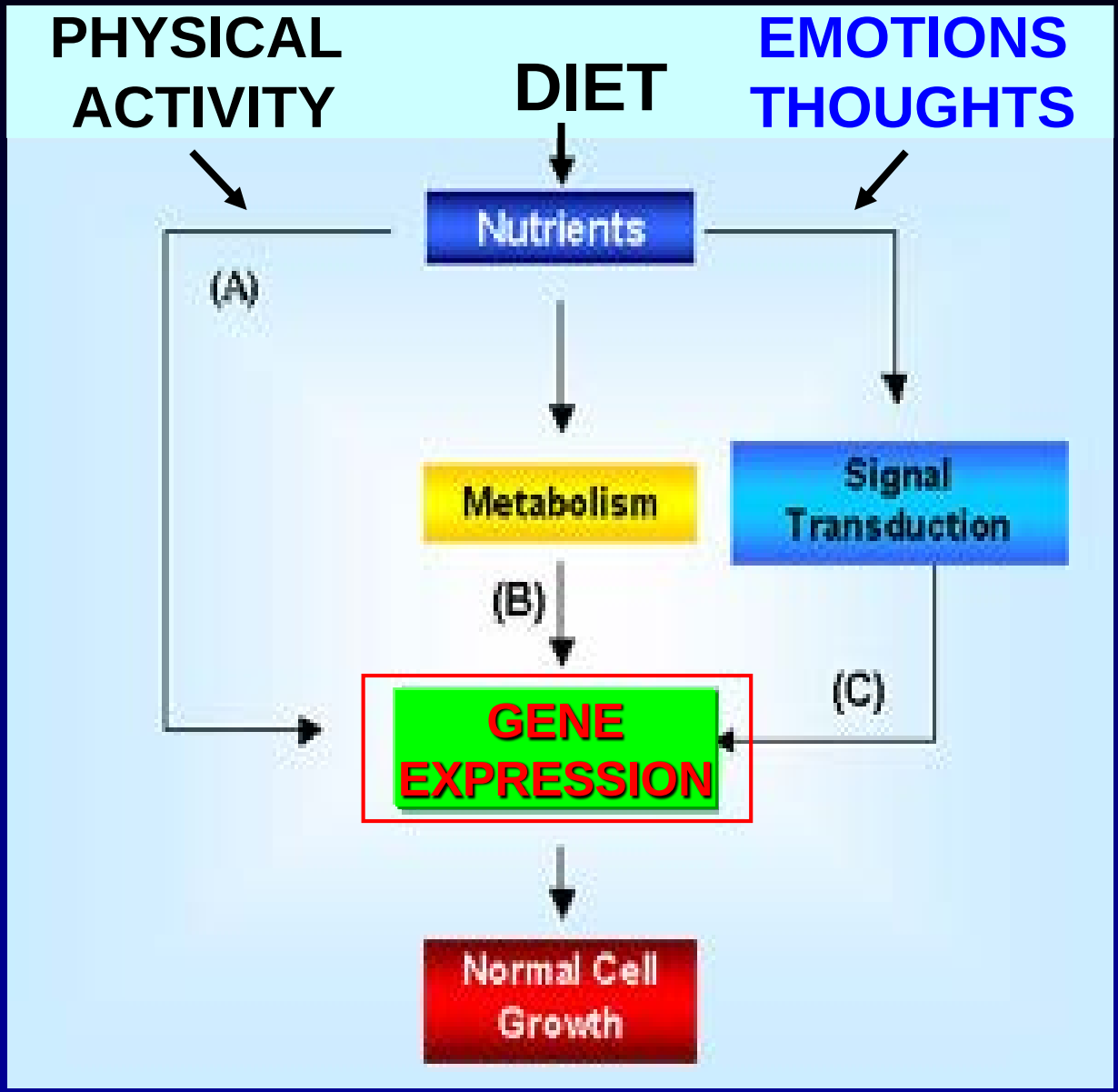


# Immune-mediated Inflammatory Diseases



# Maintaining a Healthy Immune System: *What you can do to help*

Leonard H. Calabrese, DO
R. J. Fasenmyer Chair of Clinical Immunology




Modified from http://nutrigenomics.ucdavis.edu/dietarychemicals.htm

# The "J" curve


Increased
Risk of URTI
Normal
Decreased
Sedentary
Moderate
Very high
Training load

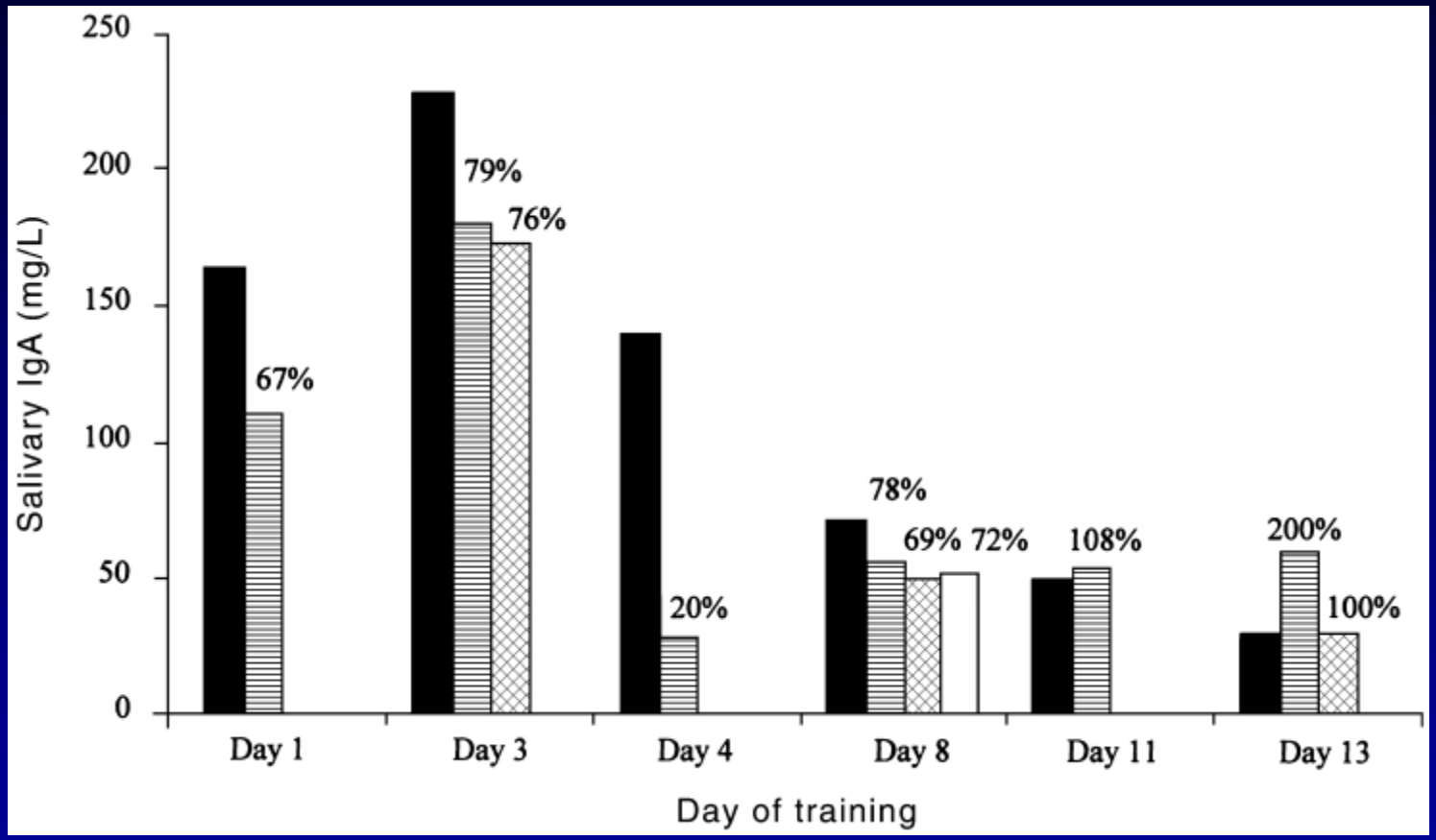
# EPIDEMIOLOGY OF INFECTIONS AND EXERCISE/TRAINING

- 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;**

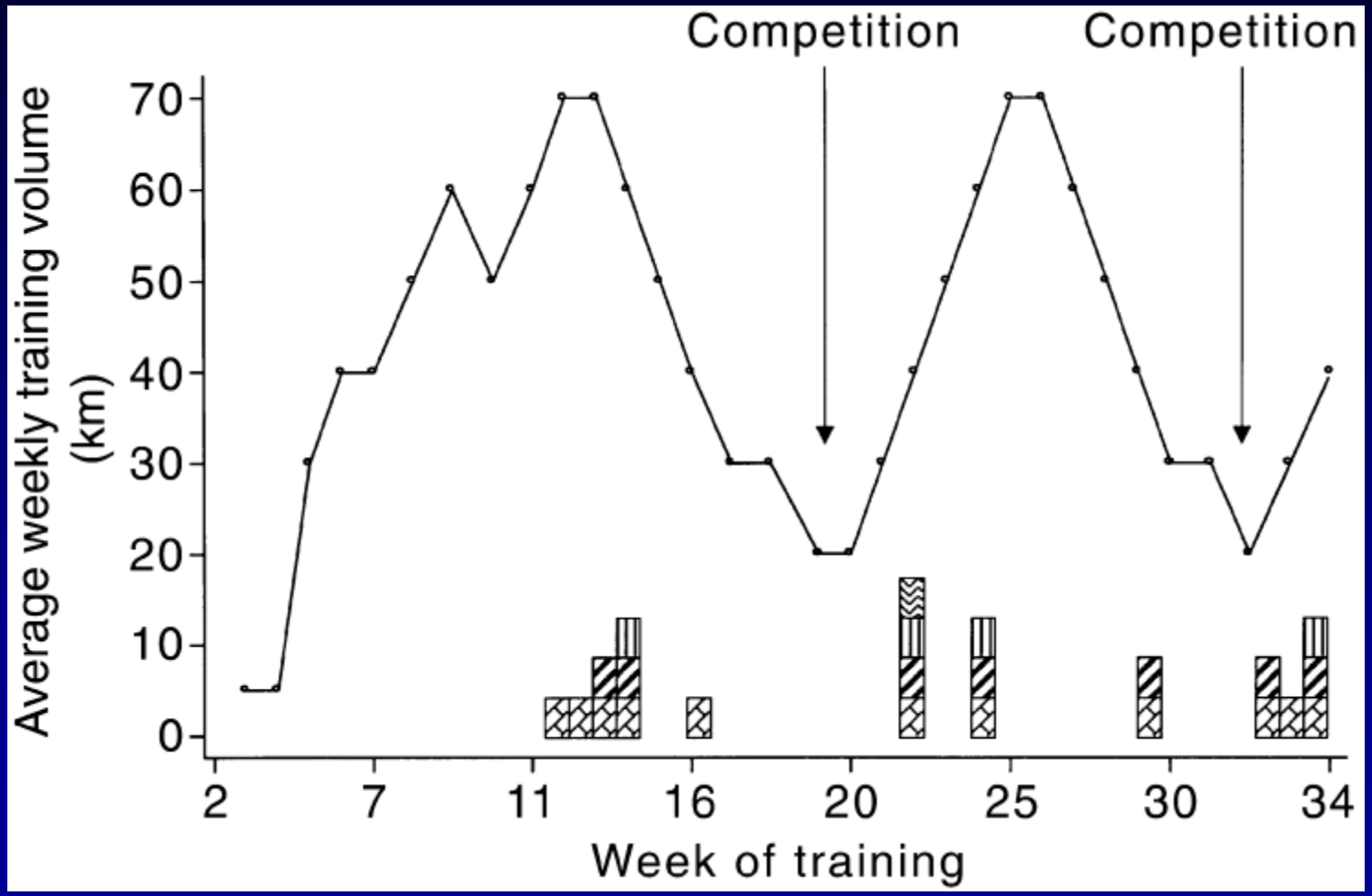



Pre-exercise salivary IgA concentrations for each training session over a 2 week period for an elite kayaker and the percentage change from the initial concentration

# 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


Increased
Risk of URTI
Normal
Decreased
Sedentary
Moderate
Very high
Training load

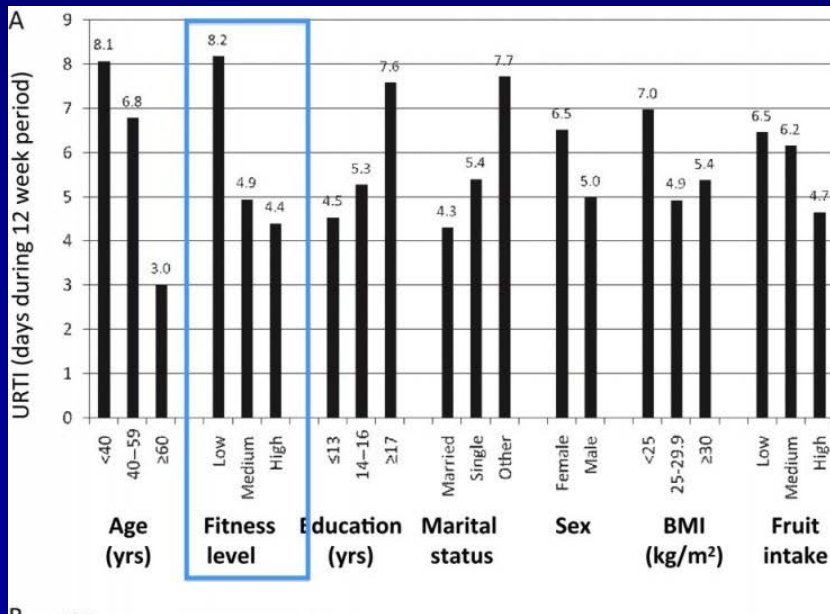
# Beneficial effects of exercise on URTI Br J Sports Med 45:987,2011

- 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)



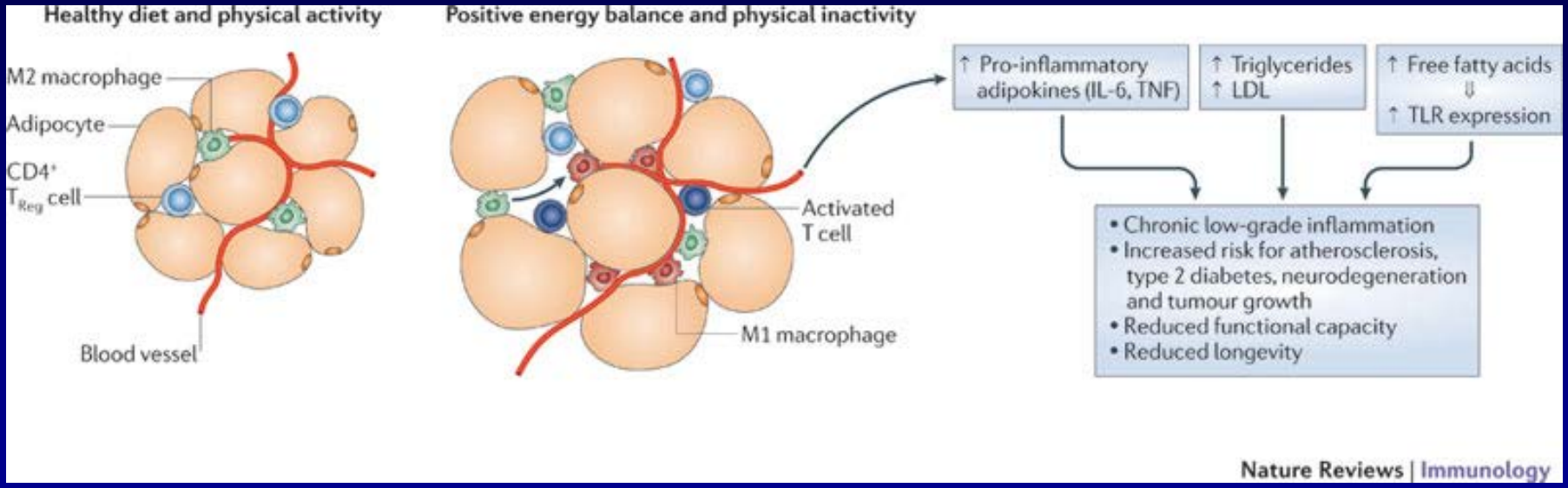
# Physical activity and immune function in elderly women

.Nieman DC, Med Sci Sports Exerc. 1993 Jul;25(7):823-31.Physical

- 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



# GUIDELINES

## 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).

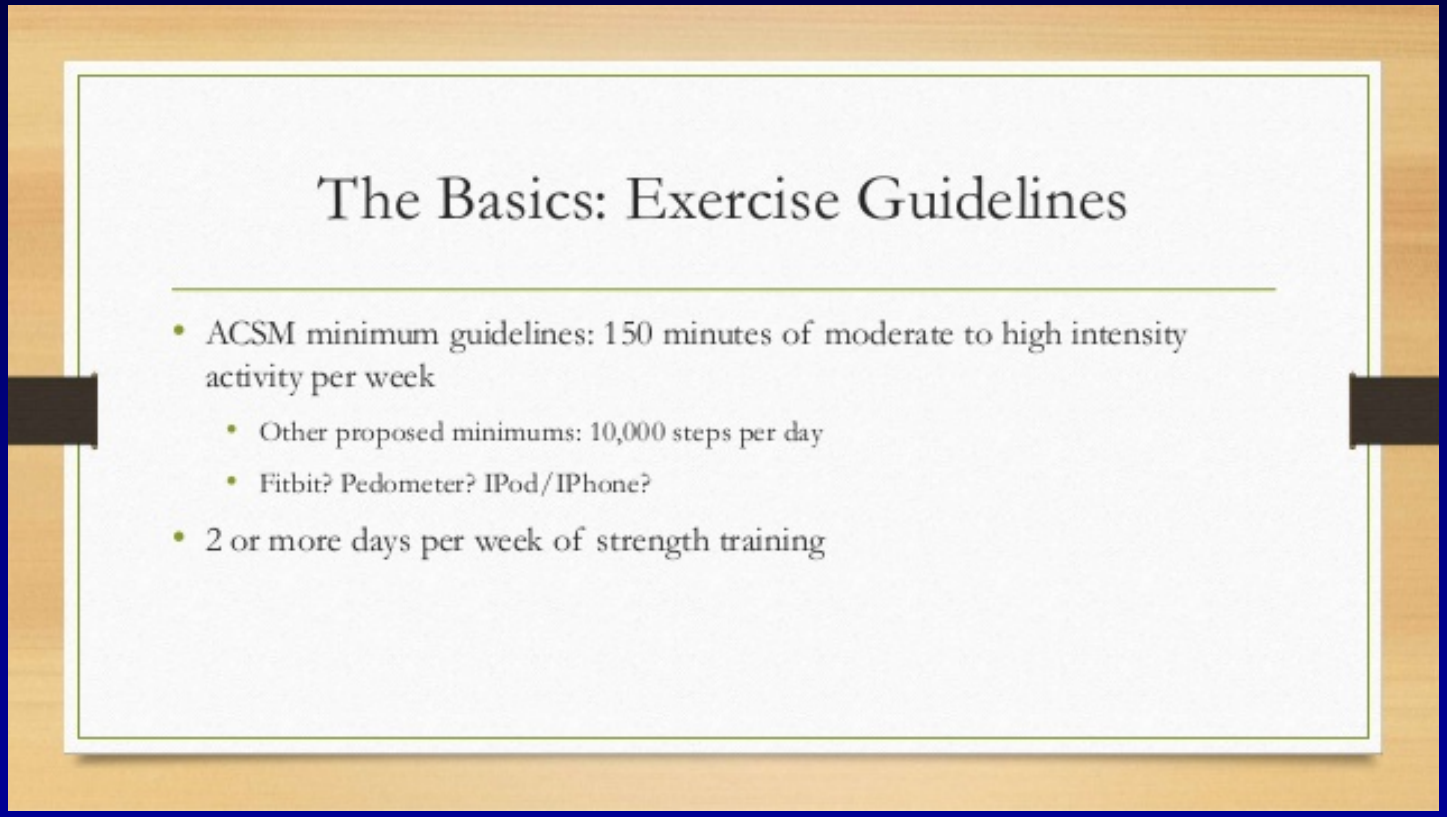
**OR**

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).

| Moderate-intensity Physical Activity (Approximately 3-6 METs) | Vigorous-intensity Physical Activity (Approximately >6 METs) |
|---|---|
| Requires a moderate amount of effort and noticeably accelerates the heart rate. | Requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate. |
| Examples of moderate-intensity exercise include: | Examples of vigorous-intensity exercise include: |
| • Brisk walking | • Running |
| • Dancing | • Walking / climbing briskly up a hill |
| • Gardening | • Fast cycling |
| • Housework and domestic chores | • Aerobics |
| • Traditional hunting and gathering | • Fast swimming |
| • Active involvement in games and sports with children / walking domestic animals | • Competitive sports and games (e.g. Traditional Games, Football, Volleyball, Hockey, Basketball) |
| • General building tasks (e.g. roofing, thatching, painting) | • Heavy shovelling or digging ditches |
| • Carrying / moving moderate loads (<20kg) | • Carrying / moving heavy loads (>20kg) |

# General USPHS Recommendations



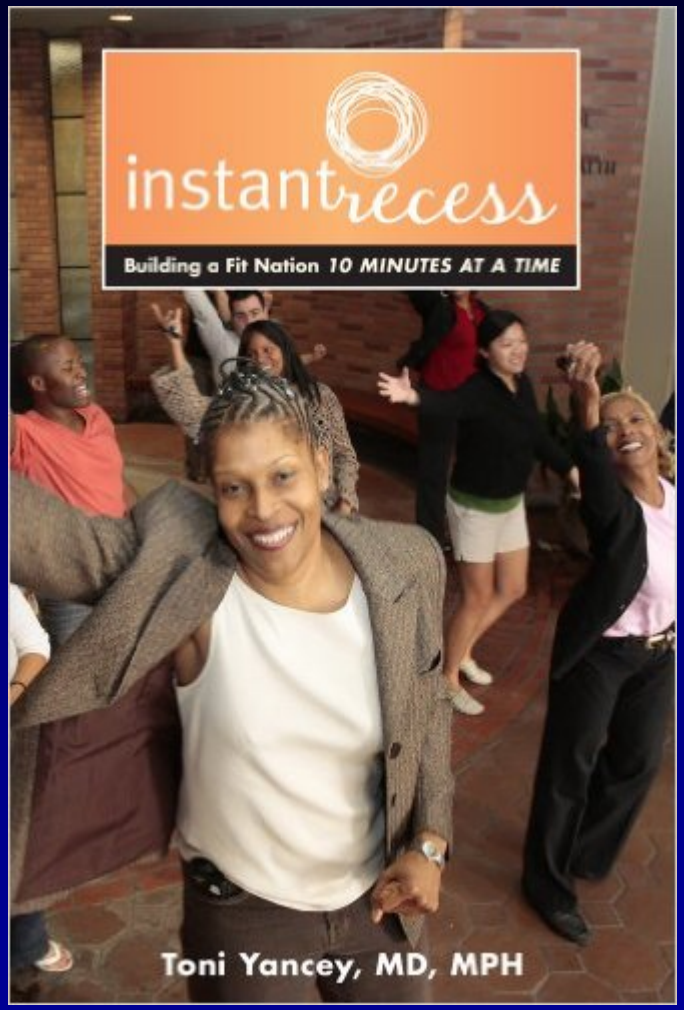
## EXAMPLES OF MODERATE AND VIGOROUS INTENSITY PHYSICAL ACTIVITIES

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

**Table 2**

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

# 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
  - Schedlowski (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

HYPOTHESIS #2

http://technorati.com/lifestyle/article/running-to-lose-weight/

# Mindfulness meditation may reduce stress, & thereby prevent or ameliorate cold-n-flu

HYPOTHESIS #1

http://theantiagingspecialist.com/destructive-stress-and-aging

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

A. E. Fiore et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm.Rep. 59 (RR-8):1-62, 2010.*

N. A. Molinari, et al. The annual impact of seasonal influenza in the US: measuring disease burden and costs. *Vaccine 25 (27):5086-5096, 2007.*

A. M. Fendrick, A. S. Monto, B. Nightengale, and M. Sarnes. The economic burden of non-influenza-related viral respiratory tract infection in the United States. *Archives of Internal Medicine. 163 (4):487-494, 2003.*

# 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

- **M**editation or
- **E**xercise to
- **P**revent
- **A**cute
- **R**espiratory
- **I**nfection

School of Medicine and Public Health
UNIVERSITY OF WISCONSIN-MADISON

Department of Family Medicine

# MEPARI

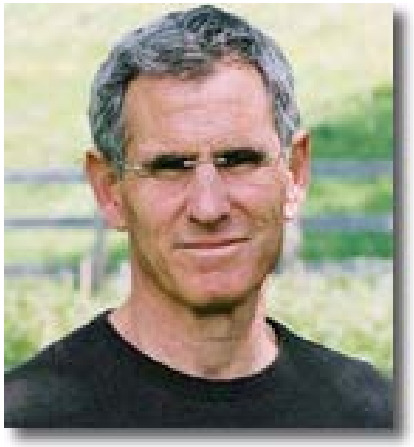
- OBJECTIVE
- To evaluate potential preventive effects of mindfulness meditation or sustained moderate intensity exercise on incidence, duration and severity of acute respiratory infection

# 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

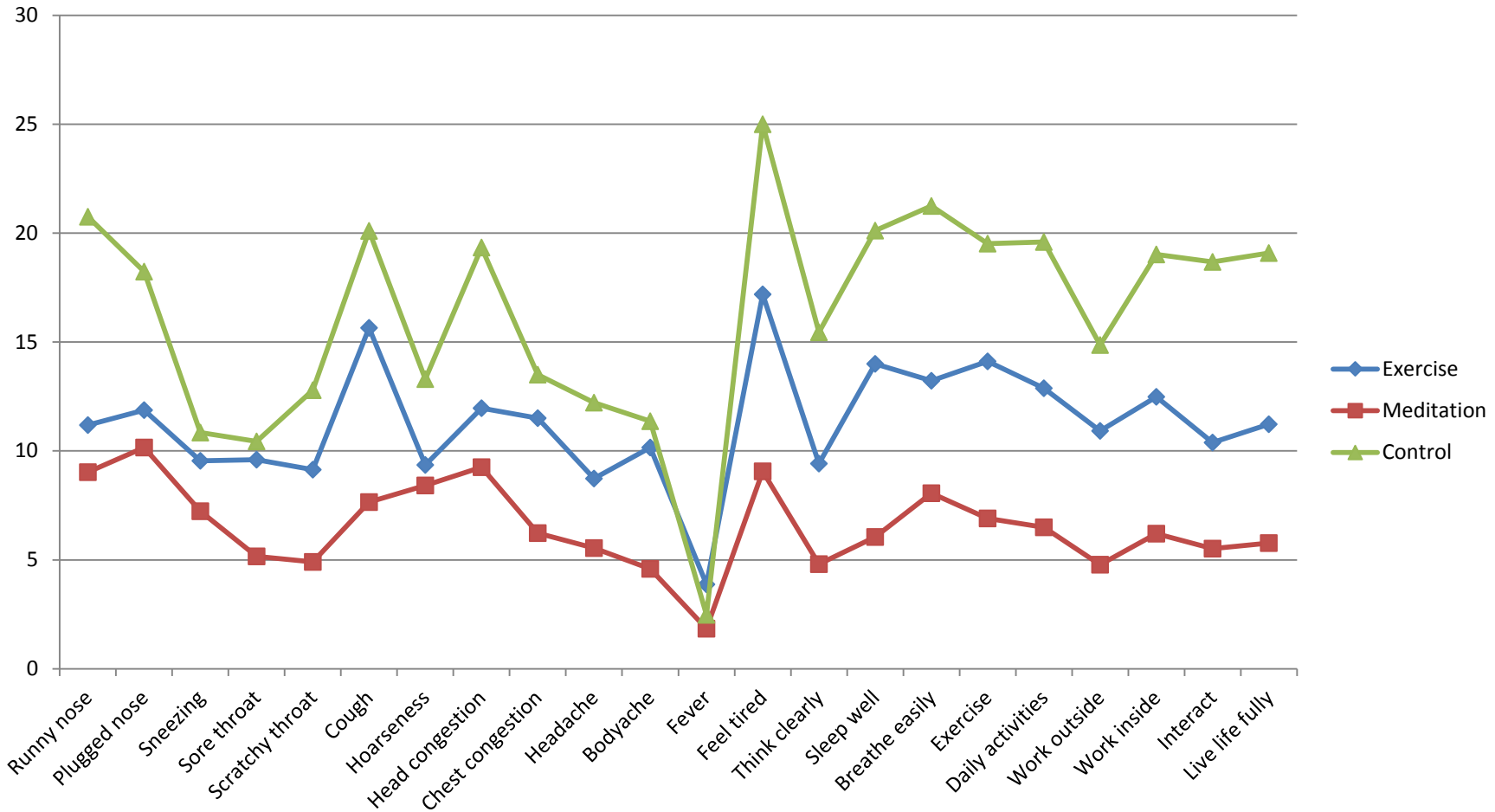
Matched to MBSR by:

- 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 to16 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

## Mean WURSS-21 item severity across all MEPARI participants




C. N. Obasi, R. Brown, T. Ewers, S. Barlow, M. Gassman, A. Zgierska, C. L. Coe, and B. Barrett. Advantage of meditation over exercise in reducing cold and flu illness is related to improved function and quality of life. *Influenza Other RespiratoryViruses, 2012.*

# 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)

D. Rakel, M. Mundt, T. Ewers, L. Fortney, A. Zgierska, M. Gassman, and B. Barrett. Value associated with mindfulness meditation and moderate exercise intervention in acute respiratory infection: The MEPARI Study. *Family Practice, 2013.*

# 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**

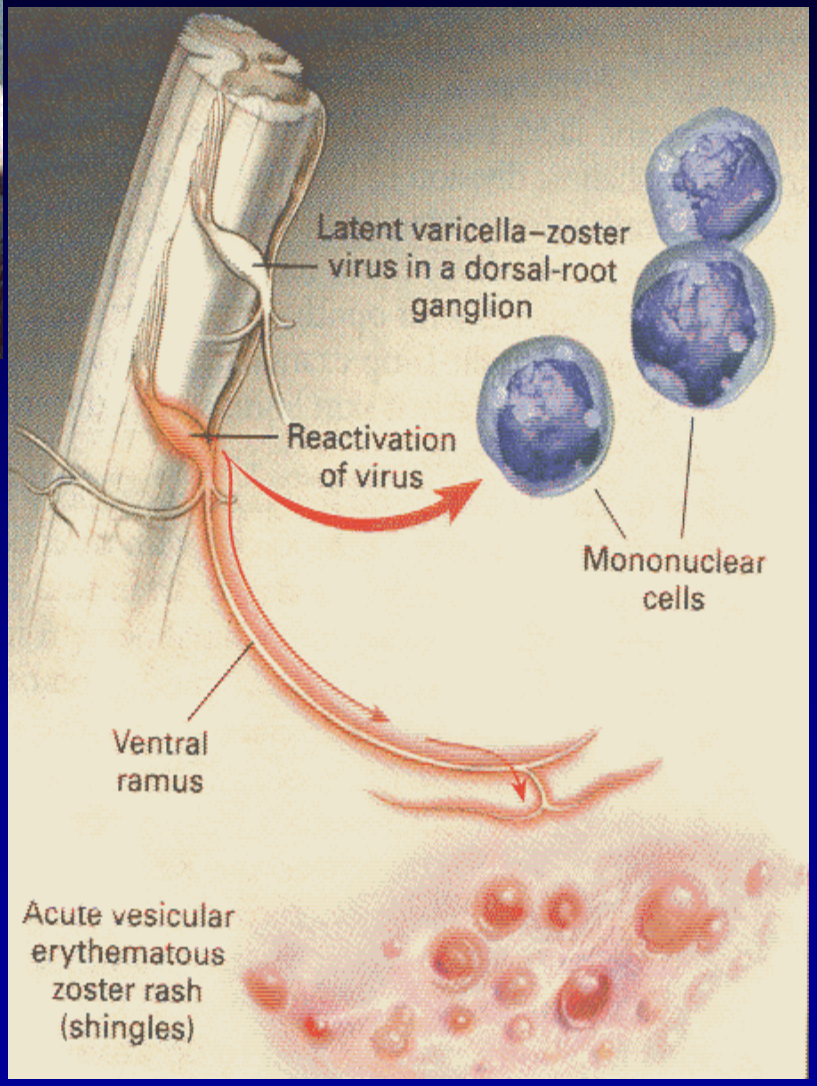
Combines physical activity with modest aerobic component with ‘meditation through movement”

Associated with documented health benefits in multiple domains and the treatment of illnesses such as fibromyalgia

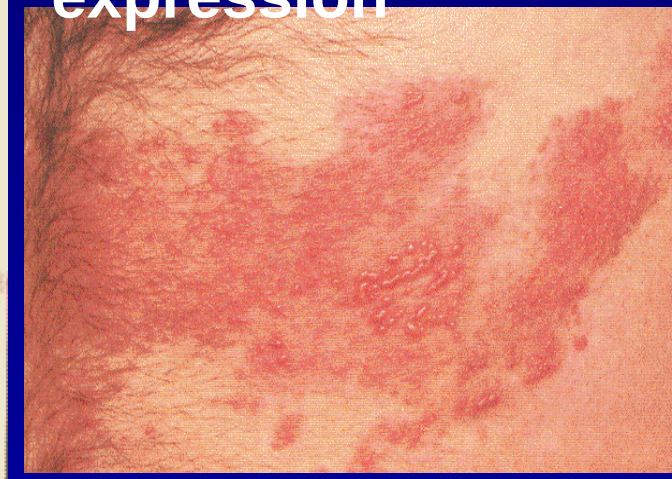
NEJM 2011

Tai Chi Chih
Westernized version

# Pathogenesis and Natural History and Latency of VZV

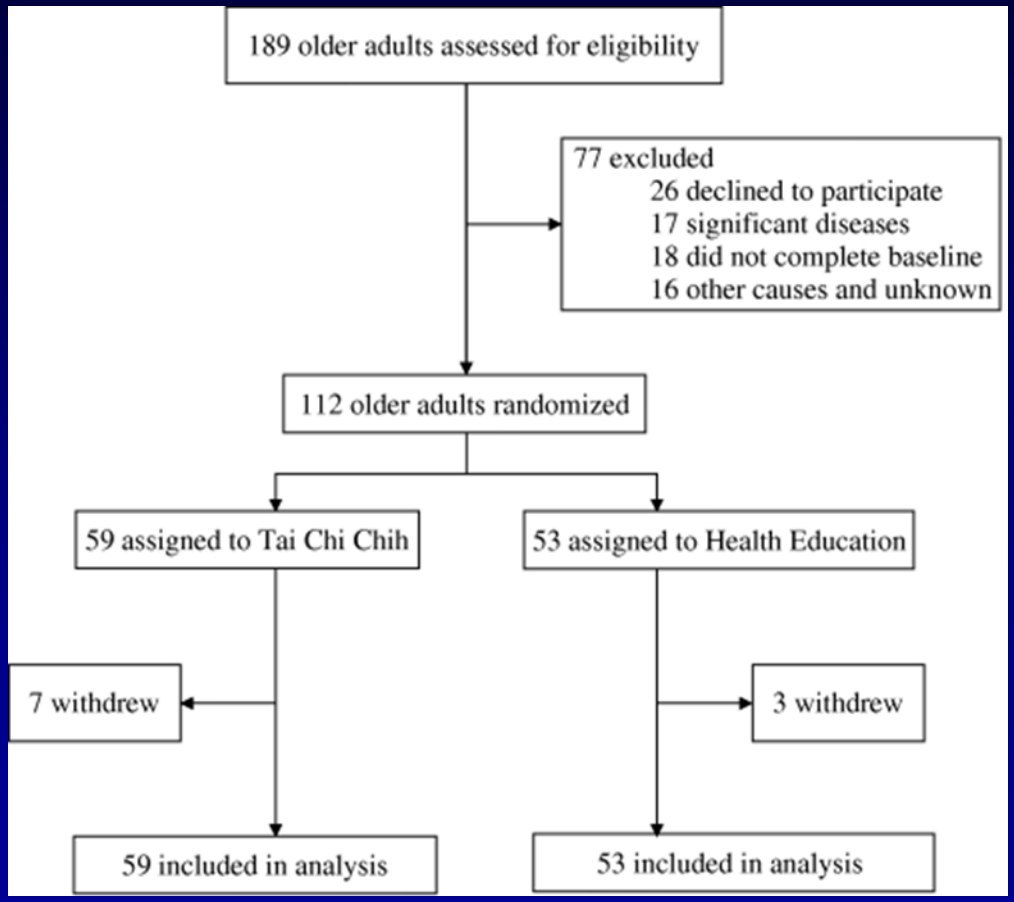



- Can not be cultured
- + S blot and PCR
- neuronal - epineuronal cells
- episomes
- select gene expression



# Shingles immunity and health functioning in the elderly: Tai Chi Chih as a behavioral treatment

## Irwin, Pike, Oxman J Am Geriatric Soc 55: 511-17,2007

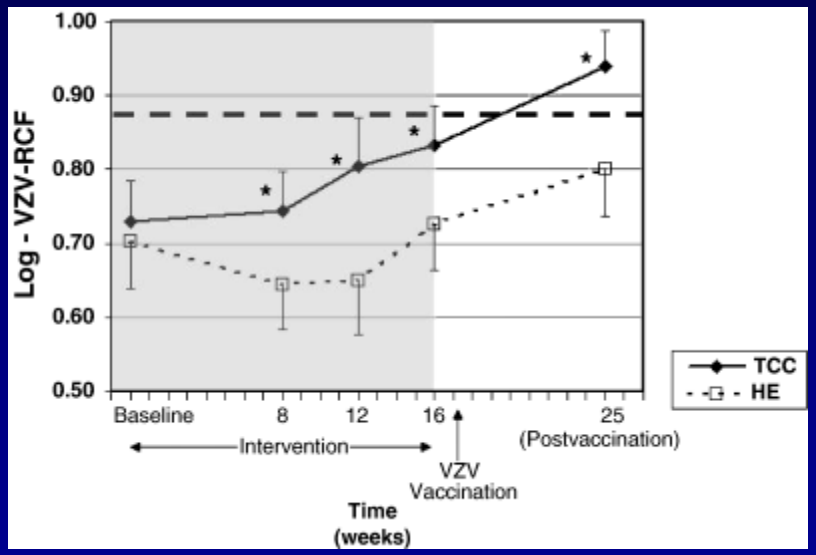


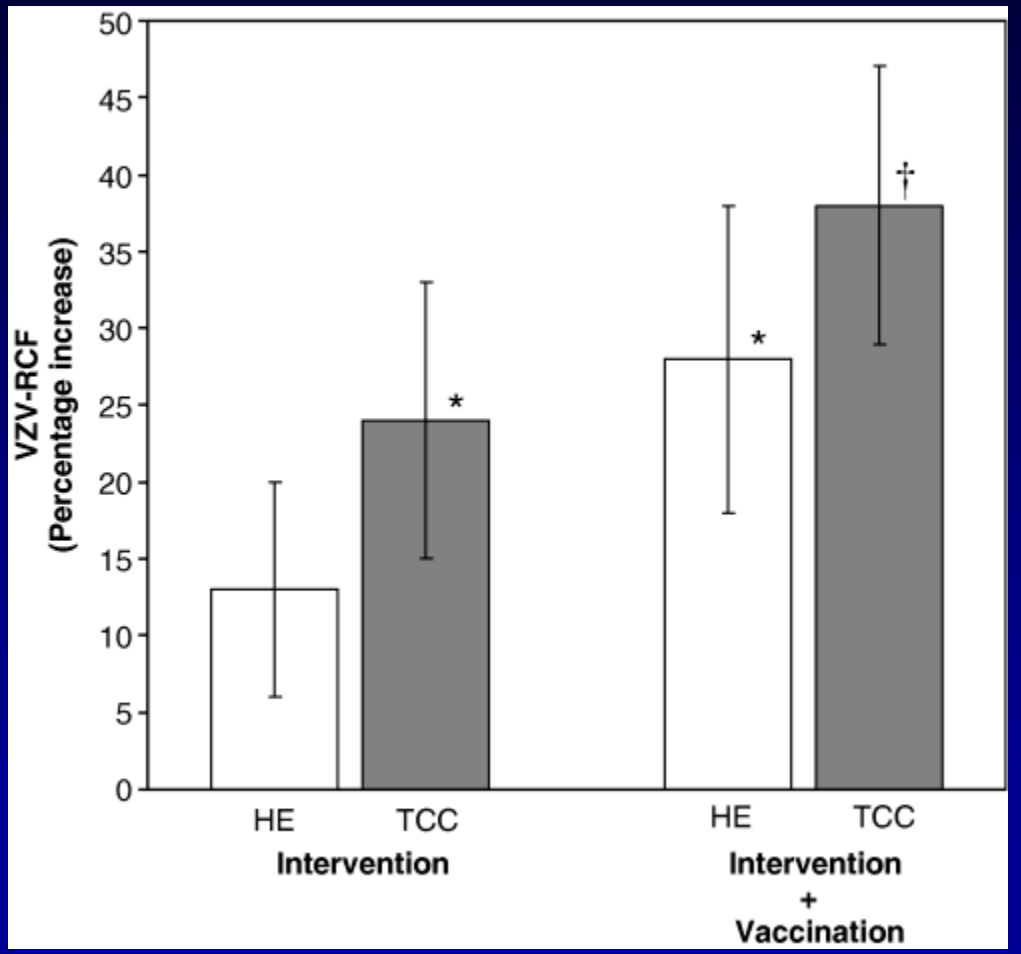

15 weeks
Randomized
20 movements
45 minutes – 3 times /week
Health education control

After 16 weeks both immunized with VARIVAX

Quantitative measurements of VZV CMI and QOL (SF36)

# VZV CMI
# VZV RCF



# 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

Shin et al. Arthritis Research & Therapy (2015) 17:380
DOI 10.1186/s13075-015-0893-x

Arthritis Research & Therapy

RESEARCH ARTICLE Open Access

# The beneficial effects of Tai Chi exercise on endothelial function and arterial stiffness in elderly women with rheumatoid arthritis

Jeong-Hun Shin[1], Yonggu Lee[2], Soon Gil Kim[1], Bo Youl Choi[3], Hye-Soon Lee[4] and So-Young Bang[4*]

**Abstract**

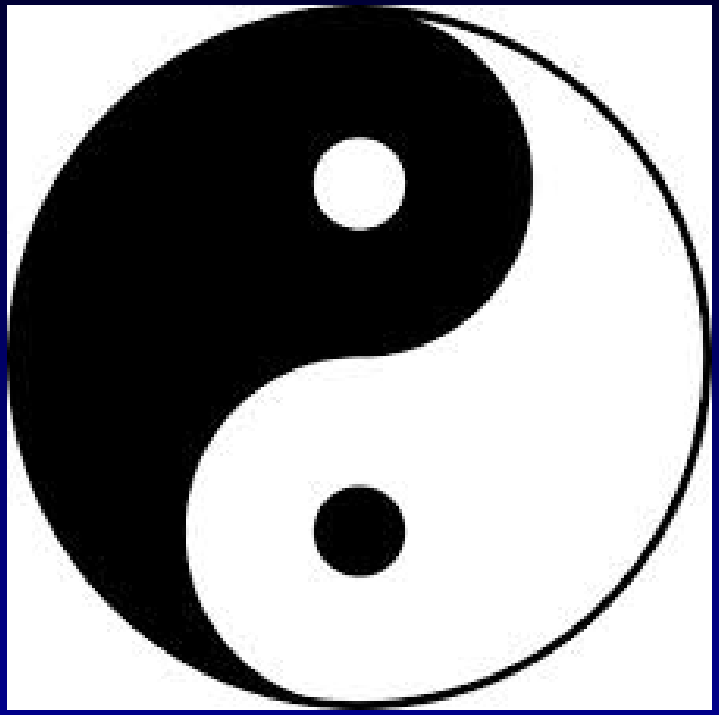
**Background:** Rheumatoid arthritis (RA) has been known to be associated with increased risk of cardiovascular disease (CVD). The aim of this study was to investigate the effects of Tai Chi exercise on CVD risk in elderly women with RA.

**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).

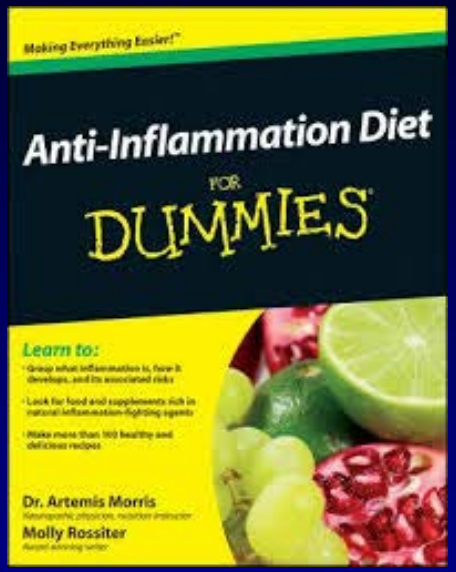
**Results:** FMD, representative of endothelial function, significantly increased in the Tai Chi exercise group (initial 5.85 ± 2.05 versus 3 months 7.75 ± 2.53 %) compared with the control group (initial 6.31 ± 2.12 versus 3 months 5.78 ± 2.13 %) ($P = 1.76 \times 10^{-3}$). Moreover, baPWV, representative of arterial stiffness, significantly decreased in the Tai Chi exercise group (initial 1693.7 ± 348.3 versus 3 months 1600.1 ± 291.0 cm/s) compared with the control group (initial 1740.3 ± 185.3 versus 3 months 1792.8 ± 326.1 cm/s) ($P = 1.57 \times 10^{-2}$). In addition, total cholesterol decreased significantly in the Tai Chi exercise group compared with the control group (−7.8 ± 15.5 versus 2.9 ± 12.2 mg/dl, $P = 2.72 \times 10^{-2}$); 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; $P = 2.22 \times 10^{-2}$) 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



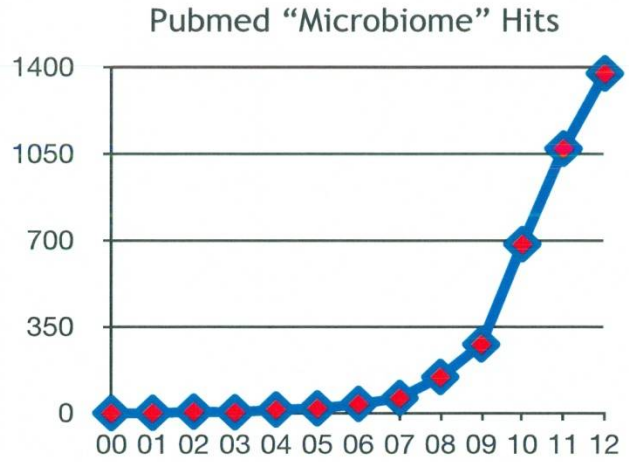

## Mediterranean Diet

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.

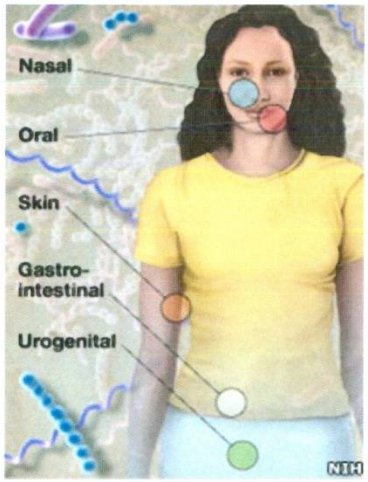

www.reduce-weight-digest.com

# Some of My Best Friends Are Germs

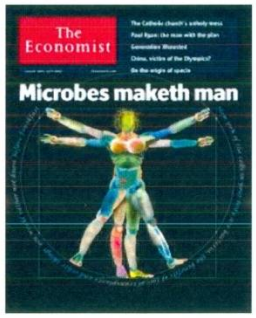
# The Rise of the Microbiome

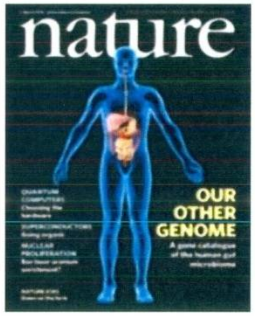


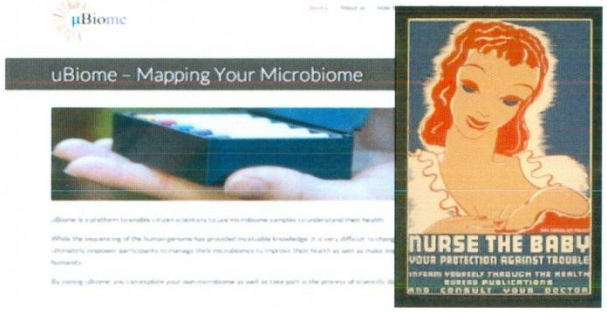

NIH HUMAN MICROBIOME PROJECT



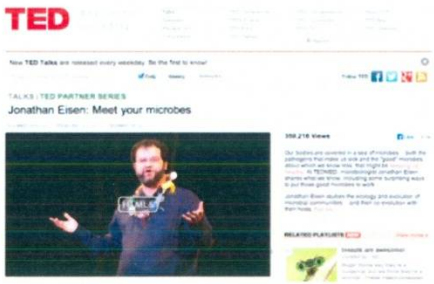


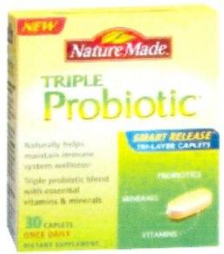






# Role of the Gut Microbiota in Immunity and Autoinflammatory Diseases

- 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

Kamanda et al. *Nat Rev Imm*. 2013;13:321.

# 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 sub lethal 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?*

Abt MC. *Immunity* . 2012;37:158.

# What I tell my patients about eating

# Mediterranean Diet

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