The “Natural” Control of Inflammation

Steven G. Pratt, MD, FACS, ABHM
Vision Institute of Canada
8th November 2008

- First described by Celsus in the first century AD
  - Rubor
  - Tumor
  - Calor
  - Dolor
  - Dysfunction (Virchon)
- Cannot survive without inflammation
- An essential part of the immune repair system

Inflammation

Beneficial – Essential function
- Engage the innate and adaptive immune systems
  - 65% of all U.S. sepsis cases occur in 12% over age 65
- Destroy pathogens
- Promote clotting
- Promote complement activation
- Initiate repair mechanisms
**Inflammation**

- Make some fire – put out the fire
- Can’t live without it – will die with it
- Balance is key

**Inflammation and…**
- AMD
- Cataracts
- HTN
- AD
- CVD
- Osteoporosis
- Obesity
- DM
- Insulin Resistance
- Cancer
- Dry Eye
- Cigarettes
- Secondhand Smoke
- Sleep Deprivation
- Sleep Apnea
- Metabolic Syndrome
- Waist Line
- IBS
- Crohns Disease
- Aging
**Pro-inflammatory Cytokines**

- hs CRP
- IL-6
- TNF-\(\alpha\)
- TNF-\(\alpha\) R1
- sICAMS
- ICAM-1
- VCAM-1
- PGE-2
- ESR

**Inflammatory Markers**

- Most vascular events occur in people without ↑ TC
- 1/5 of all vascular events occur in individuals without any traditional risk factors
- ↑ Levels of inflammation and atherosclerosis seen in those as young as 15

**Controlling the “Fire” Fats**

- Balance your essential fatty acids (EFA’s)
- EFAs = n-3 + n-6
Fats

- **N-3's (marine) =** DHA, EPA, “Others”
  - Wild salmon
  - Herring
  - Sardines
  - Mackerel
  - Tuna
  - Halibut

Fats

- **N-3’s (plant) =** Alpha Linolenic Acid (ALA)
  - Walnuts
  - Flaxseeds
  - Soybeans
  - Spinach / Purslane
  - Wheat germ
  - Pecans
  - Canola oil

Fats

- **ALA → EPA → DHA**
- Conversion rate 1-15% maximum
- ↓ Conversion rate when EFA ratio >1:3

Fats

- **N-6’s**
  - Grain fed beef & pork
  - Corn & oil
  - Sunflower seeds & oil
  - Soybeans & oil
  - Cotton seed & oil
**Fats**

**Balance: the Key**

- N-3’s anti-inflammatory
- N-6’s pro-inflammatory
- SFA’s and Trans fats are pro-inflammatory
- Ideal n-3 / n-6 = 1:1 → 1:3
- Typical American diet 1:15 → 1:25

**Fats**

American Heart Association:

- Limit SFA’s to <7% of total daily calories
- Limit TFA’s to <1%
  - There is no “safe amount”

**Fats**

Food & Nutrition Board – Institute of Medicine:

- 1.6 g/d ALA for adult males
- 1.1 g/d ALA for adult females
- 160 mg EPA, DHA for adult males
- 110 mg EPA, DHA for adult females

**Fats**

My Recommendations:

- 1-4 g/d fish oil for adult males
- 1-2 g/d fish oil for adult females
  * From a combination of cold water fish and supplements
- 1-3 Tbsp/d ground flaxseeds for adult males & females
- Walnuts and green leafies multiple times/wk
- 2 Tbsp/d EVOO
**Controlling the “Fire” Fiber to the Rescue – Again**

- Fiber lowers hs CRP
- ↓ Risk for inflammatory diseases
  - Obesity
  - DM / Insulin Resistance
  - CVD
  - Atherosclerosis
  - Metabolic Syndrome

**Metabolic Syndrome**

- Waist circumference >40 inches in men and >35 inches in women
- Triglyceride level of 150 mg/dL or higher
- High-density lipoprotein (HDL) level of <40 mg/dL in men and <50 mg/dL in women
- Blood pressure of 130/85 mm/Hg or higher, or if you are undergoing treatment for hypertension
- Fasting plasma glucose level of 100 mg/dL or higher

**Pro-inflammatory Foods**

- White grains, pasta
- Saturated fat
- Trans fats
- Processed foods
- Omega 6 fats
- High-glycemic index foods
**Put out the “Fire”**

**First Cold Pressed Extra-Virgin Olive Oil**

- The primary fat (up to 40% of total calories) in the traditional Mediterranean diet (Crete)
  - Improve lipid profiles
  - ↓ BP
  - ↓ Insulin resistance
  - ↓ Expression and or activation of pro-inflammatory biomarkers
  - ↓ Oxidative stress
  - 2 Tbsp/d

**Put out the “Fire”**

**Sleep**

- ↓ Sleep ↑ IL-6, TNF-α, TNF-αR1, hs CRP
- 3 days of total sleep deprivation (88 hrs) – hs CRP levels indicating ↑ risk for CVD/stroke
- 4 hrs sleep/night for 10 days = hs CRP levels associated with high CVD risk
- Sleep and hs CRP – a dose dependent relationship
- Sleep quality and ↑ IL-6
- Insomnia and ↑ IL-6
**Skeletal Muscle – Blood Sugar – Inflammation**

- Skeletal muscle the primary regulator of blood sugar
- Blood sugar is a pro-inflammatory event
- Sarcopenia = a degenerative loss of skeletal muscle that begins around age 50
  - Not a disease, but a normal process of aging
  - 24% in persons <70
  - >50% in person >80
  - Low grade inflammation an important contributor
- Exercise (both aerobic & resistance) and Superfoods to the Rescue

**Inflammation and...**

- Caloric restriction
- Caloric mimetics
  - Resveratrol
  - Quercetin
- “GALT”
  - Role of pre-probiotics
  - Sets the stage for inflammation
  - Non-fat yogurt
  - Dan Active Immunity
  - Sustenex
- Nutrigenomics
  - N-3’s
  - Berries
  - Spice

**Controlling the “Fire” Flavonols**

- A subclass of Flavonoids
- Quercetin – a major anti-inflammatory
  - Red > yellow onions
  - Apples (skin)
  - Cranberries
  - Blueberries
  - Tea
  - Broccoli
  - Buckwheat
  - Cilantro

**Resveratrol**

- Red wine (2-5 mg/L)
- Purple grapes juice
- Cranberries
- Blueberries
- Peanut skin
Love Those Whole Grains

- Habitual whole grain consumption
  - ↓ Risk for coronary heart disease
  - ↓ For T2DM
- Whole grains contain fiber, vitamins, minerals, polyphenols, phytoestrogens, anti-oxidants, other phytochemicals
  - ↓ Oxidative stress
  - ↓ Pro-inflammatory cytokines

Love Those Whole Grains

- Study of 41,836 females ages 55-69 over 17 yr
  - 35% ↓ risk of death in the highest consumers (19 or more servings/wk vs. 4-7 servings/wk) from inflammatory* diseases (exclude CHD, cancer)
- Includes infectious disease, RA, gout, COPD, asthma, ulcerative colitis, Crohn disease, T1DM, T2DM, neurodegenerative disease

Put out the “Fire” 4 Tocotrienols & 4 Tocopherols

- Vitamin E is an essential component of our anti-inflammatory "state"
- Plays a critical role against oxidative stress
- In a study of 698 community-living persons 65 yrs or older, low serum vitamin E (alpha tocopherol) was associated with subsequent decline in physical function
  - ↓ PA = ↑ inflammation = disability = “slippery slope”
  - ? Vitamin D₃ plays similar role
  - In this study, dietary vitamin E, not supplement

Put out the “Fire” 4 Tocotrienols & 4 Tocopherols

- Alpha and Gamma Tocopherol reduce oxidative stress, inflammation in metabolic syndrome
  - Synergy at work
  - ↓ hs CRP & TNF-α

Jacobs, et al. AM J CLIN NUTR. 2007;85:1606


**Put out the “Fire” Vitamin D₃**

- Inverse relation between serum vitamin 25-hydroxy-vitamin D and many pro-inflammatory diseases

**Centenarians**

- Stave off the deleterious sequelae of inflammation
- 3 types
  - Survivors (onset of disease before age 80 = 42%)
  - Delayer (onset of disease age 80 or older = 45%)
  - Escaper (reach 100 without disease = 13%)
- In general, reach 100 without certain cancers, MI, stroke, diabetes, metabolic syndrome

**Aging & Inflammation**

- Menopause is associated with...
  - ↑ Body weight, total body fat, % body fat, and BMI
  - ↓ Fat-free mass (muscle & bone)
- Men
  - Little change in body weight but total body fat ↑ and lean body mass ↓ (muscle & bone)
* Physical activity associated with ↓ body weight, ↓ total body fat, ↓ % body fat, ↓ BMI and ↑ lean body mass (muscle & bone)
* Long term obesity (inflammation) ↓ life span
**Optimal Biomarkers**

- Will not be achieved in a pro-inflammatory state
  - BP <115/75 (old 140/80)
  - LDL-C 50-70 mg/dL (old <100)
  - FBS 75 mg/dL (<100 mg)
  - Hs CRP <1.0 mg/L (*measure >once)

**How to ↓ hs CRP**

- Mediterranean (Superfoods) diet and lifestyle
- Walnuts
- Berries
- ↑ Fiber
- ↓ Weight
- ↓ Waist
- PA
- If you smoke = stop
- Sleep
- Statins
- Sweet bing cherries
- Apples
**hs CRP**

- Manufactured in the liver
- The most well-documented biomarker with clinical application of inflammation
- The body of evidence in support of hs CRP dwarfs that for other inflammatory biomarkers
- The young (15-34) are also at risk when elevated
- Can predict disease progression in the short run (e.g. heart failure, vascular dementia) and also future disease (e.g. HBP in women, metabolic syndrome in men)

**16 Way to Decrease Inflammation**

1. Ave 7-8 quality hrs sleep/night
2. 10% ↓ weight if BMI over 25
3. Min 30 min/d moderate exercise most days
   Better = 60-90 min/d exercise most days
4. Weight training 2-3x /wk
5. Adequate quantities dietary fiber
6. Eat high n-3 fatty acid fish 4x/wk, 3.5 oz/serving, (e.g. Wild Salmon best, then sardines, herring, tuna) and take 1-3 g fish oil capsules daily.
7. 2 Tbsp ground flaxseed meal most days
8. 1 - 1½ oz walnuts 5x/wk
9. 1 c berries, cherries or purple grapes, or 4-8 oz 100% pomegranate juice (or purple grape juice) daily
   Better yet, bathe each meal with berries, cherries, grapes, pomegranate juice
10. Fasting blood sugar 75 mg/dL
11. 2 Tbsp extra-virgin cold pressed olive oil most days
12. High carotenoid diet
13. Spice it up
14. Prebiotics / probiotics
15. Fruits & veggies – “unlimited”
16. Dark chocolate 😊
Sources


Sources


Sources


Sources