“Thoughts on Preventive Cardiology”

- Arterial Health
- Endothelium
- Adipose Tissue
- CVD Risk Factors

Herbert A. Insel, M.D. F.A.C.C.

Cardiovascular Disease (CVD)

- CVD = **Heart attacks** and **strokes**
- **#1** Cause of death and disability in U.S. as well as worldwide
- Caused by **atherosclerosis** and subsequently **ischemia/infarct**

Timeline of CVD Occurrence

- Endothelial Dysfunction
- Atherosclerosis
- Ischemia/infarct
- **Organ Damage**

“Thoughts on Preventive Cardiology”

- **Sir William Osler:** “Father of Modern Medicine”- **“You are only as old as your arteries!”**

- The health of your arteries determines the potential for future adverse cardiovascular events

Endothelium/Endothelial Cell

- Largest "**organ**" in the body
- Not just an inert, passive conduit for blood flow
- Biologically/Metabolically extremely active
- Ultimately determines the development/occurrence of **CVD**

“The Great Eight” (Modifiable)

- **1.** Hypertension
- **2.** Dyslipidemia
- **3.** Diabetes
- **4.** Cigarette smoking
- **5.** Weight
- **6.** Diet
- **7.** Activity level
- **8.** Mental well-being

Classical Risk Factors
Diabetes mellitus
Dyslipidemia
Smoking
Hypertension
Aging

Novel/Emerging Risk Factors
Infection/Inflammation
Physical inactivity
Post-prandial state
Homocysteine
Obesity

Intrinsic susceptibility – Genetic and environmental factors

Endothelial Dysfunction

Impaired vasomotion/tone

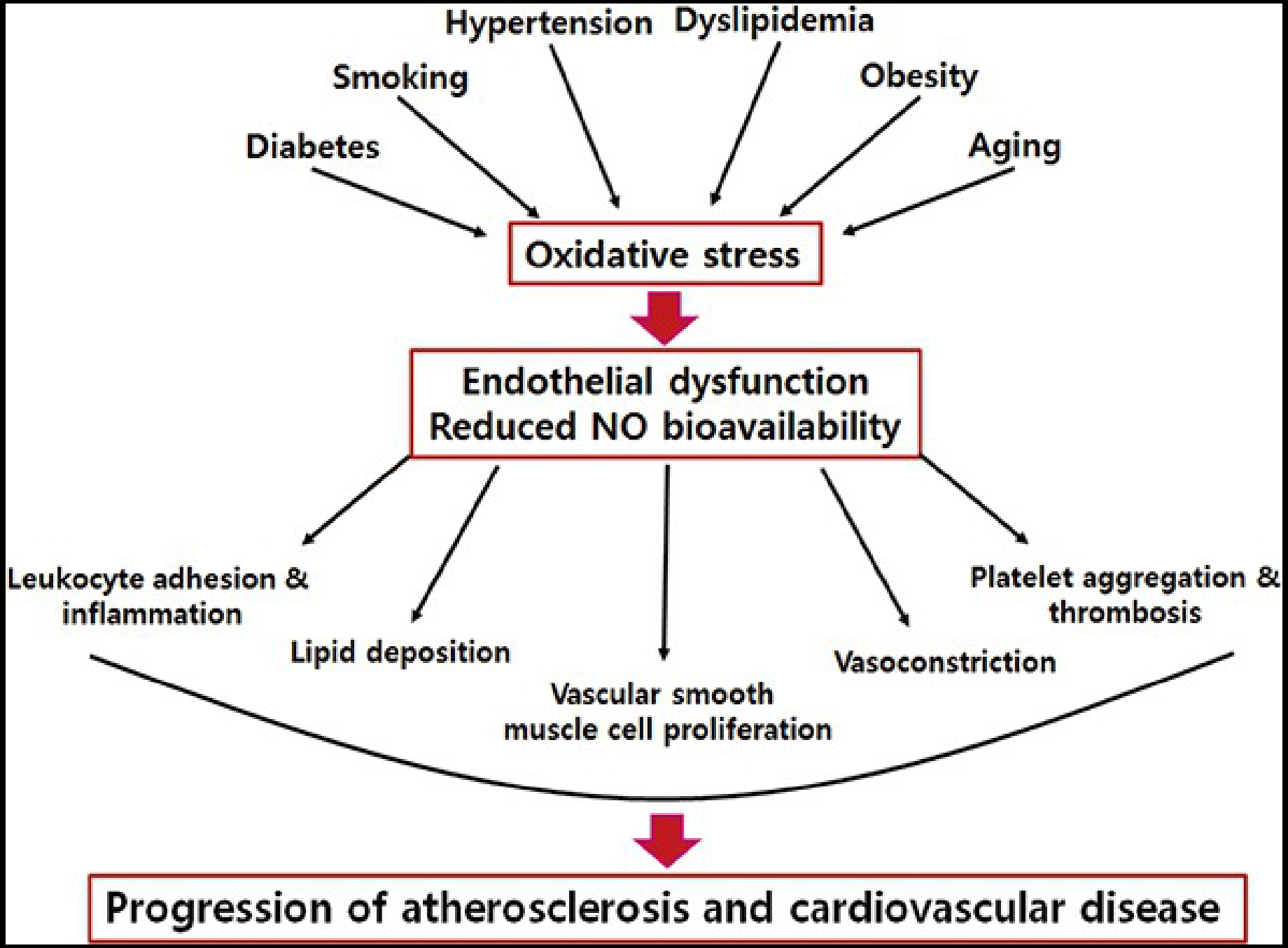
Prothrombotic state

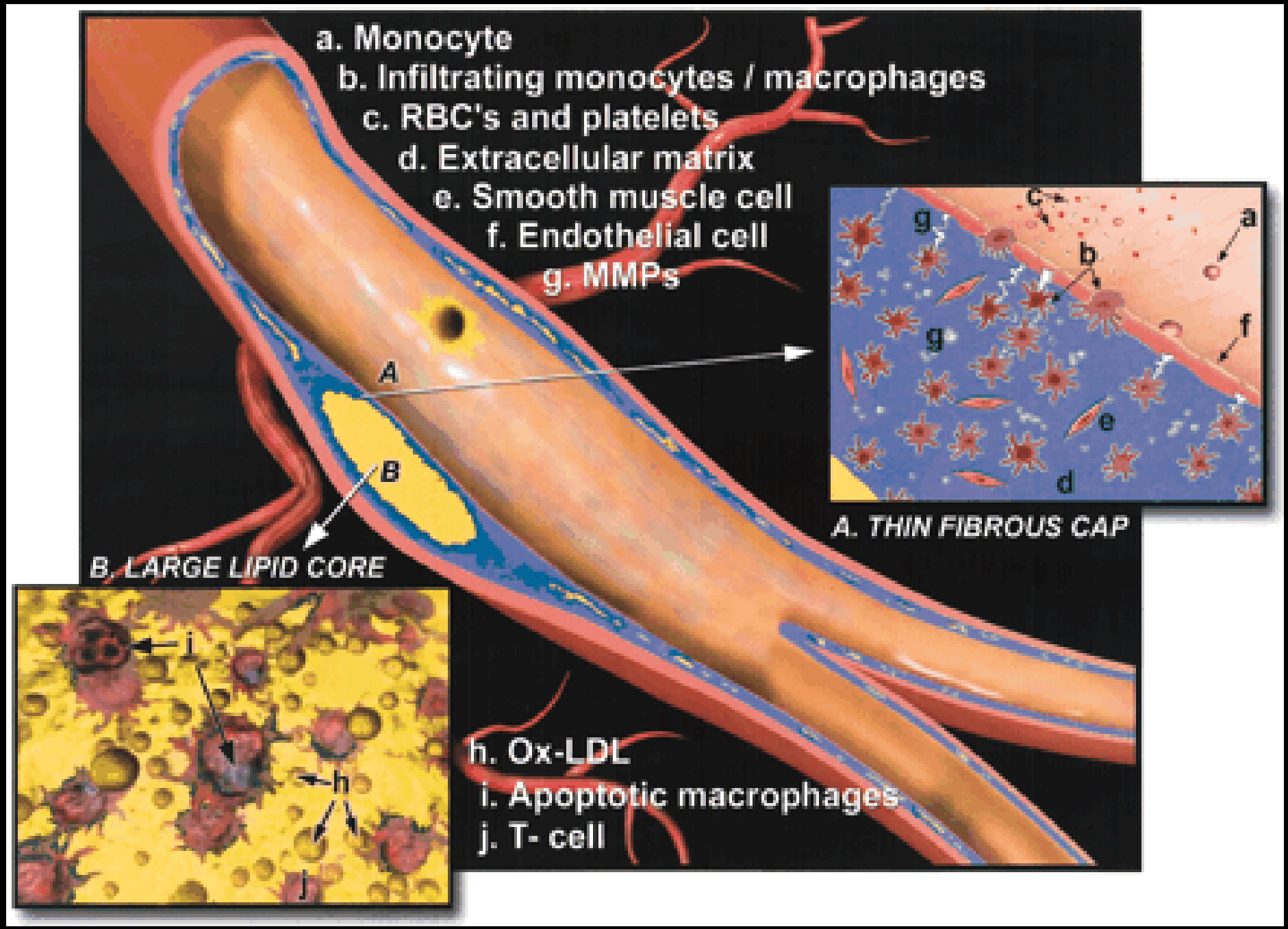
Pro-Inflammatory State

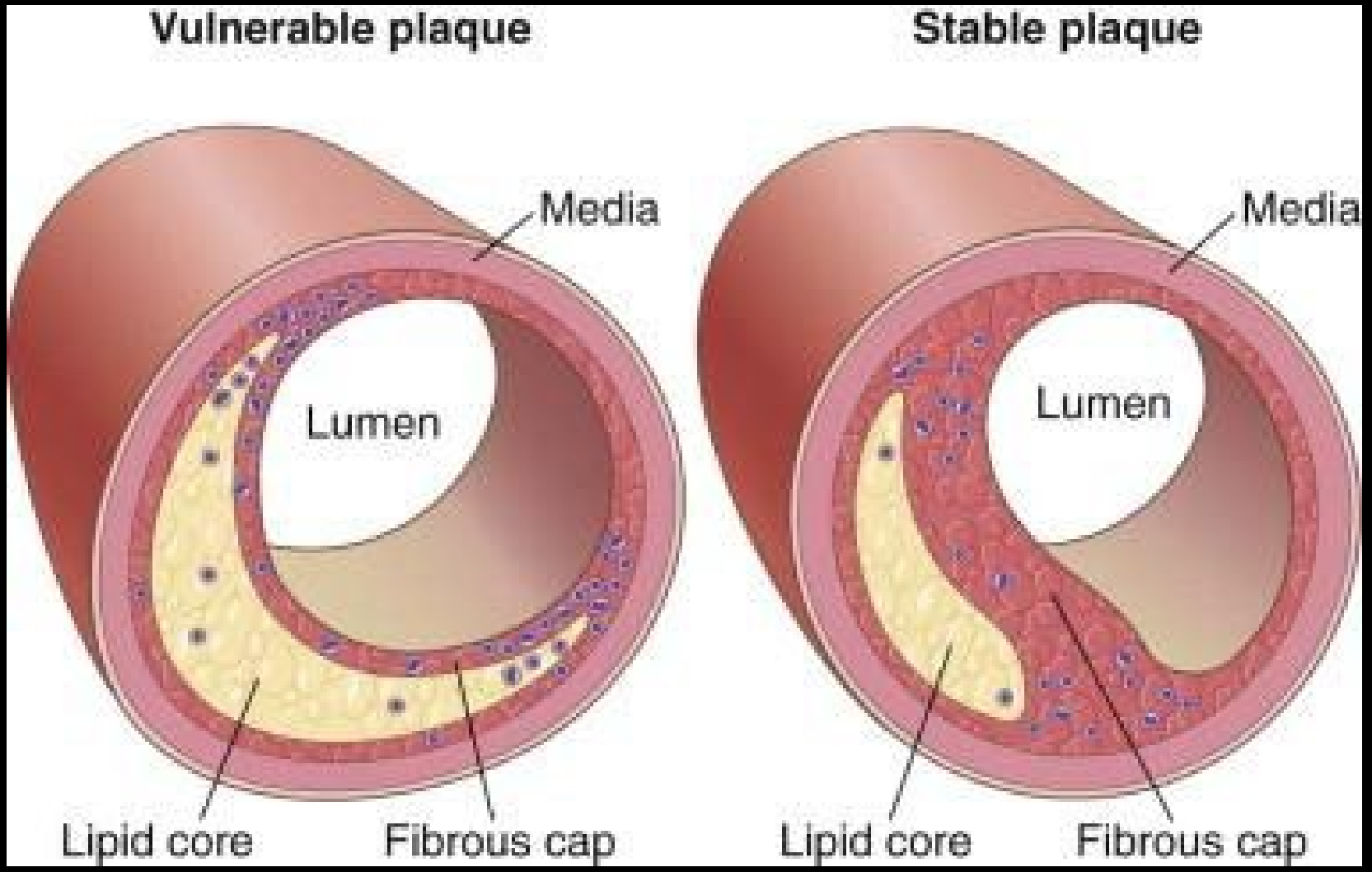
Proliferation in arterial wall

Atherosclerotic Lesion Formation and Progression
Plaque Activation/Rupture
Decreased Blood Flow due to Thrombosis and Vasospasm

Cardiovascular Disease Events


Hypertension
Dyslipidemia
Smoking
Obesity
Diabetes
Aging
Oxidative stress
Endothelial dysfunction
Reduced NO bioavailability
Leukocyte adhesion & inflammation
Lipid deposition
Vascular smooth muscle cell proliferation
Vasoconstriction
Platelet aggregation & thrombosis
Progression of atherosclerosis and cardiovascular disease


a. Monocyte
b. Infiltrating monocytes / macrophages
c. RBC's and platelets
d. Extracellular matrix
e. Smooth muscle cell
f. Endothelial cell
g. MMPs
A
B
A. THIN FIBROUS CAP
B. LARGE LIPID CORE
h. Ox-LDL
i. Apoptotic macrophages
j. T- cell


Vulnerable plaque
Media
Lumen
Lipid core
Fibrous cap
Stable plaque
Media
Lumen
Lipid core
Fibrous cap

Dr. Insel Says:

- Your arteries go by:

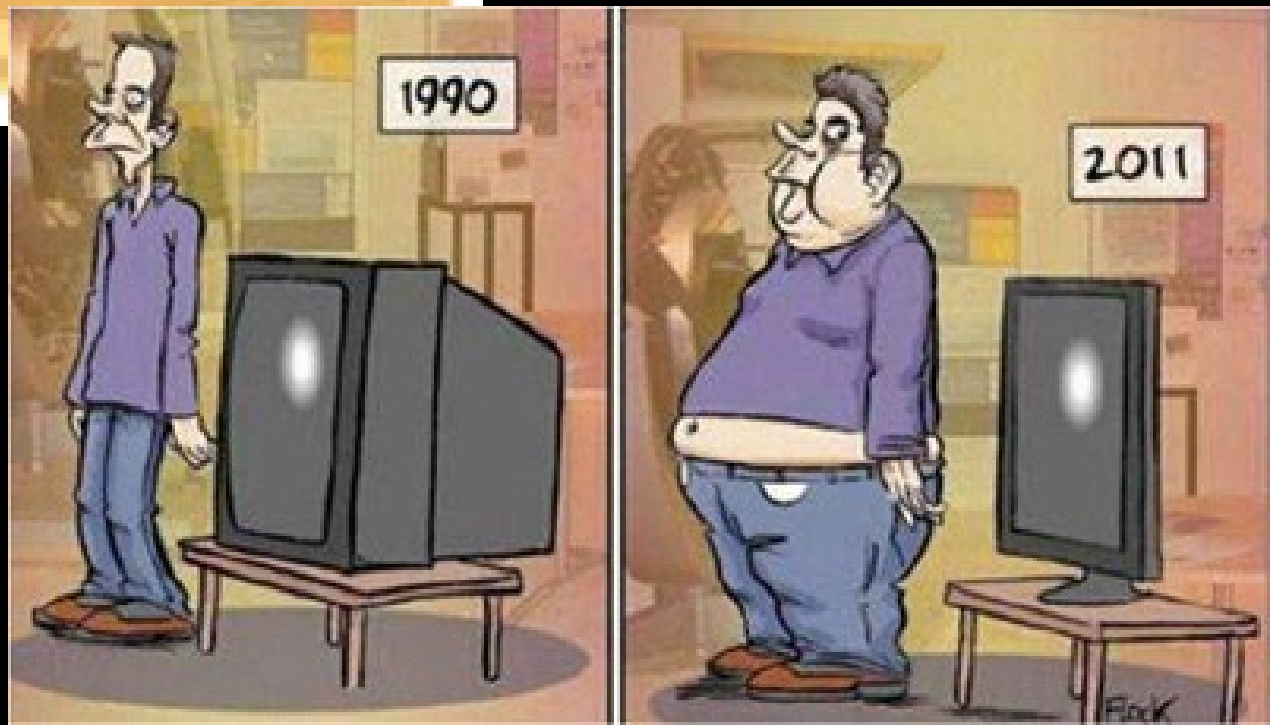
  “What have you done for me lately!”

  “It’s never too late!”


GLOBAL THREAT
WAITING AREA
OBESITY
BIRD
FLU
GLOBAL
WARMING
JEFF
PARKER
FLORIDA
TODAY
caglecartoons.com

Obesity in the U.S. has increased from 1/3 of the adult population to closer to 40%!!!

As our TV size has diminished our waist size has increased!!!



Adipose Tissue/Adipocyte

- Not just an inert, passive fat storage system
- Biologically/metabolically extremely active
- Produces/secretes many substances that **influence other organ systems**, potentiates inflammatory and pro-thrombotic responses that can **affect the endothelium and cause disease**

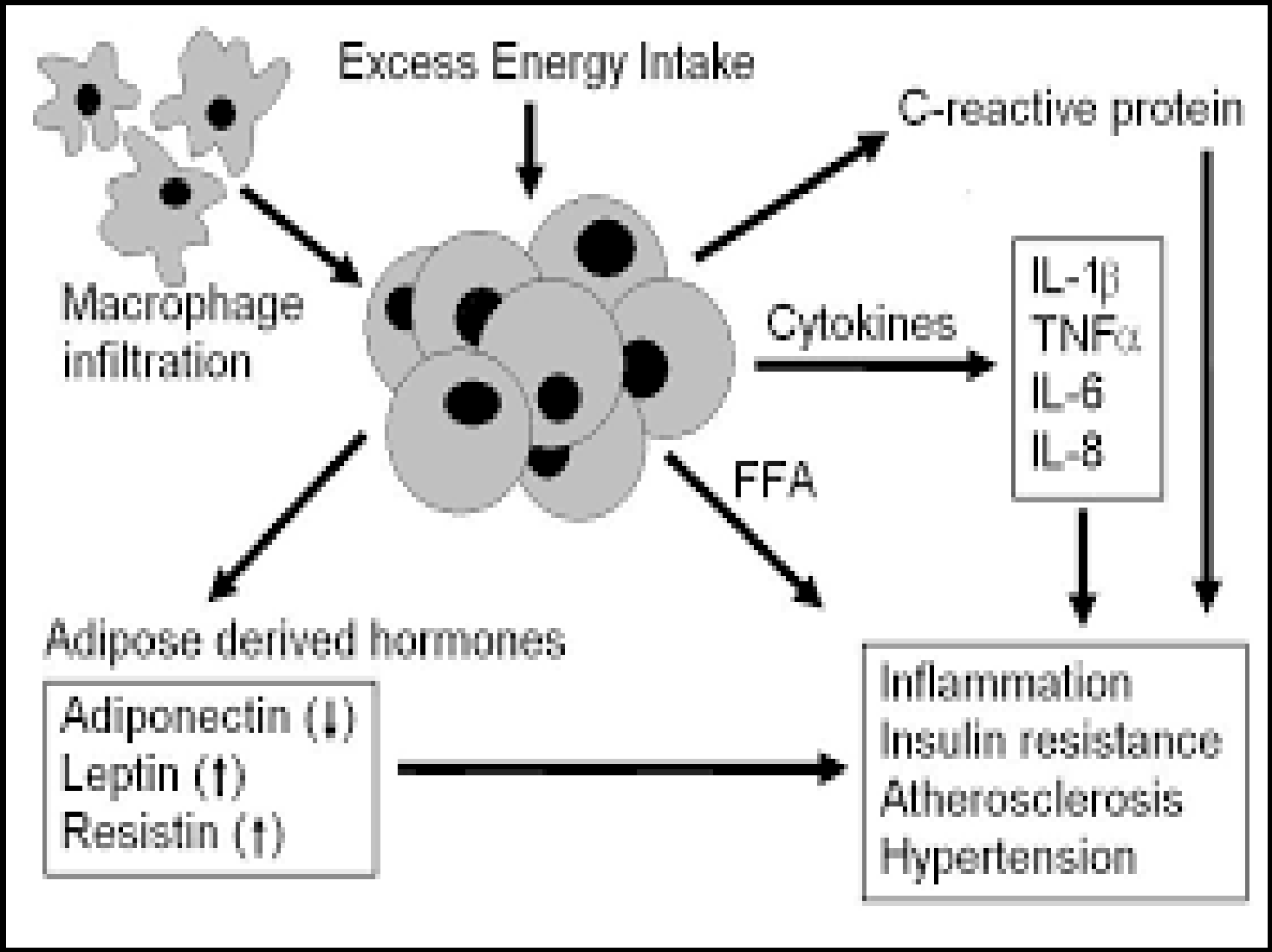
Adipose Tissue/Adipocyte

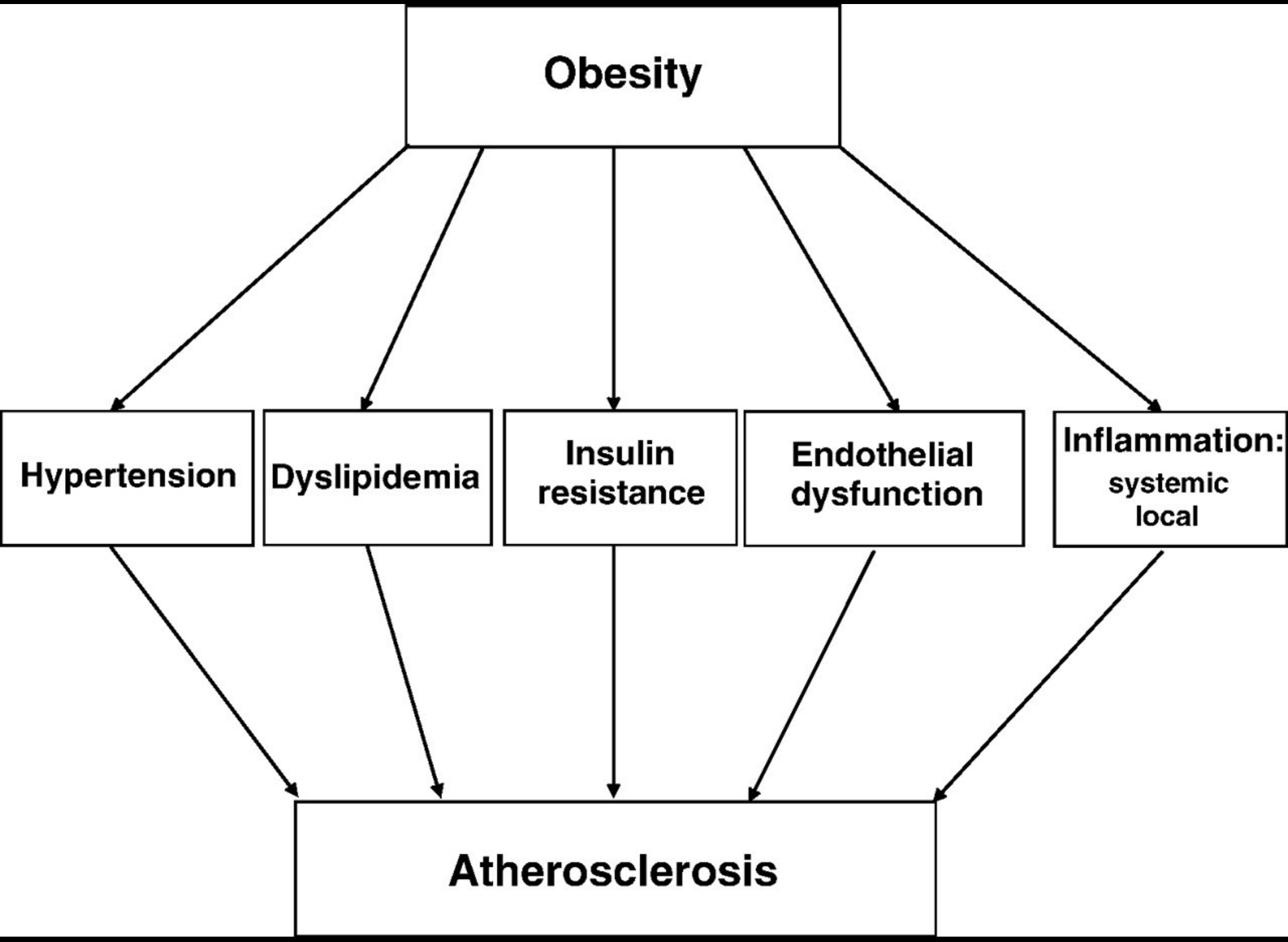
- Two Types of Fat ("All fat is not created equal"):
- **Subcutaneous Fat:** (Just under the skin); Better at fat storage
- **Visceral Fat:** (Internal; Around abdominal organs); "Sick Fat"; "Adiposopathy"
- You can be "thin" on the outside and "fat" on the inside!

The two kinds of body fat

Subcutaneous fat
(under the skin)

Visceral fat
(around the internal organs)


Excess Energy Intake
C-reactive protein
Macrophage infiltration
Cytokines
IL-1β
TNFα
IL-6
IL-8
FFA
Adipose derived hormones
Adiponectin (↓)
Leptin (↑)
Resistin (↑)
Inflammation
Insulin resistance
Atherosclerosis
Hypertension


Obesity
Hypertension
Dyslipidemia
Insulin resistance
Endothelial dysfunction
Inflammation:
systemic
local
Atherosclerosis


OBESITY
CORONARY HEART DISEASE
DIABETES
CANCERS
HYPERTENSION
HIGH CHOLESTEROL
SLEEP APNEA
RESPIRATORY PROBLEMS
QUALITY OF LIFE
ARTHRITIS
HIGH BLOOD PRESSURE

Stress (Mental Well-Being) and CVD

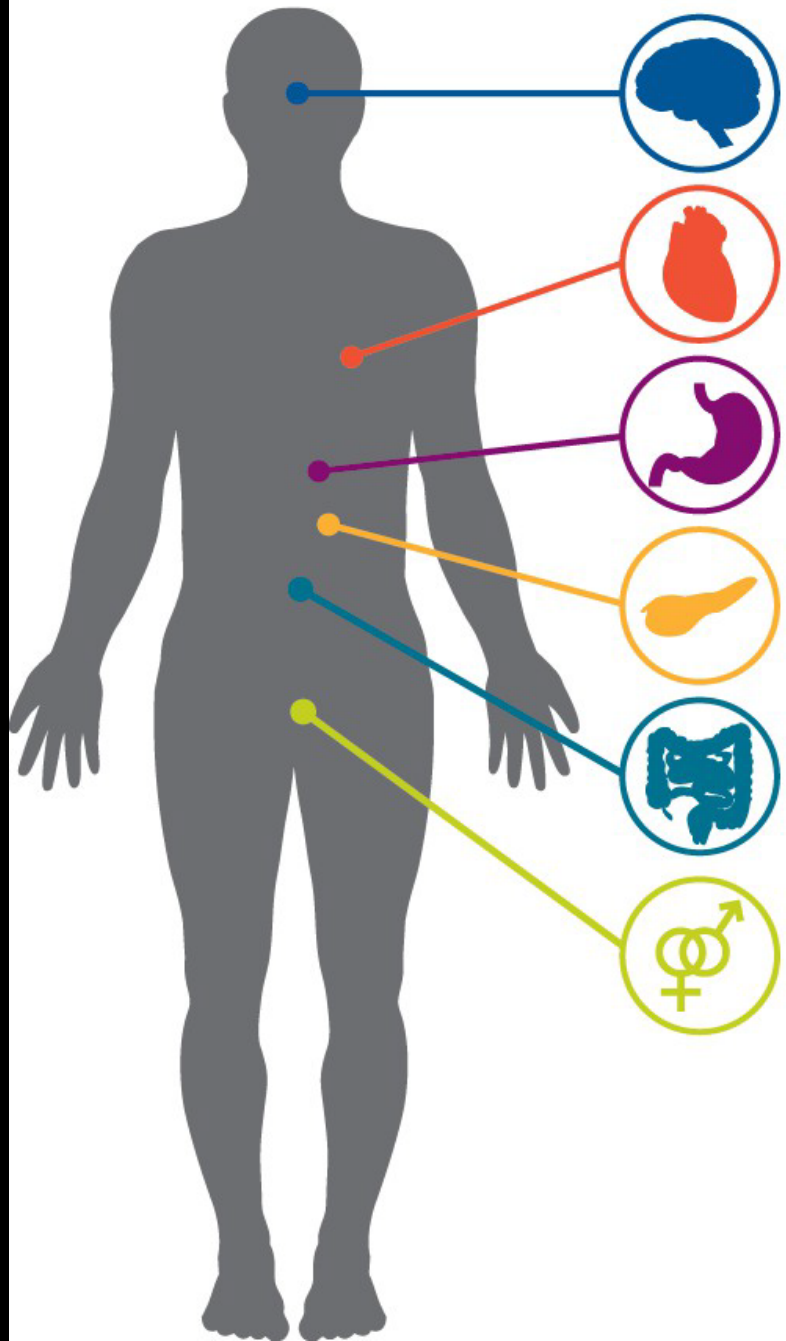
- Integral member of the "Great Eight"
- Similar adverse consequences as other components

EFFECTS OF STRESS

- Health problems caused by stress:
  - Heart diseases
  - Digestive problems
  - Sleep problems
  - Depression
  - Auto immune diseases


Overtime
Sick
Tired
Dread
Health
No Time
Headache
Bills
Payments
Stress
Stress
No Sleep
Debt
Work
Fear
Worry
Job
Anxiety
Retirement
Savings
Anxiety
Expectations
Overdue
Insuran
Time Management
Fear
Late Nights

Effects of Stress on the Body



Brain and Nerves: Headaches, feelings of despair, lack of energy, sadness, nervousness, anger, irritability, trouble concentrating, memory problems, difficulty sleeping, mental health disorders (anxiety, panic attacks, depression, etc.)

Heart: Faster heartbeat or palpitations, rise in blood pressure, increased risk of high cholesterol and heart attack

Stomach: Nausea, stomach ache, heartburn, weight gain, increased or decreased appetite

Pancreas: Increased risk of diabetes

Intestines: Diarrhea, constipation and other digestive problems

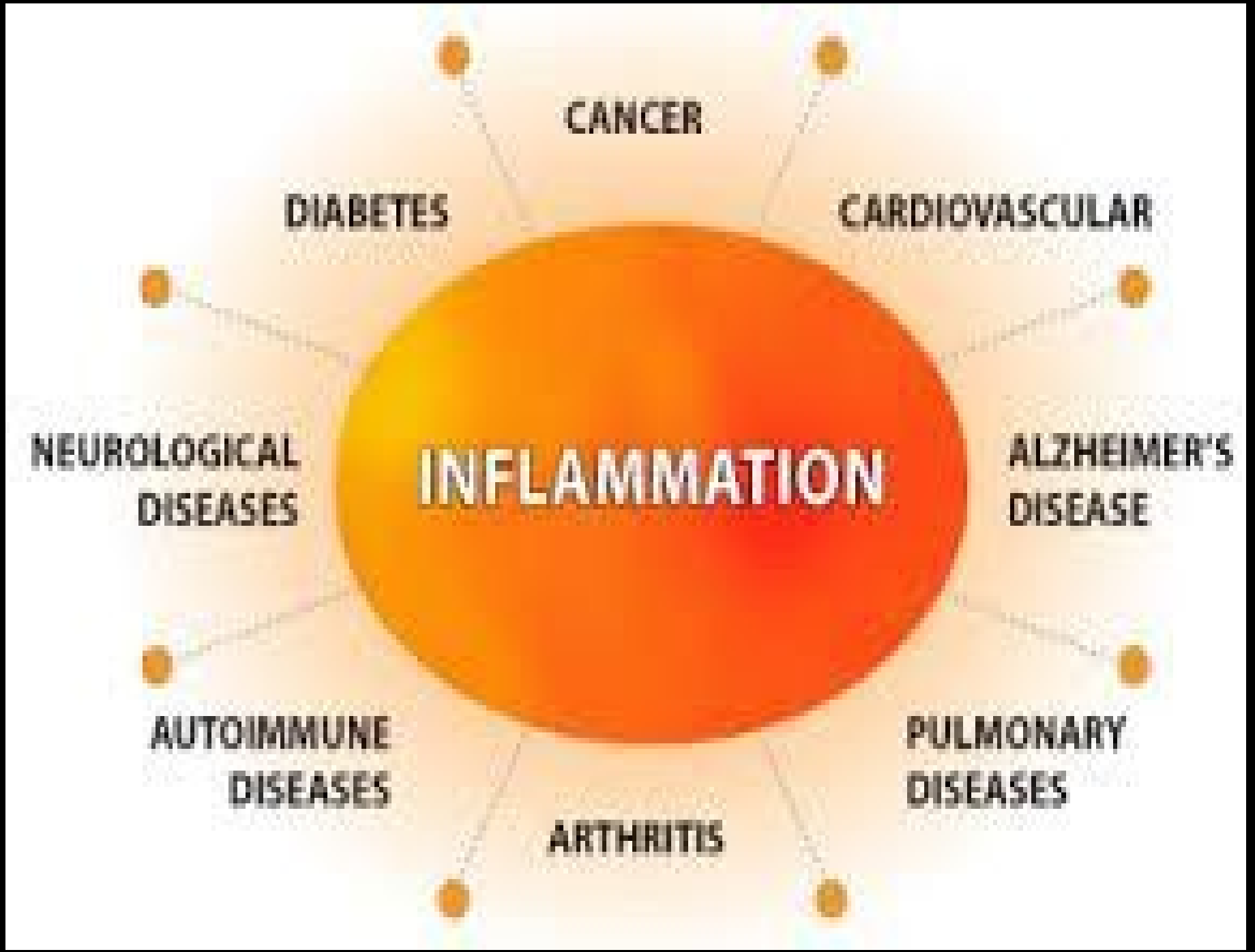
Reproductive Organs: For women-irregular or painful periods, reduced sexual desire. For men-impotence, low sperm production, reduced sexual desire

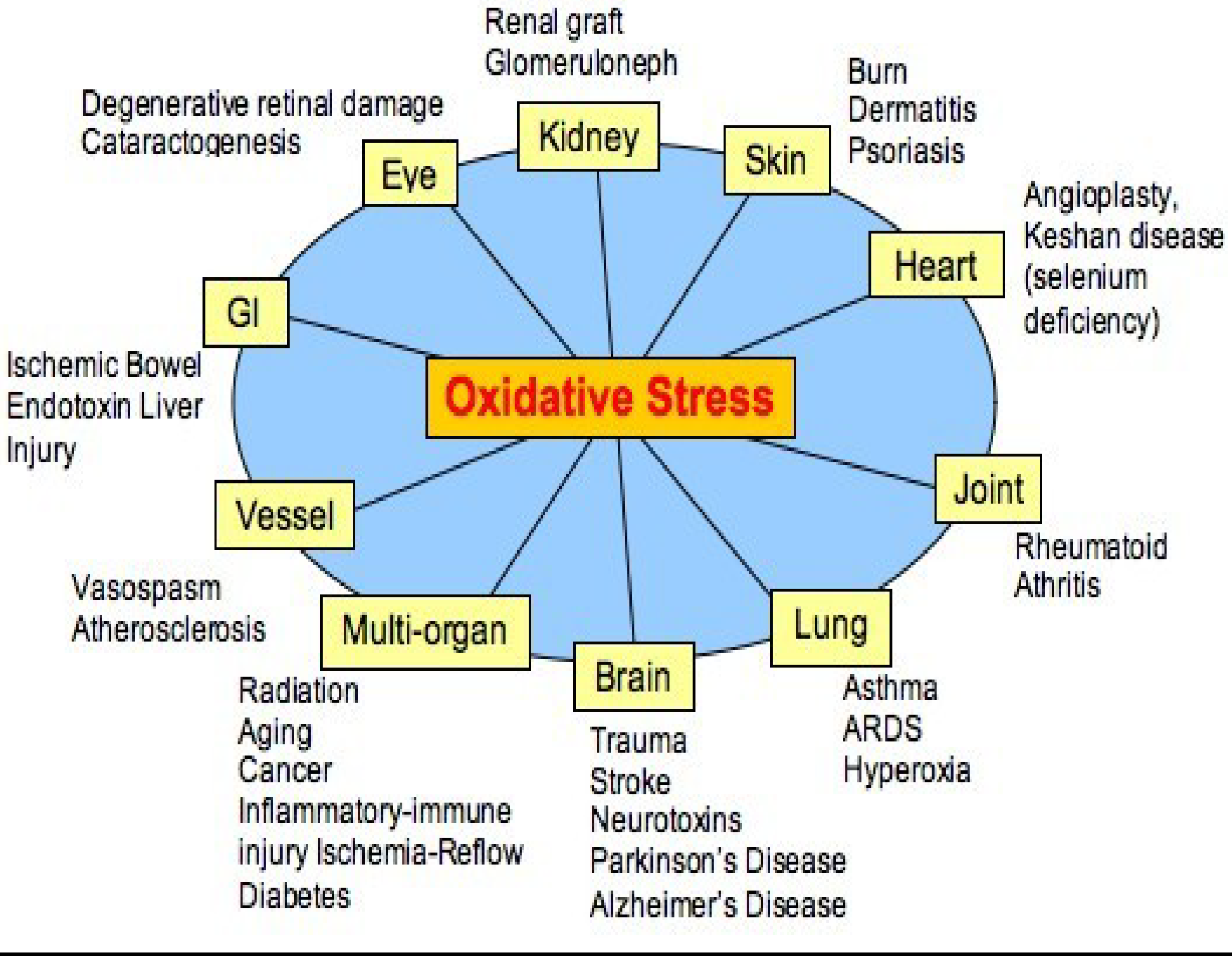
Other: Acne and other skin problems, muscle aches and tension, increased risk for low bone density and weakened immune system (making it harder to fight off or recover from illnesses)

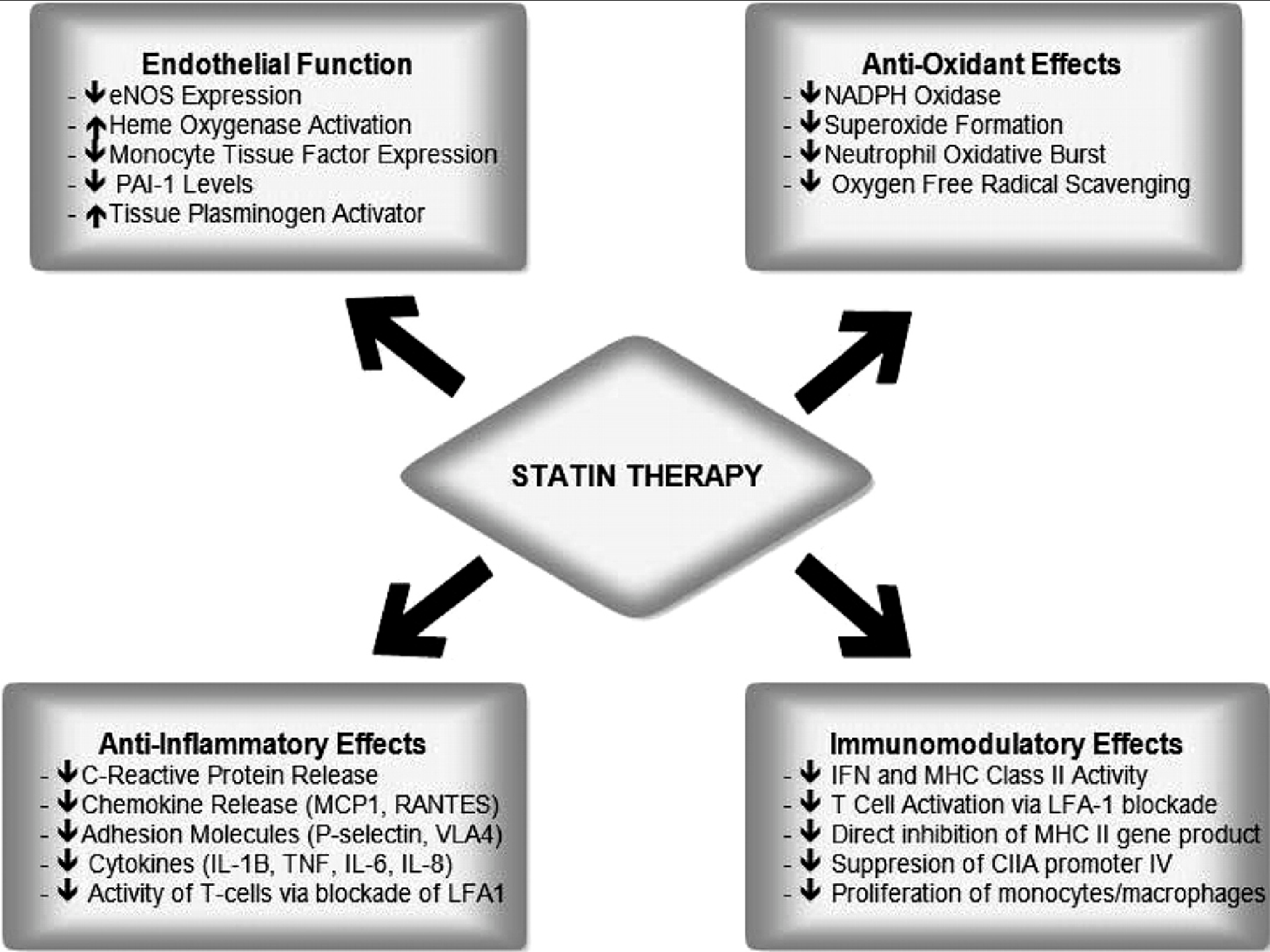

Therapy
Spa
Exercise
Hobby
Meditation
Yoga
Nature
Time Management
Music
Stress Management

Adverse Effects of "The Great Eight"

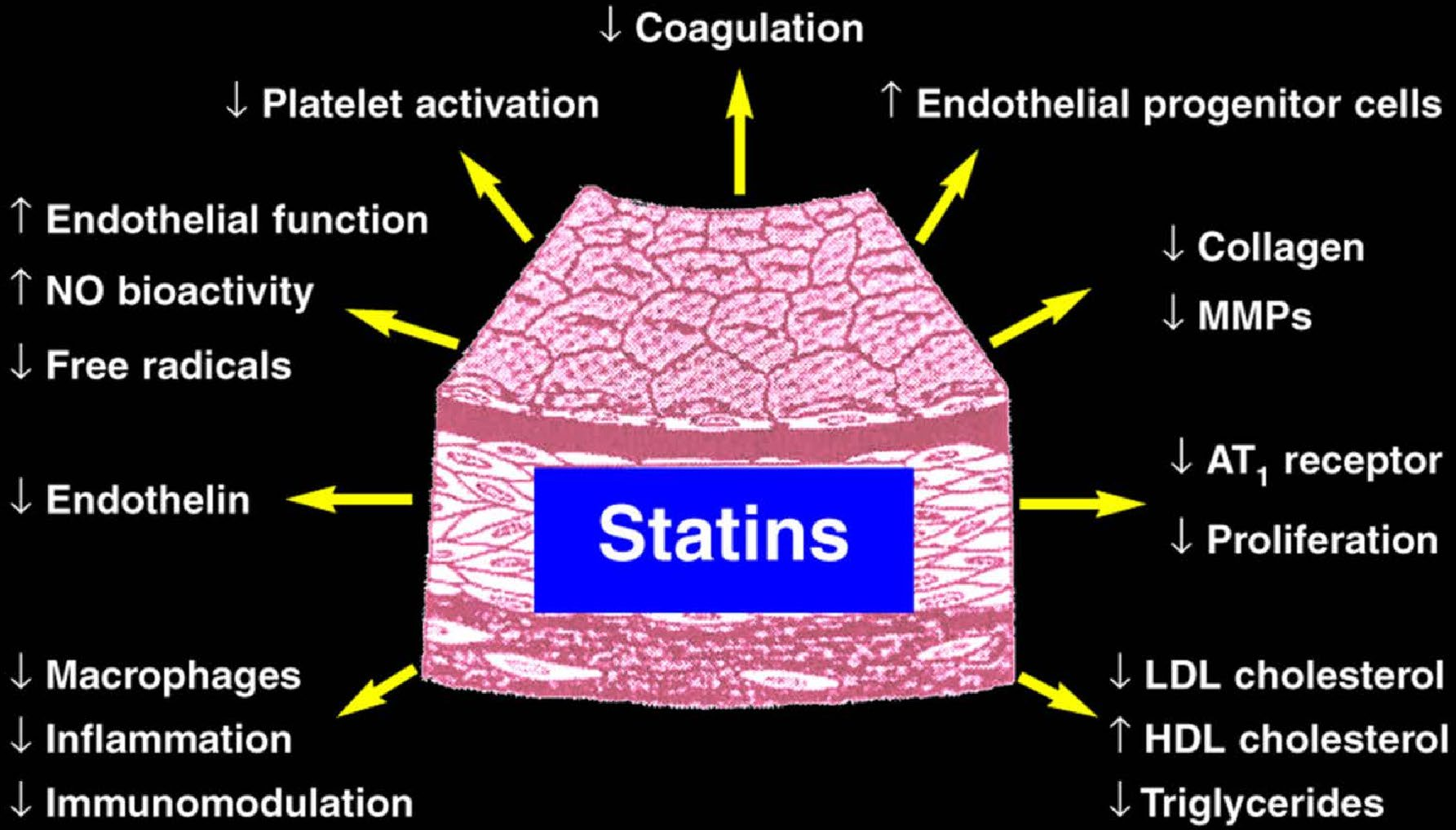
- Leads to a pro-inflammatory state
- Leads to oxidative stress
- Leads to endothelial dysfunction
- Leads to development of CVD


CANCER
DIABETES
CARDIOVASCULAR
NEUROLOGICAL DISEASES
INFLAMMATION
ALZHEIMER'S DISEASE
AUTOIMMUNE DISEASES
PULMONARY DISEASES
ARTHRITIS


Renal graft
Glomeruloneph
Degenerative retinal damage
Cataractogenesis
Kidney
Eye
Skin
Burn
Dermatitis
Psoriasis
Angioplasty,
Keshan disease
(selenium
deficiency)
Heart
GI
Ischemic Bowel
Endotoxin Liver
Injury
Oxidative Stress
Joint
Rheumatoid
Athritis
Vessel
Vasospasm
Atherosclerosis
Multi-organ
Lung
Brain
Radiation
Aging
Cancer
Inflammatory-immune
injury Ischemia-Reflow
Diabetes
Trauma
Stroke
Neurotoxins
Parkinson's Disease
Alzheimer's Disease
Asthma
ARDS
Hyperoxia


Endothelial Function
- ↓eNOS Expression
- ↑Heme Oxygenase Activation
- ↕Monocyte Tissue Factor Expression
- ↓ PAI-1 Levels
- ↑Tissue Plasminogen Activator
Anti-Oxidant Effects
- ↓NADPH Oxidase
- ↓Superoxide Formation
- ↓Neutrophil Oxidative Burst
- ↓ Oxygen Free Radical Scavenging
STATIN THERAPY
Anti-Inflammatory Effects
- ↓C-Reactive Protein Release
- ↓Chemokine Release (MCP1, RANTES)
- ↓Adhesion Molecules (P-selectin, VLA4)
- ↓ Cytokines (IL-1B, TNF, IL-6, IL-8)
- ↓ Activity of T-cells via blockade of LFA1
Immunomodulatory Effects
- ↓ IFN and MHC Class II Activity
- ↓ T Cell Activation via LFA-1 blockade
- ↓ Direct inhibition of MHC II gene product
- ↓ Suppresion of CIIA promoter IV
- ↓ Proliferation of monocytes/macrophages

Pleiotropic effects of statins on the vessel wall



MMPs = matrix metalloproteinases

Wassmann S, Nickenig G. *Endothelium*. 2003;10:23-33.

Beneficial Effects of Prudent Lifestyle Modification and Medical Therapy

- Minimizes **Oxidative Stress**
- Minimizes **Inflammation**
- **Improves endothelial function**
- **Reduces development of CVD**

Cardio/Aerobic

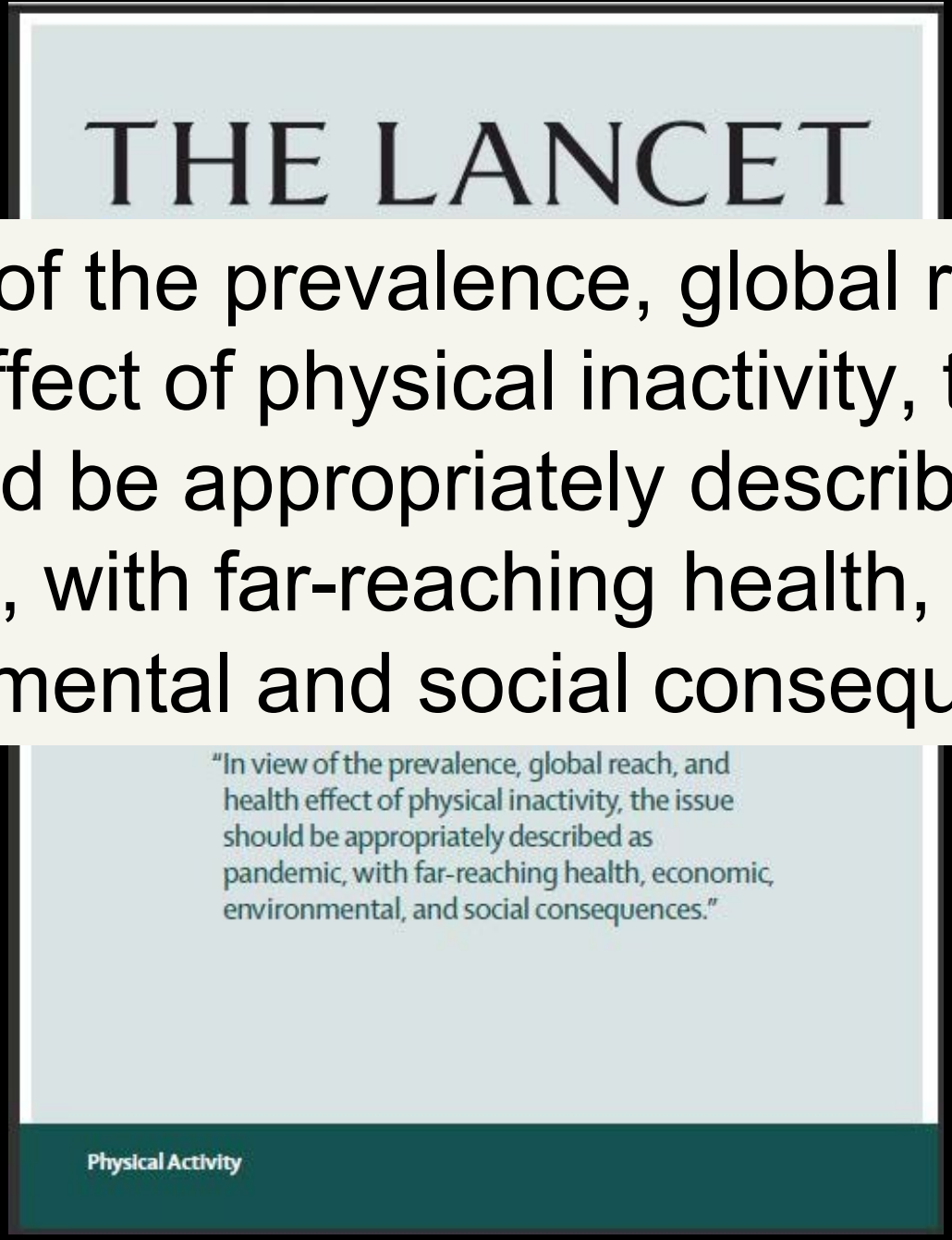
Resistance/Strength

It's not that diabetes, heart disease and obesity runs in your family. It's that no one runs in your family.

someecards
user card

Health Burden of Inactivity Vs. Smoking

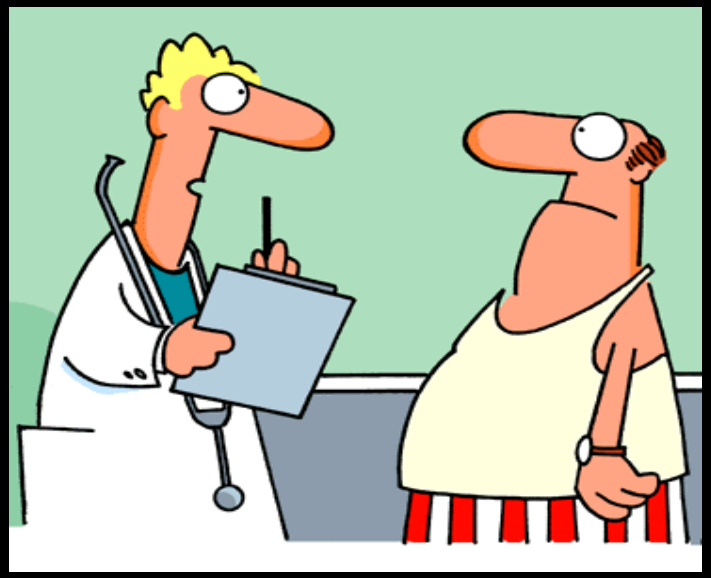
- One day of being inactive has roughly an equivalent health burden to smoking 3 cigarettes.
- So, being inactive for a whole week has equivalent health burden to smoking a pack of cigarettes.
  - Do you advise your patients not to smoke?



"In view of the prevalence, global reach and health effect of physical inactivity, the issue should be appropriately described as Pandemic, with far-reaching health, economic, environmental and social consequences."

Common Barriers to Exercise

- Competing demands (work/kids/spouse)
- Not enough time
- Too tired
- Physical limitations
- Too boring
- Sedentary habits



"What fits your busy schedule better, exercising ½ hour a day or being dead 24 hours a day?"

Do You Really Think We have a Chance Without Exercise?

- Obesity
- Coronary artery disease
- Diabetes
- Hypertension
- Cancer
- Depression and anxiety
- Arthritis
- Osteoporosis
- Etc, etc, etc…

NO!

Exercise and Health

- Did you know?
  - Physicians with healthy personal habits are more likely to counsel patients to adopt such habits.
  - Patients find doctors with healthier exercise and diet habits to be more believable and motivating toward healthy patient lifestyles.
  - **Doctors who exercise and eat right are better doctors!**
- Healthy Doc = Healthy Patient
  - Dr. Erica Frank
  - Professor and Canada Research Chair

Breaking Down the Barriers

- **Make exercise a habit, not an option.**
- 150 min per week is goal – not starting point; so start small:
  - 1-2 days per week
  - Three 10-min bouts
- Simple recipe for getting your exercise:
  - AM; park car 10 min from office, walk in
  - Lunch; walk 5 min out, eat, walk back
  - PM; Walk 10 min back to car

Breaking Down the Barriers

- Make weekends count!
  - Change mindset; weekends are for fitness
  - Walk 60 min on Sat or Sun, only need 90 more minutes during week
- Bump up the intensity!
  - 25 min of vigorous exercise (jog) done 3x per wk
  - 30 min of moderate (brisk walk) done 5x per wk
- More ideas:
  - Find an exercise partner
  - Get good shoes and nice workout clothes
  - Set goals (fun run or walk, sprint triathlon)

Exercise *Is* Medicine: *Physicians should prescribe it, Patients should take it!*

- **Exercise** is the long sought **vaccine** to prevent chronic disease and extend life.

- If we had a pill that conferred the proven health benefits of exercise, physicians would prescribe it to every patient and healthcare systems would find a way to make sure every patient had access to this **wonder drug**.

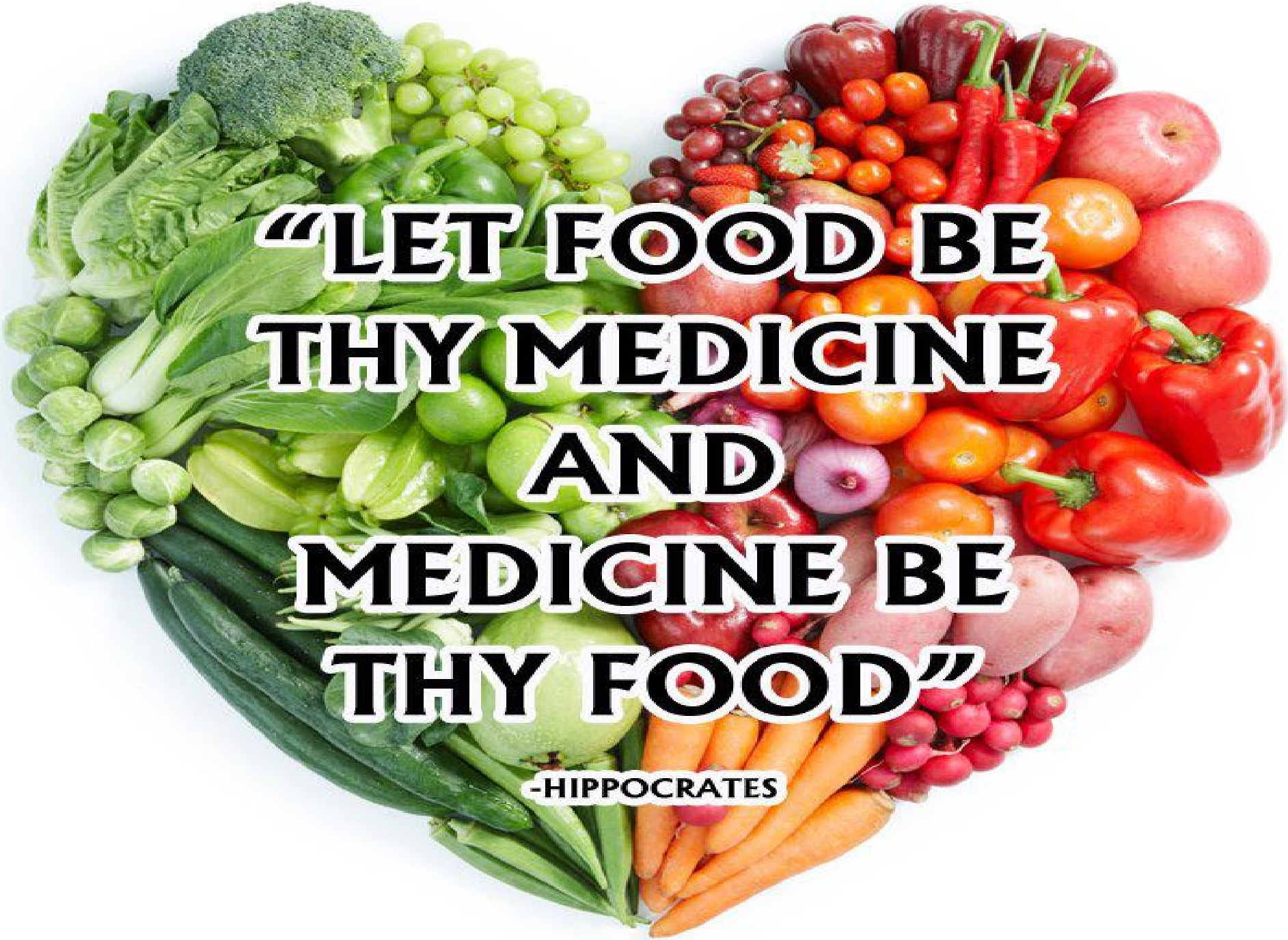
Diet and CVD

- Research has consistently shown that the Mediterranean Diet is effective in reducing the risk of CVD and overall mortality

- When it comes to weight loss two principles come to mind:
  1. Move more
  2. Eat less

Mediterranean Food Pyramid


Relationships
Career
Fruits
Whole Grains
Vegetables
Protein
Water
Fats & Oils
Spirituality
Physical Activity
Integrative Nutrition™ Plate


"LET FOOD BE
THY MEDICINE
AND
MEDICINE BE
THY FOOD"
-HIPPOCRATES

Benefits of eating healthy, exercising routinely and adherence to appropriate medical therapy for CVD risk factors

- **"Let food be thy medicine and medicine be thy food"** – Hippocrates: 4th century B.C.

- **"Let exercise be thy medicine and be routine as thy food"** – Dr. Insel: 21st century A.D.

“Thoughts on Preventive Cardiology”

- "You are only as old as your arteries"
- "Remember The Great Eight"
- "It's never too late"

The Future of Preventive Cardiology

- Looking beyond CVD risk factors
- Direct, non-invasive, office-based, accurate, reproducible assessment of endothelial function/dysfunction
- Therapies targeted to directly/specifically improve endothelial function/arterial health

Coronary Artery Calcium Scoring

Evaluation beyond traditional risk factors

Quick; No contrast; Low radiation

Independent predictor of future CVD/MACE

Assessment of calcified plaque only

Coronary Artery Calcium Scoring

0	No calcification
1-10	Minimal calcification
11-100	Mild calcification
101- 400	Moderate calcification
Over 400	Severe calcification

Coronary Artery Calcium Scoring

Who should we refer for a Coronary artery calcium test/scan?

EHE Health Criteria

Borderline or Intermediate ASCVD risk

Non-calcified Coronary Artery Plaques (NCPs)

NCPs are considered precursor lesions for calcified plaque

The absence of CAC and the presence of NCPs can vary between 6-46% (multiple reports)

NCPs

Early detection of coronary artery plaque before its progression to calcification can allow early interventions towards regression

This will eventually translate into a lower incidence of future CVD events

Coronary CTAs (CCTAs)

CCTA can identify soft/NCP's

Soft/non-calcified/vulnerable plaques are more likely to rupture and cause acute cardiac events

Identified by thin fibrous caps, large lipid burden and presence of inflammatory cells

Research is indicated to determine the utility of CCTA in individuals with zero/minimal CAC