BREAST WELLNESS
A FUNCTIONAL APPROACH TO CANCER

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FUNCTIONAL MEDICINE

- Prevention
- Underlying Causes
- Science Based
- Biochemical Individuality
- Patient Centered (Not Disease Centered)
- Interconnections in our body
  - Inflammation and heart disease
  - Gut and immune system

ASKS WHY???

FUNCTIONAL MEDICINE - 7 KEYS

- Hormonal
- Detoxification
- Immune System
- Inflammation
- Digestion
- Oxidative Stress
- Structural

Not just breast cancer…….

but breast cancers

ESTROGEN

- As estrogen exposure increases so does our risk of breast cancer
  - Number of periods in your lifetime
  - BCPs >5 years or current use
  - HRT - 8.6% decrease in postmenopausal ER+ breast cancer since 2001
  - Endocrine Disrupters

Estrogen

Endocrine Disrupters -

Substances that mimic or disturb the activity or binding of our hormones

- Xenoestrogen - synthetic chemicals that act as endocrine disrupters
- Plastics -
  - BPA - Bisphenol A - #7
  - PVC - Polyvinyl chlorine - phthalates

- Pesticides

  carcinogens and endocrine disruptors

What can you do?

- Buy organic
  - Decreased pesticide exposure
  - Decreased growth hormone exposure
    - Decrease animal products in general
- Use glass whenever possible
- Do not heat or microwave plastic
- Switch to non plastic reusable water bottles
- Avoid pesticides on your lawn and garden

ESTROGEN

- As estrogen exposure increases so does our risk of breast cancer
  - Number of periods in your lifetime
  - BCPs >5 years or current use
  - HRT
  - Endocrine Disrupters
  - **Weight - % body fat**

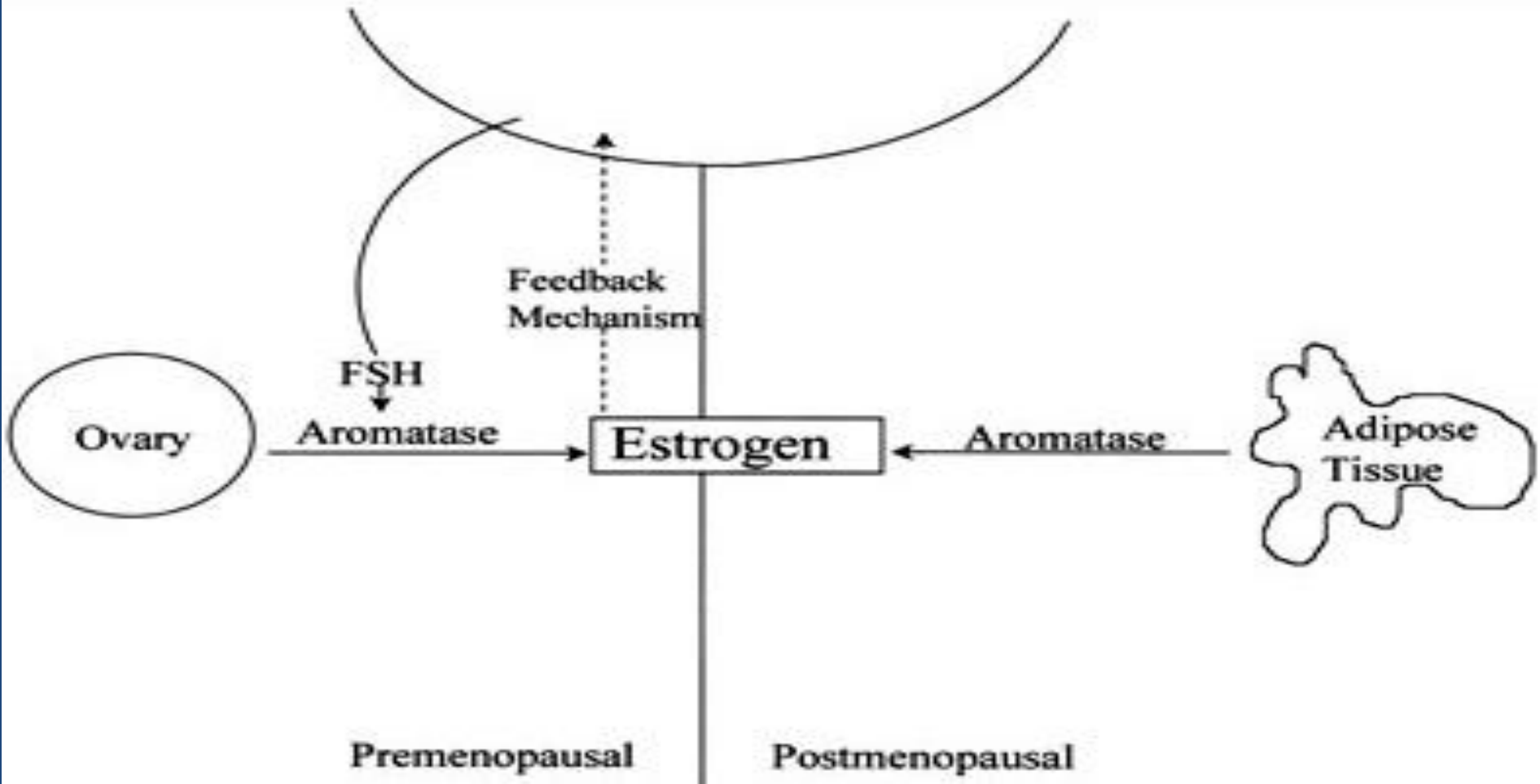
WEIGHT

- Increase weight by 22 or more pounds since age 18… 30% increased risk of breast cancer than women gained 5 or less pounds
  - » JAMA. 2006. 296:193

- Women with the highest BMI had a 35 percent increase in risk of triple-negative breast cancer and a 39 percent increase in the risk of estrogen receptor-positive breast cancer.
- Women with the highest levels of physical activity had reduced risks of both triple-negative breast cancer and estrogen receptor-positive breast cancer
  - – Phipps AI, Chlebowski RT, Prentice R et al. Body size, physical activity, and risk of triple-negative and estrogen receptor-positive breast cancer. Cancer Epidemiology, Biomarkers, & Prevention. Early online publication March 1, 2011
- Breast cancer survivors who were overweight or obese were more likely to have their cancer recur than thinner survivors.
  - » Journal of Clinical Oncology. 2002. Vol. 20, No. 15: 3302-3316

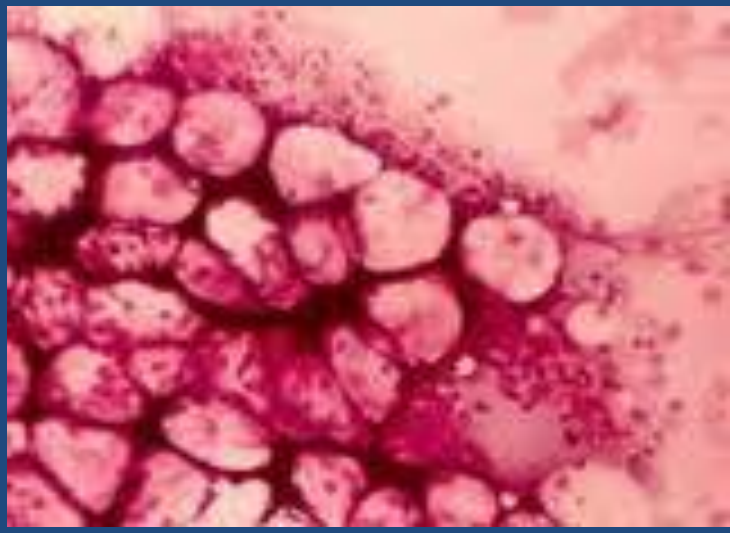
WHY?

- Aromatase and Insulin Resistance



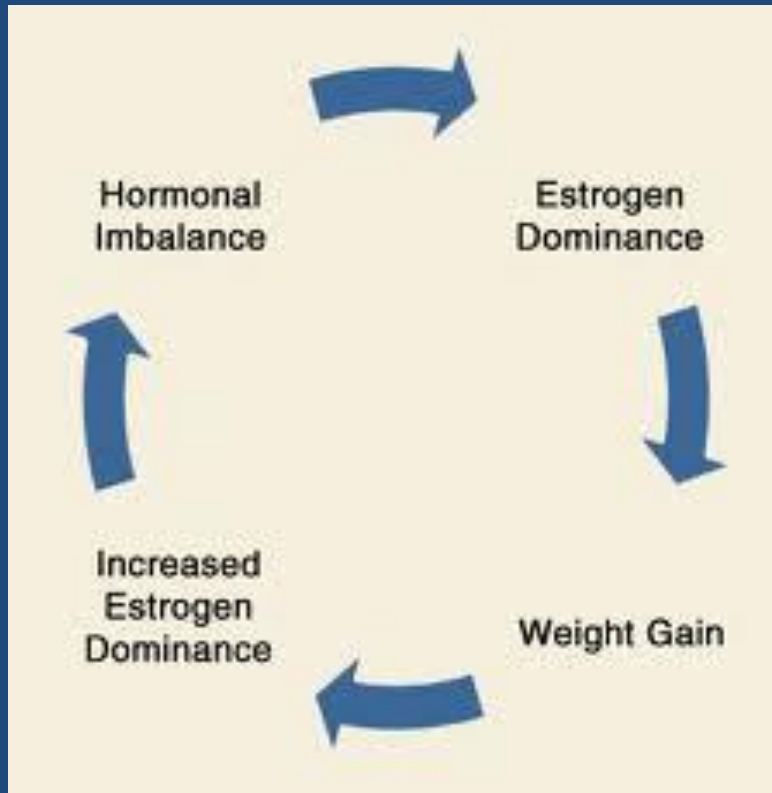
Decrease Aromatase

- Lower % body fat
  - Maintain healthy weight
  - Resistance exercise
- Decrease inflammation
  - Omega 3 fats
  - Avoid trans fats
  - Decrease saturated fat
  - Lower % body fat
    inflammation made in fat
  - Turmeric
  - Aspirin ?

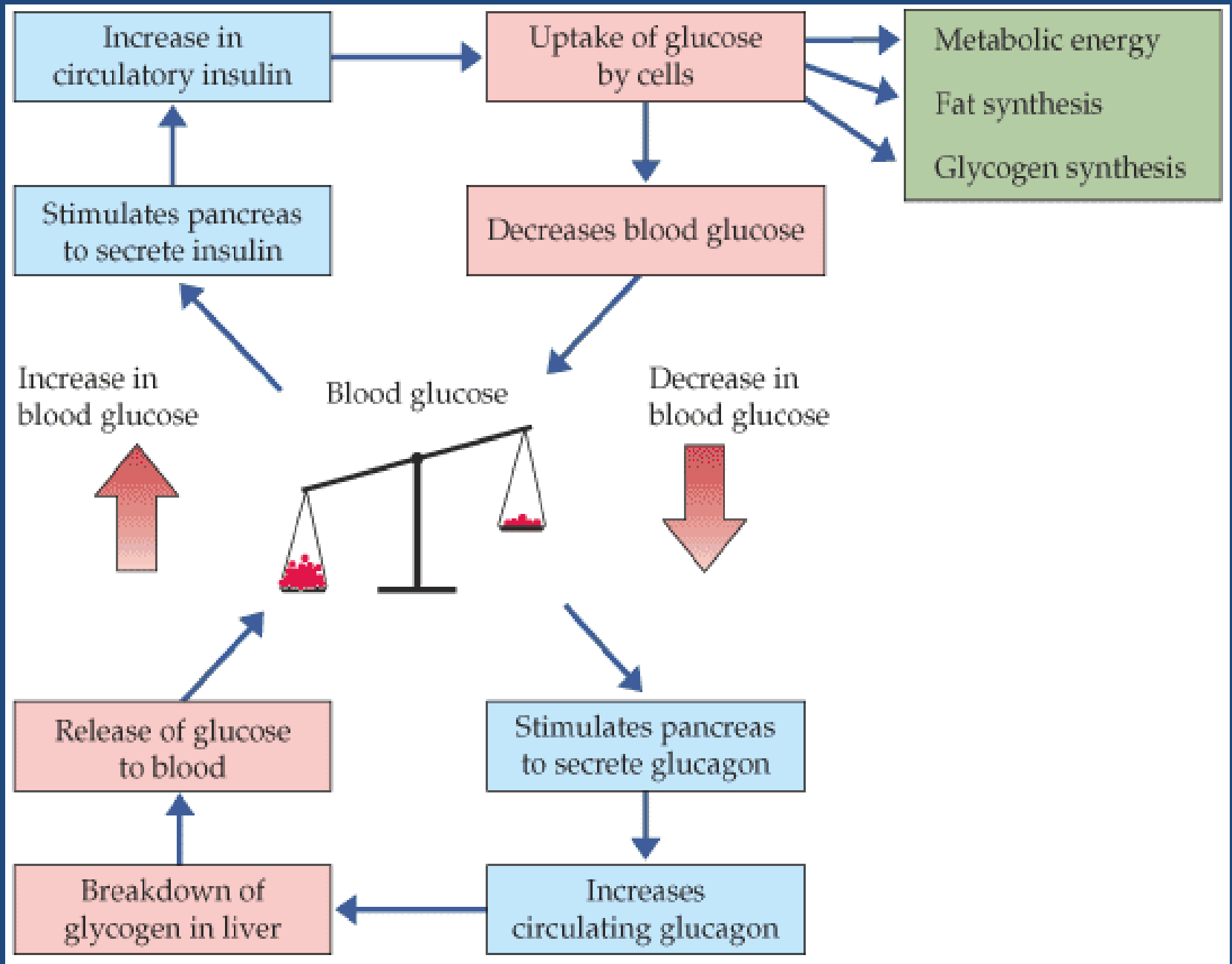


SHBG

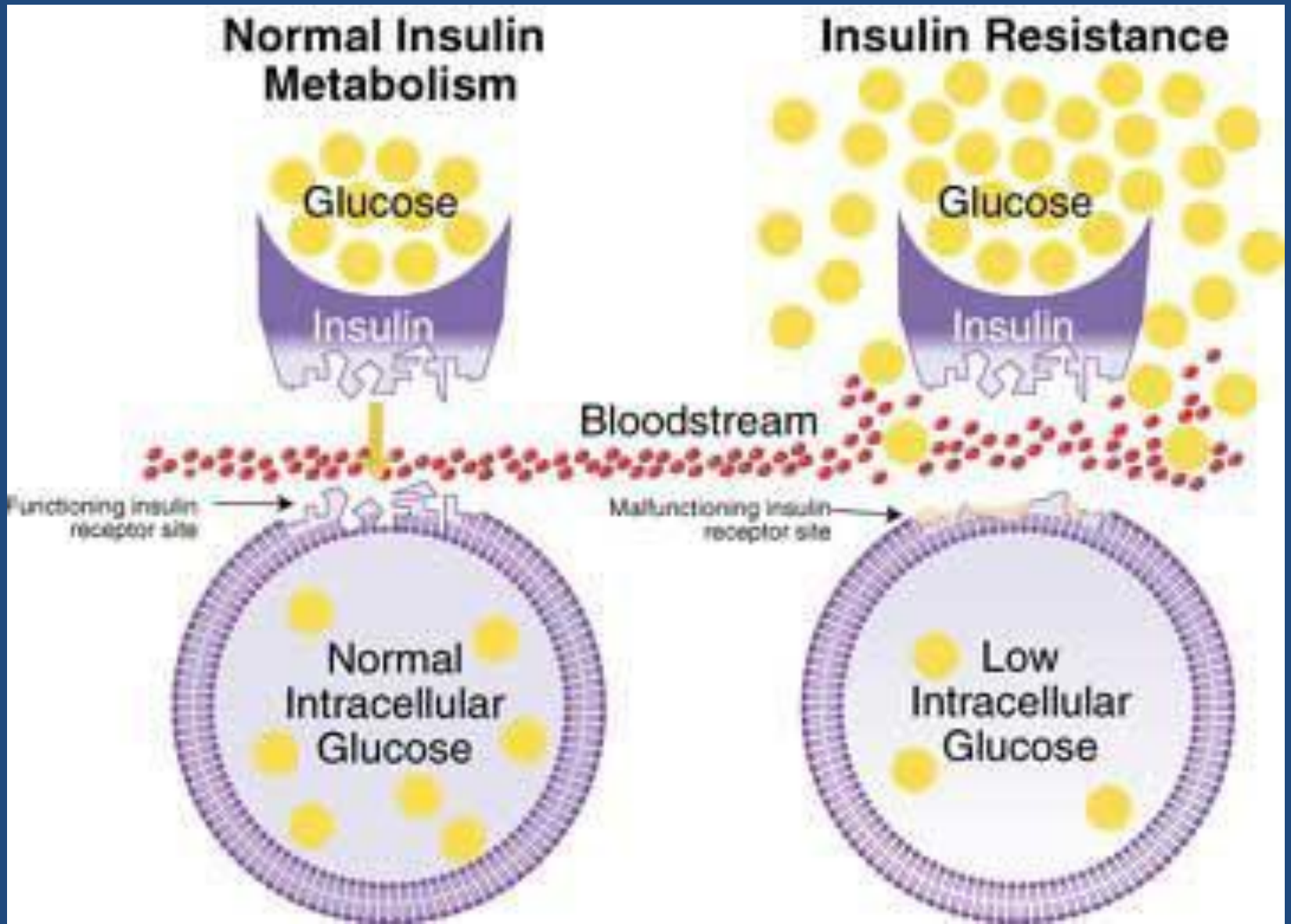
- Sex Hormone Binding Globulin
- Increased level = lower free estrogen
  - Maintain a healthy weight
  - Vegetarian lower fat diet
  - Improve Insulin Sensitivity



Blood Sugar Regulation



Insulin Resistance



Insulin Resistance

- Women with higher levels of insulin were 2.5 x more likes to have breast cancer over the next 7 years than women with the lowest insulin levels
  - 800 women without diabetes
  - not taking estrogen
    - J. Natl. Cancer Inst. 101:48, 2009.

Diabetes Care 33:1304, 2010.

Insulin Resistance

- Abdominal weight gain
- Fatigue
- Feeling tired after a meal
- Harder time losing weight
- Cravings for foods
- Hot Flashes
- Energy Swings
- Low blood sugar

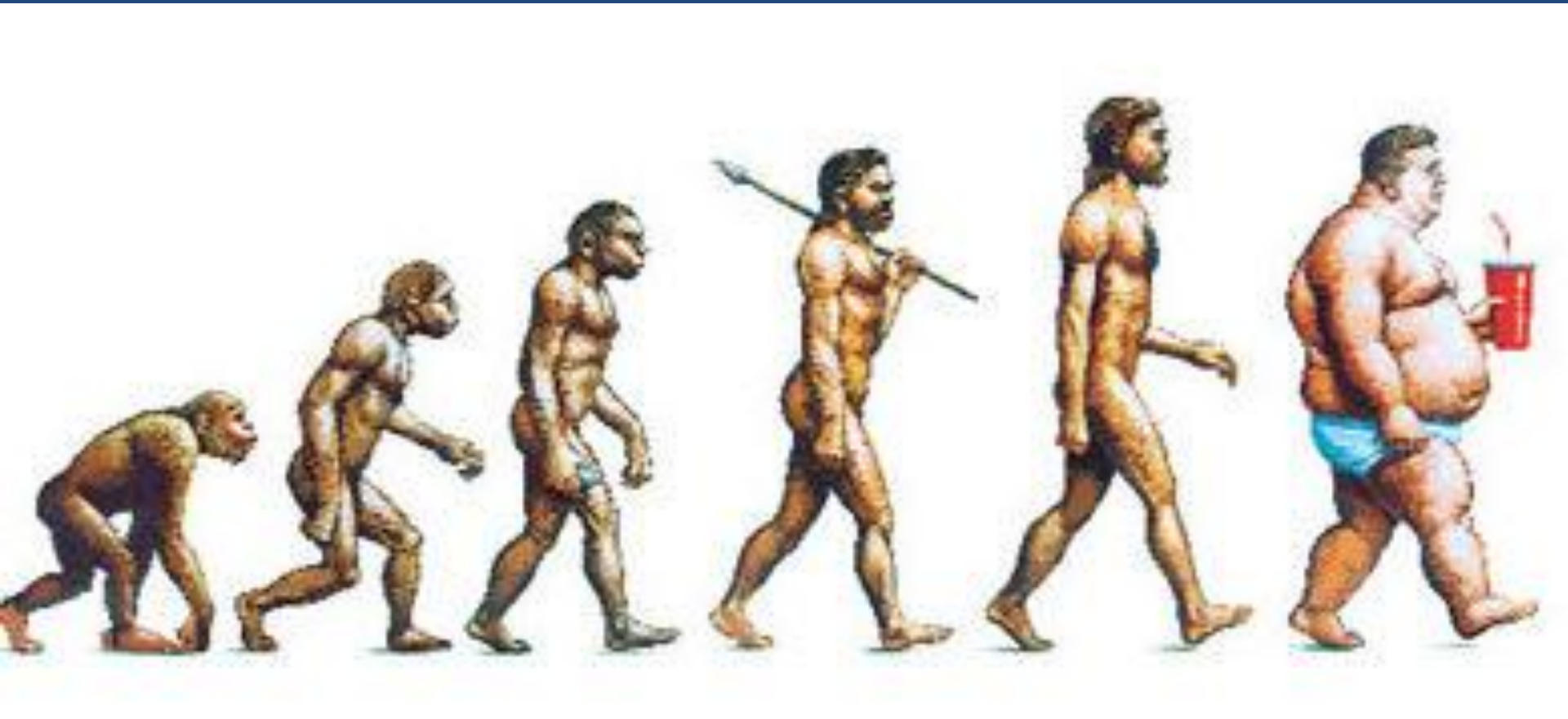
Who Is At Risk?

- **Epidemic**
  - 5% of children
  - 34% of adults over age 20
  - 51% of people over age 60

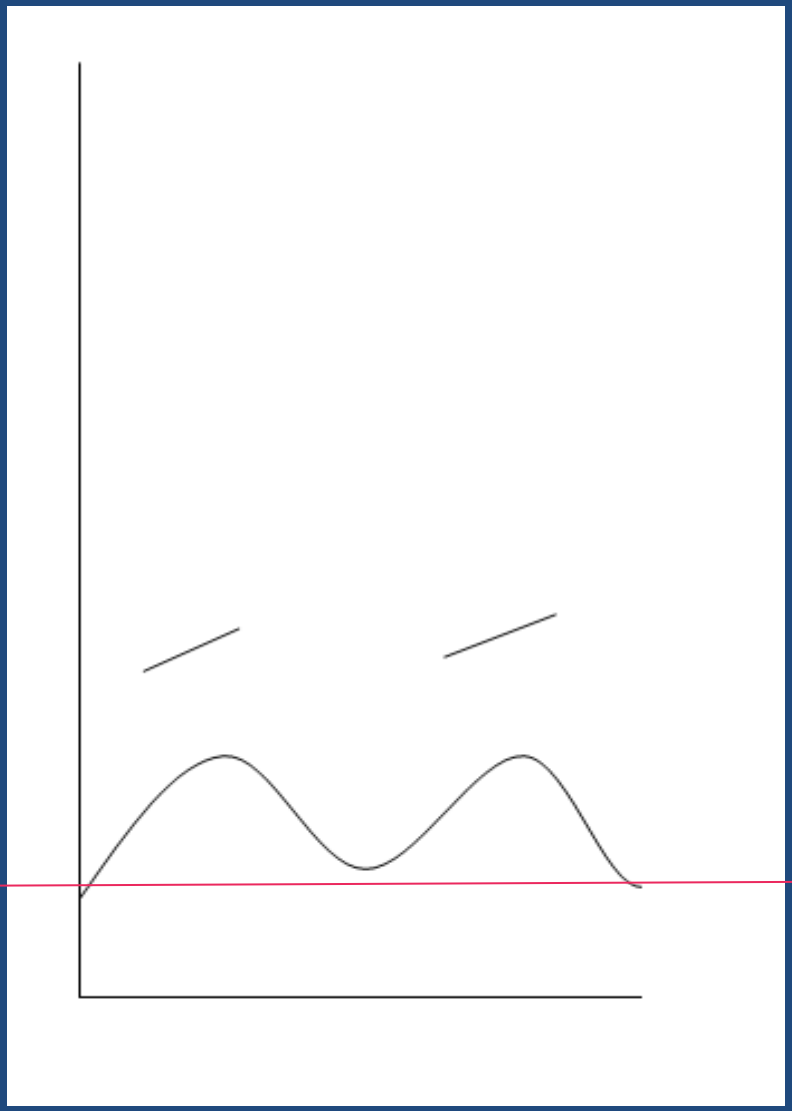
    National Health Statistics Report, CDC. No 13, May 2009

- **Lifestyle**
  - Weight gain
  - Poor Diet
  - Lack of exercise
  - Stress
  - Sleep deprivation
  - Dysbiosis
  - Toxin

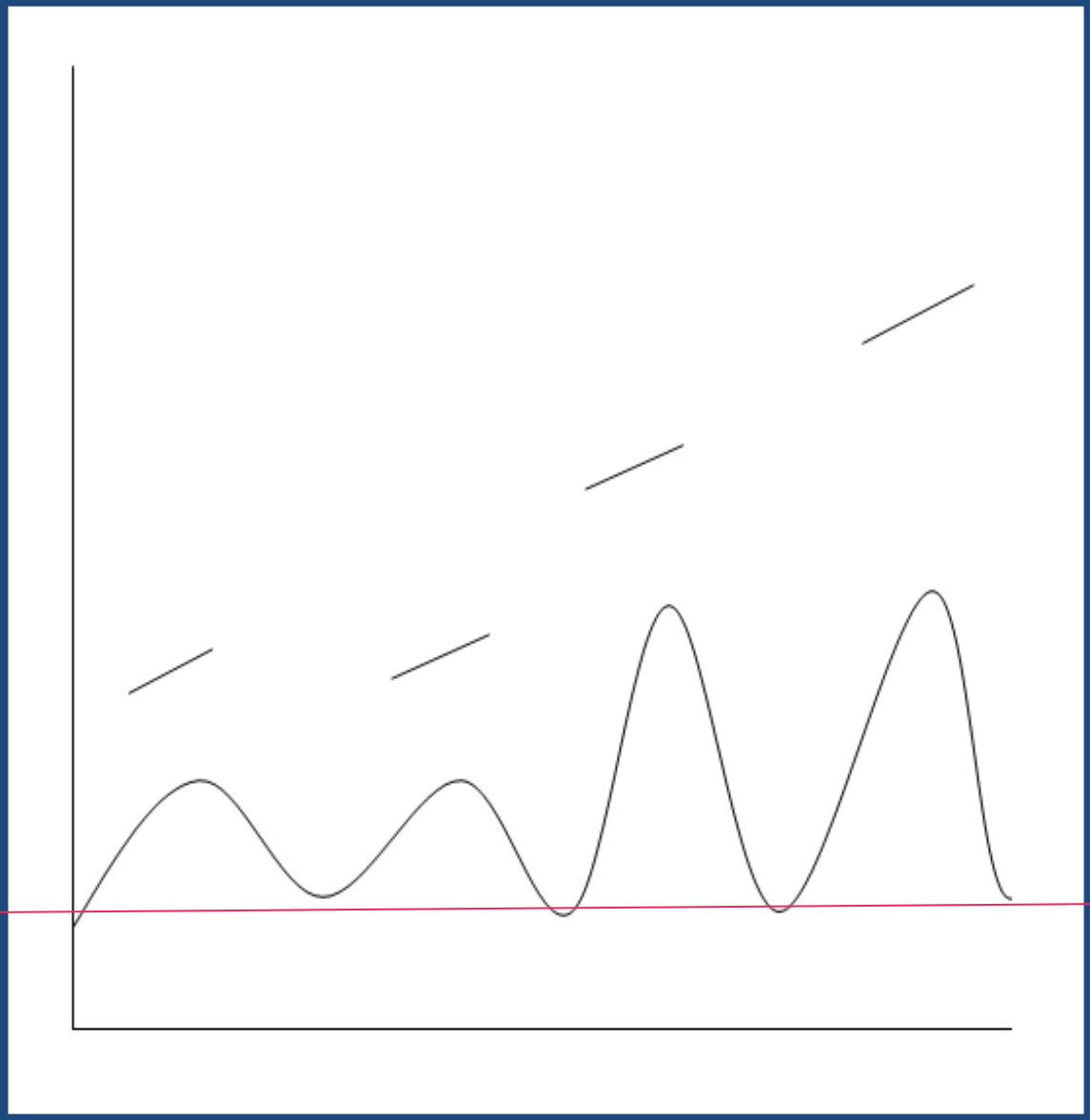
Our Genes Haven't Changed, But Our Environment Has…



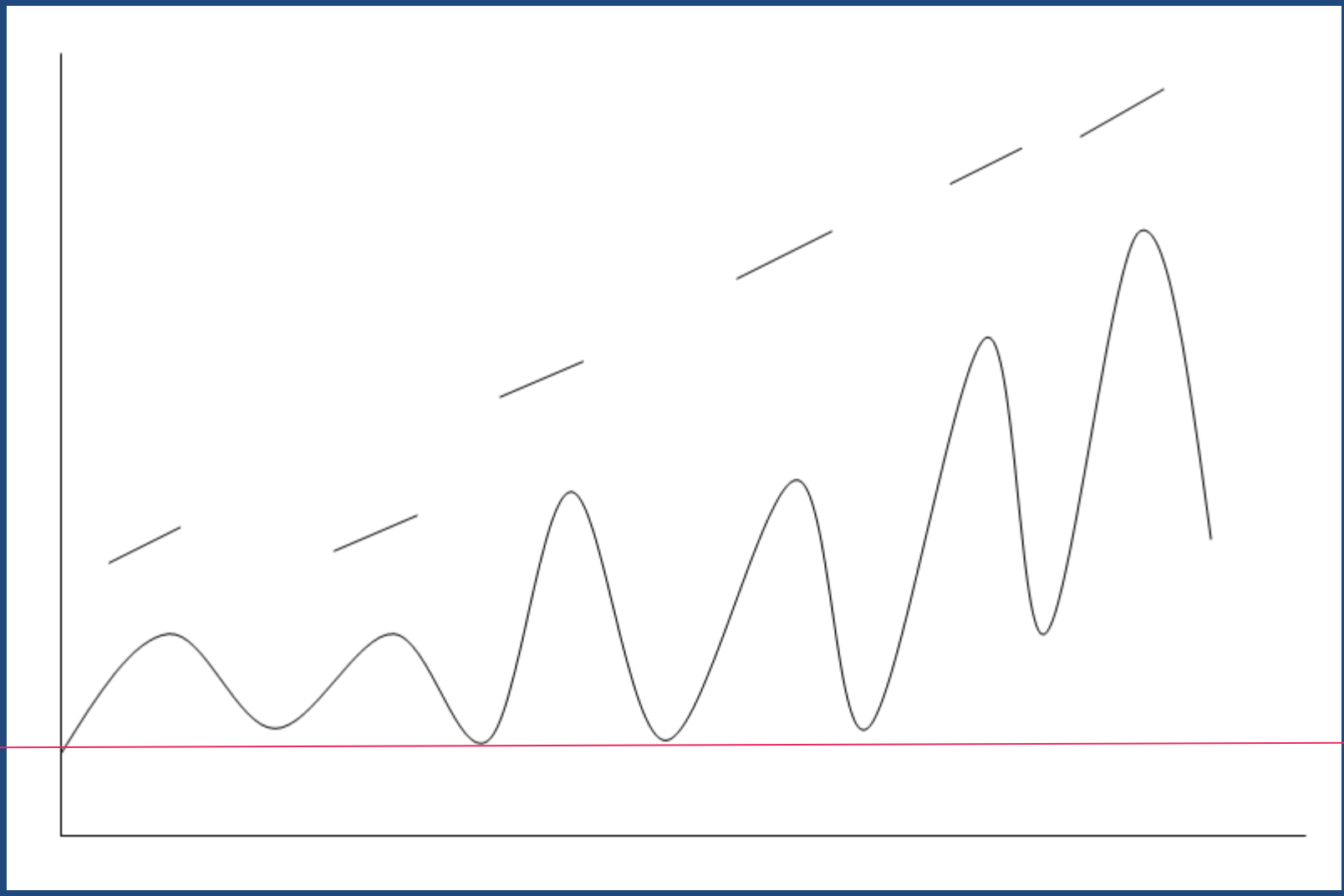
Normal blood sugar and insulin levels



Insulin Resistance



Normal → Insulin Resistance → Diabetes



METABOLIC SYNDROME

3 out of the 5

1. Impaired glucose tolerance –
   - fasting blood sugar > 100 or high insulin
2. Elevated blood pressure
   - >130/85 or on medication
3. Central Obesity = Apple shape
   - Waist circumference >35” women
   - Waist / Hip ratio > .80 women
4. Elevated Triglycerides > 150
5. Low HDL < 50 women

How Can I Improve Insulin Sensitivity?

- Increase fiber - 35 grams daily
- Protein - at each meal
- Regular Meals
- Increase omega 3 fats
- Eliminate Trans fats (partially hydrogenated fats)
- Nutrient dense foods
- 40 minutes of exercise daily
- Get 7-9 hours of sleep per night
- Manage stress

Glycemic Load Linked To Breast Cancer Risk

- *61,000 women over 17 years*
- *Highest Glycemic Load had about 80% increased risk of getting ER+ breast cancer*

Int J Cancer 2009;125:153-157.

ESTROGEN METABOLISM

- 2 OH Estrone - protective
- 4 OH Estrone - promote tissue proliferation and carcinogenic
- 16 OH Estrone - promotes tissue proliferation and carcinogenic

- 2/16 ratio > 2 optimal

Improve Estrogen Metabolism

- Increase cruciferous vegetables
  I3C and DIM and Sulforaphane
- Fish oil
- Daily exercise
- Ground flax seed
- Healthy soy

Our Genes

- BRCA 1 and 2

- COMT
- CYP1B1
- GSTM1
- MTHFR

DETOXIFICATION

- Phase I - certain people have higher risk
  - Avoid Estrogen Disrupters
  - Avoid Cigarette smoke
  - Decrease Charbroiled Meats - Heterocyclic aromatic amines
  - Limit Alcohol

ALCOHOL

-As alcohol intake increases so does our risk

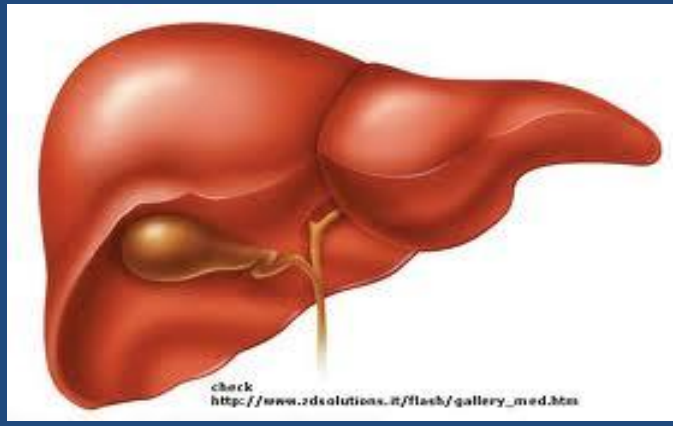
-For every 1 drink increase per day, a women's risk of getting breast cancer increased by 12%

J Nat Cancer Inst.2009;101:296-305

- >2 drinks per day = 3x increased risk
- Annals of Int Medicine 11/02.

ALCOHOL - Why?

- Liver and detox impact
- Increase free estrogen
  - by decreasing SHBG
- Associated with other unhealthy lifestyles
- Decrease B vitamins
  - important for methylation



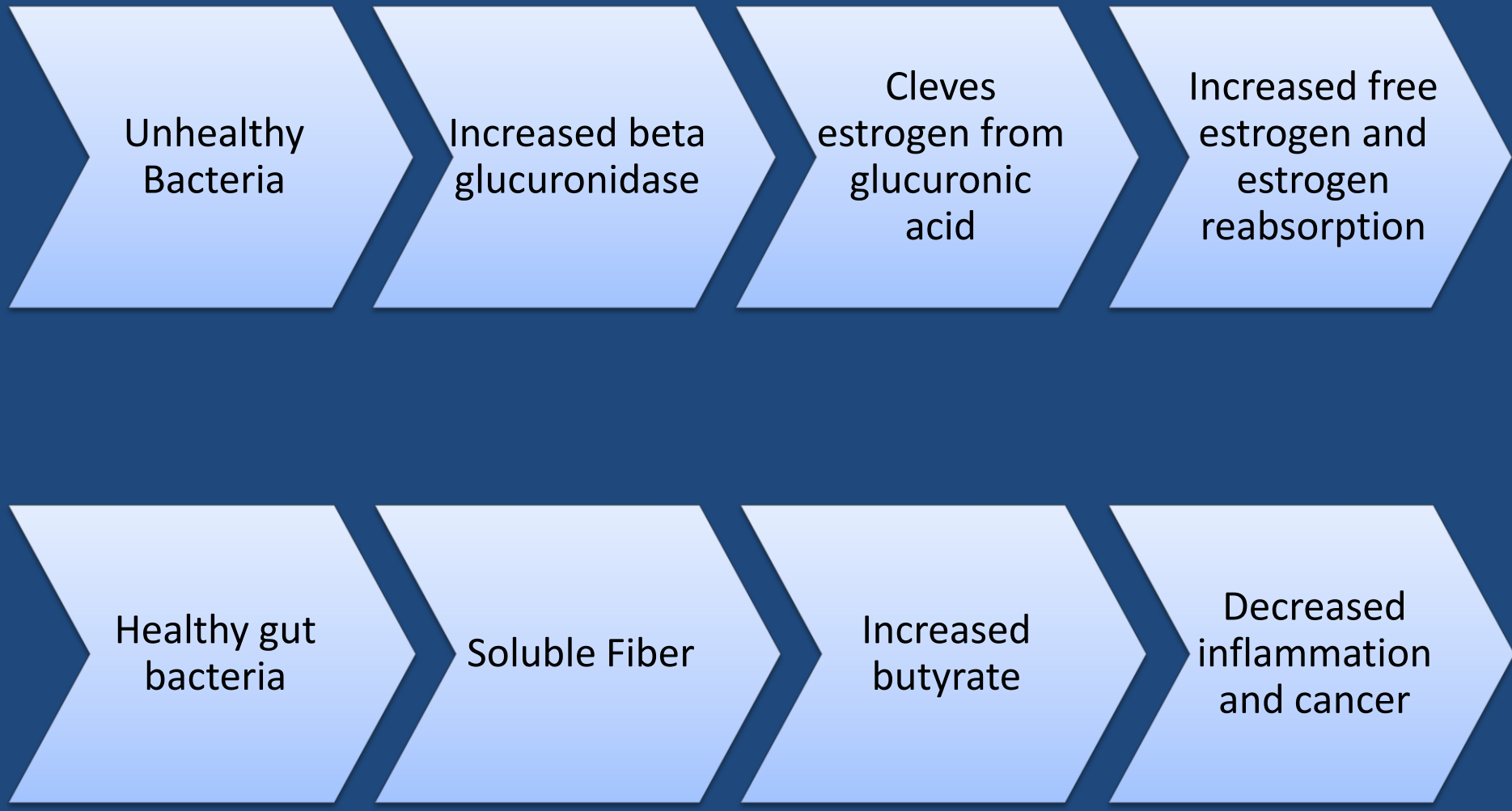
DETOXIFICATION

- Phase II
  - Methylation
    - Need adequate folate, B12, B6
    - Alcohol increases B vitamin needs
    - Genes - MTHFR
    - Check homocysteine
    - Methylmalonic acid
  - Sulfation
    - Cysteine ---- glutathione
  - Glucuronidation
    - Calcium d glucurate
    - 1000mg 2x day

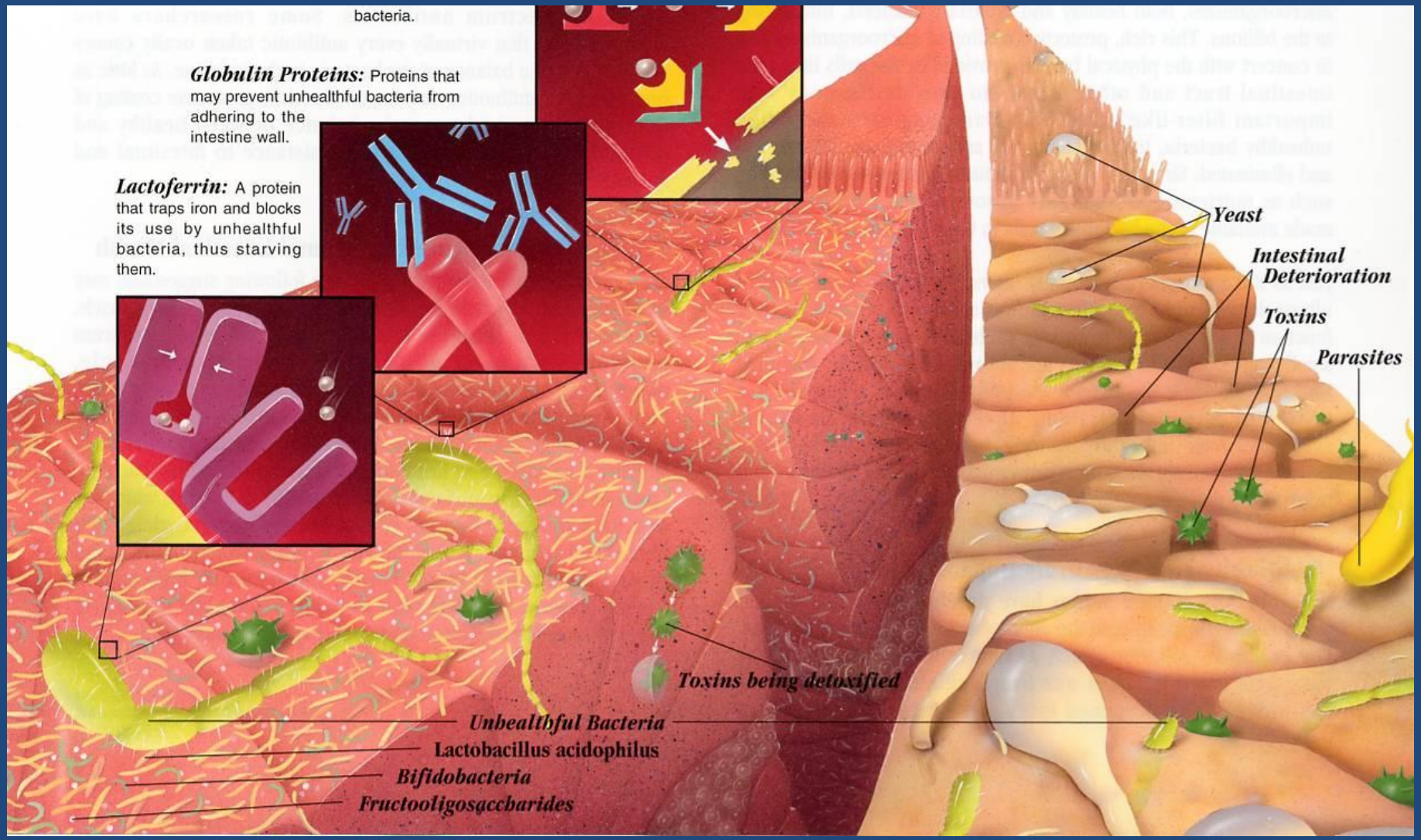
Glucuronidation

- Glucuronic Acid conjugates with estrogen
- E-GA - excreted in the stool

- Beta glucuronidase - cleave E-GA and increases free estrogen
- Beta glucuronidase is elevated:
  - high meat / low fiber diets
  - Imbalanced gut flora
  - Pathogenic gut flora


Unhealthy Bacteria
Increased beta glucuronidase
Cleves estrogen from glucuronic acid
Increased free estrogen and estrogen reabsorption
Healthy gut bacteria
Soluble Fiber
Increased butyrate
Decreased inflammation and cancer

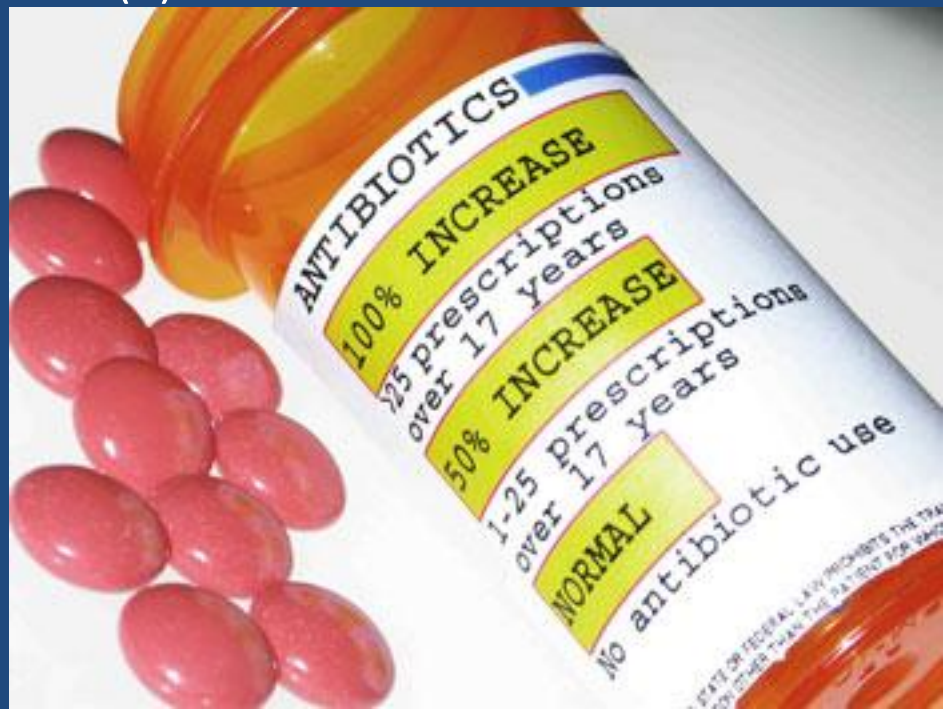
Gut Microbiome



Antibiotics and Breast Cancer

- 17 year period -
  - > 25 scripts -- 2 x increased risk
  - 1-25 scripts --- 1.5 x increased risk
    - Int. J Cancer 2008. Nov 1: 123(9):2152-5.

- Immune system ?
- Damage to Gut



Heal The Gut

- Limit Antibiotic Use
- High Fiber Diet
- Decrease Red meat - <18 oz/wk (AICR)
- Probiotics
- Nutrients
- Remove inflammatory foods
- Treat infections

Increase Inflammation = Increase Cancer

Coussens LM, Werb. Inflammation and Cancer. *Nature* 2002; 420:860-7.

<u>Signs of Inflammation</u>

Increased CRP
Increased ESR
Water retention
Bloating
Joint Pain
Asthma
Eczema
Digestive Distress
Abdominal weight gain…

hsCRP

- hsCRP is a better marker than stage of disease

- < 1.0 40% alive after 3 years
- >1.0 none survived

- Associated with increased angiogenesis, invasion, metastasis

- McMillan DC, etal. Nutr Cancer. 2001;41(1-2):64-69.

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Baseline C-Reactive Protein Is Associated With Incident Cancer and Survival in Patients With Cancer

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From the Department of Clinical Biochemistry, Herlev Hospital, and The Copenhagen City Heart Study, Bispebjerg Hospital, Copenhagen University Hospital; and Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark.

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Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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The Appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF version (via Adobe® Reader®).

0732-183X/09/2713-2217/$20.00

DOI: 10.1200/JCO.2008.19.8440

ABSTRACT

Purpose

We tested the hypothesis that baseline plasma levels of C-reactive protein (CRP) are associated with risk of incident cancer in the general population and early death in patients with cancer.

Patients and Methods

A total of 10,408 individuals from the Danish general population who had CRP measured at baseline were observed for up to 16 years; 1,624 developed cancer, and of these, 998 patients died during follow-

diagnosis at baselin

Results

Baseline CRP level

adjusted hazard rat

for lung cancer, 1.9

cancer. Correspond

levels were 1.3 (95%

CI, 0.5 to 1.7), resp

cancer were 1.8 (95

CI, 1.1 to 1.7) for the

early death in patie

(interaction; P = .0

Conclusion

Elevated levels of C

type, of lung cance

CRP associate wi

without metastase

J Clin Oncol 27:22

Elevated levels of CRP in cancer-free individuals are associated with increased risk of cancer of any type, of lung cancer, and possibly of colorectal cancer. Moreover, elevated levels of baseline CRP associate with early death after a diagnosis of any cancer, particularly in patients without metastases.

J Clin Oncol 27:2217-2224. © 2009 by American Society of Clinical Oncology

INTRODUCTION

C-reactive protein (C

that is elevated during

tory disease, trauma,

and cancer[1]; CRP is pr

to elevated cytokine

stimulus.[2] Two hypotheses have been proposed to explain the relationship between elevated CRP levels and cancer.[3] The first hypothesis states that elevated CRP levels are a result of an underlying cancer or a premalignant state, whereas the second hypothesis states that chronic inflammation and elevated CRP might have a causal role in carcinogenesis.

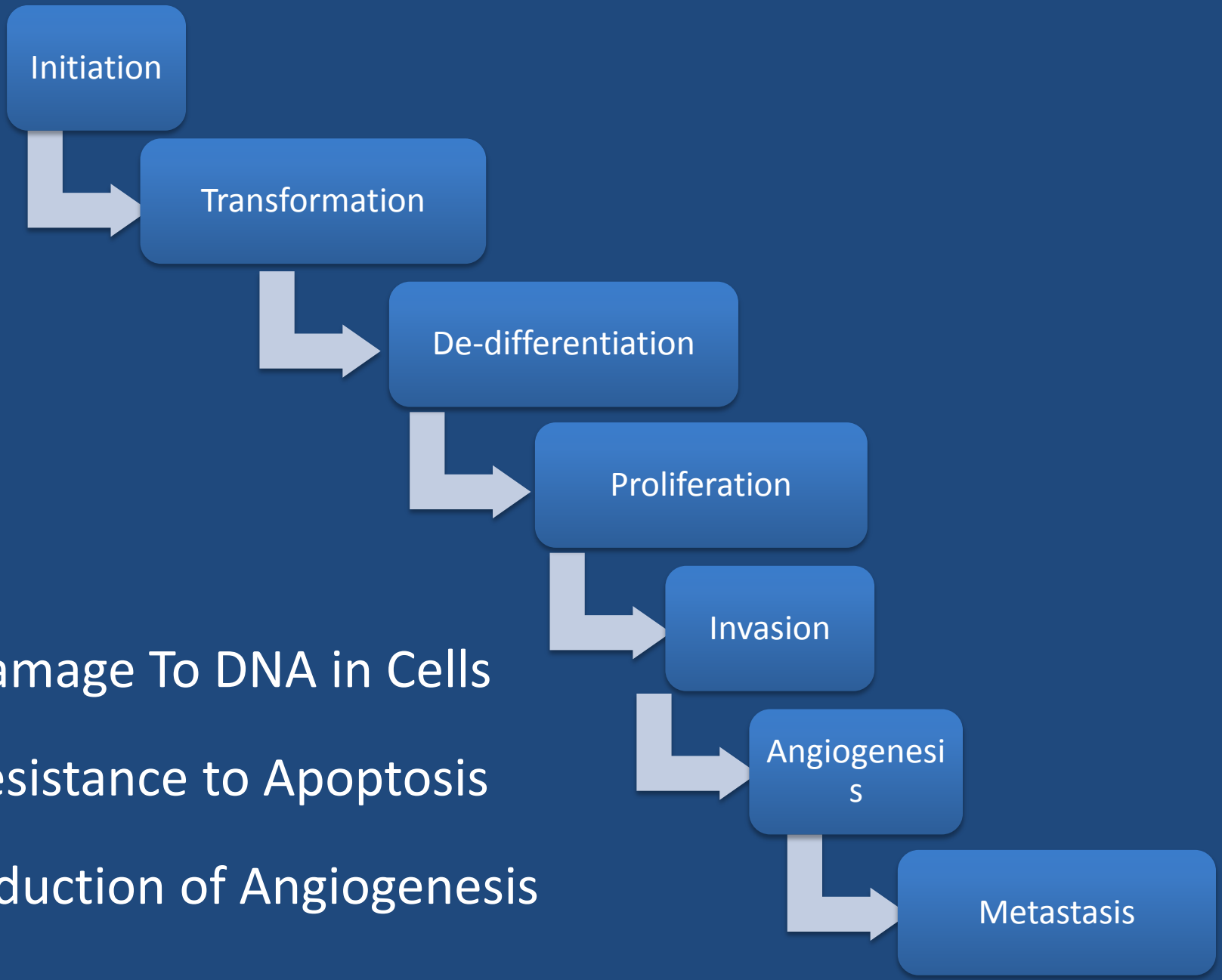
Case-control studies have reported higher levels of CRP in patients with cancer compared with controls,[3] whereas results from prospective studies are conflicting, with some studies suggesting that CRP is not merely a marker of prevalent cancer, but poor survival in patients with cancer[4-6]; however, in only two of these studies including few participants were CRP measured with a high-sensitivity assay,[7,19] allowing examination of associations in the high-normal interval just greater than 1 mg/L. Thus it is still unclear whether, and to which extent, CRP levels are associated with incident cancer as well as early death in patients with cancer.

We tested the hypothesis that baseline plasma levels of CRP in the general population are associated with risk of incident cancer, including the three

Chronic Inflammation: A Common and Important Factor in the Pathogenesis of Neoplasia

Recurrent or persistent inflammation may induce, promote, or influence susceptibility to carcinogenesis by causing DNA damage, inciting tissue reparative proliferation, and/or creating a stromal "soil" that is enriched with cytokines and growth factors. Future research on the complex cascade of cellular and humoral factors participating in the chronic inflammatory process will further understanding of the pathogenesis of various cancers and potentially provide a rationale for targeted chemopreventive interventions.

David Schottenfeld, MD, MSc; Jennifer Beebe-Dimmer, PhD, MPH
CA Cancer J Clin 2006;56:69–83



+Damage To DNA in Cells

+Resistance to Apoptosis

+Induction of Angiogenesis

STOP Progression To Cancer

- 30-50% of healthy women aged 40-50 premalignant microscopic breast tumors on autopsy.
  - Black WC, Welch HG. Advances in diagnostic imaging and overestimations of disease prevalence and the benefits of therapy. *N Engl J Med* 1993;328:1237-43.

- Some tumors regress

- Unhealthy Soil:
  - high insulin, sugar, omega 6, IGF milk and meat
- Healthy Soil
  - Phytonutrients, low inflammation, high omega 3, green tea, beta glucans

Decrease Inflammation

- Avoid refined and processed foods
- Decrease % Body Fat
- Increase Omega 3 fats
- Decrease Omega 6 and saturated fats and eliminate trans fats
- Turmeric, resveratrol, ginger and green tea
- Decrease stress and increase sleep

Int.J. Behav. Med.
DOI 10.1007/s12529-010-9079-8

Effects of a Weight Loss Intervention on Body Mass, Fitness, and Inflammatory Biomarkers in Overweight or Obese Breast Cancer Survivors

Bilgé Pakiz · Shirley W. Flatt · Wayne A. Bardwell · Cheryl L. Rock · Paul J. Mills

Abstract

Background Obesity is characterized by chronic mild inflammation and may influence the risk and progression of cancer.

Purpose The current study is an exploratory analysis of the effect of a weight loss intervention that emphasized increased physical activity on inflammatory cytokines (tumor necrosis factor-α [TNF-α], interleukin-6 [IL-6], interleukin-8 [IL-8], and vascular endothelial growth factor [VEGF]) at the end of the 16-week intervention period in overweight breast cancer survivors.

Methods Study participants averaged 56 years of age (N=68). Intervention participants (n=44 vs. 24 controls) participated in a cognitive behavioral therapy-based weight management program as part of an exploratory randomized trial. The intervention incorporated strategies to promote increased physical activity and diet modification. Baseline and 16-week data included height, weight, body composition, physical activity level, and biomarkers IL-6, IL-8, TNF-α, and VEGF.

Results Weight loss was significantly greater in the intervention group than controls (−5.7 [3.5] vs. 0.2 [4.1] kg, P<0.001). Paired t tests noted favorable changes in physical

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Published online: 19 February 2011

for second primary cancers, and comorbidities, such as diabetes, cardiovascular disease, and osteoporosis, are issues that need to be considered in long-term management of these women [3, 4].

Overweight or obesity is a negative prognostic factor in both pre- and postmenopausal breast cancer [5, 6], and it is increasingly being recognized as a medical condition that is characterized by chronic mild inflammation [7]. Several

Effects of a Weight Loss Intervention on Body Mass, Fitness, and Inflammatory Biomarkers in Overweight or Obese Breast Cancer Survivors

Favorable changes in cytokine levels were observed in association with weight loss in this exploratory study with overweight breast cancer survivors.

Pakiz B, etal. Int J Behav Med 2011 Feb 11.

Phytochemicals

Phytochemicals - plant metabolites that defend against microbes

- Organic has more phytochemicals -- Stress
- Increase host defense against DNA damaging molecules. Reduce oncogenic potential of carcinogens.
- Cruciferous vegies, Cucumin, Resveratrol have pro-apoptotic activity against cells
- Anti-Angiogenesis - Green tea - >3 cups, Raspberries, Strawberries and Blueberries
- Pomegranate – ellagic acid – prevents proliferation and blocks VEGF

8 - 10 1/2 cups per day

STRESS!

STRESS – Increased Cortisol

- Decreased SHBG -- increased free estrogen
- Increased insulin resistance and abdominal fat
- Increased IL-6 - inflammatory cytokine
    - Increased Inflammation = Increase Cancer Risk
- Lower NK (natural killer) cell activity
  - NK cells find and kill new cancer cells
    - Stronger a women's NK cell activity is the higher rate of survival from breast cancer after 12 years
      - Head JF. Assessment of Immunologic Competence and Host Reactivity Against Tumor Antigens In Breast Cancer Patients. *Annals of the NY Acad of Sciences* 690(1993)340-42.
    - Increased Social Support = Increased NK activity

Tumor rejection in rats after inescapable or escapable shock.

Visintainer, Madelon A.; Volpicelli, Joseph R.; Seligman, Martin Science. Vol 216(4544), Apr 1982, 437-439.

- Rats with cancer cells grafted to cause 50% to die
- 3 groups
- Shock and no control - 27% rejected tumor
- No electric shock - 54% rejected tumor
- Electric shock but had a lever to stop it - 63% rejected the tumor

Sleep

SLEEP

- Sleep deprivation =

Cortisol and Insulin

NK cells and melatonin

Melatonin = Anticancer and antioxidant effects

EXERCISE

How Much?

- 4 hrs per week = less risk
- 3-5 hours per week = improved survival for women who have had breast cancer
- Vigorous exercise + BMI < 25
  - 20% decreased risk

JAMA – 2005
Breast Ca Research 2008

DIET

- Reduced calorie diets = reduced risk
  - Oxidative Stress
- High fiber, low fat diets = decreased estrogen in body
- High fat diet - increased reoccurrence ER- cancer

WINS - Women Intervention Nutrition Study

- Soy in adolescents = lower risk
- Green tea - ECGC - anti-angiogenesis and antioxidant

Supplements

- Vitamin D -
  - 25OH vit D > 52 = 50% decreased risk breast cancer than if vit D <12ng/dl
  - Garland etal. AACR 2006
- Probiotic
- DIM / I3C
- Sulforaphane
- Calcium d glucurate
- Fish oil – 1000mg EPA + DHA
- B vitamins

1/3rd of all cancers can be prevented…at least!

- Exercising Regularly
- Eating Healthy Foods with Increased Fruits and Vegetables
- Maintaining a Healthy Weight
  - Decrease breast cancer by 38%

- Policy and Action for Cancer Prevention - Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective. 2007 WCRF / AICR

Government Role

- Increase Availability of Farmer's Markets
- Increase Bike Lanes and Walking Paths
- Get Rid of Vending Machines in Schools
- End Advertising of Junk Food To Kids
- Take High Fructose Corn Syrup out of products
- Ban Trans Fats
- Decrease toxic chemicals allowed in our environment.

What Can We Do?

- Choose Whole Foods
- Get 3-5 hours of Exercise Per Week
- Increase Fiber Intake to 35gm daily
- Have Protein at Every Meal - include vegetarian options - beans, nuts as well as fish, lean poultry and eggs.
- Maintain a Healthy Weight

What Can We Do?

- Get a Good Night Sleep
- Choose Organic Foods
- Avoid Excess Toxins
- Take Probiotics
- Limit Your Alcohol Intake
  - <1 drink per day or 5 per week.

THANK YOU !

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