



UNIVERSITY OF
ARKANSAS
— THE YOU OF A —



Stress and Breast Cancer

Ro DiBrezza

Director, Human Performance Lab

2010 Advances in Breast Cancer Research

National Science Foundation

University of Arkansas

October 26-29

Outline



- A few stats
- Stress – for better or for worse
- Cortisol – stress – breast cancer
- What can we do...if anything
- Our research

You might not know...



- About 1,970 new cases of invasive breast cancer will be diagnosed in **men** in 2010
- More than 1 in 4 cancers in women (about 28%) is breast cancer
- 70-80% of breast cancers in women are due to genetic abnormalities, rather than from hereditary causes
- White women are more likely to be diagnosed than African American women, but are less likely to die from it
- Women of other ethnic backgrounds have lower incidences
- In 2010, there are more than 2.5 million breast cancer survivors in the U.S.

Good News – Bad News



Although incidence rates have been decreasing since 1991, in 2010 there will still be roughly 262,000 women diagnosed with breast cancer and nearly 40,000 will die from it.

Risk Factors



- The good:
 - Having children and breast-feeding
 - Pregnancy before age 30
 - Physical activity and exercise
- The not so good:
 - Alcohol
 - Overweight and obesity
 - Hormone therapy after menopause
 - Stress ????

What is Stress?



- Stress: any disruption to homeostasis
- Non-specific response of the body to any demand for change
 - Body does not differentiate between physiological and psychological stress
 - Different people have different reactions to same stimulus
- Estimated that 75-90% of primary care physician visits are for stress-related problems



G.A.S.

Alarm

Resistance

Exhaustion

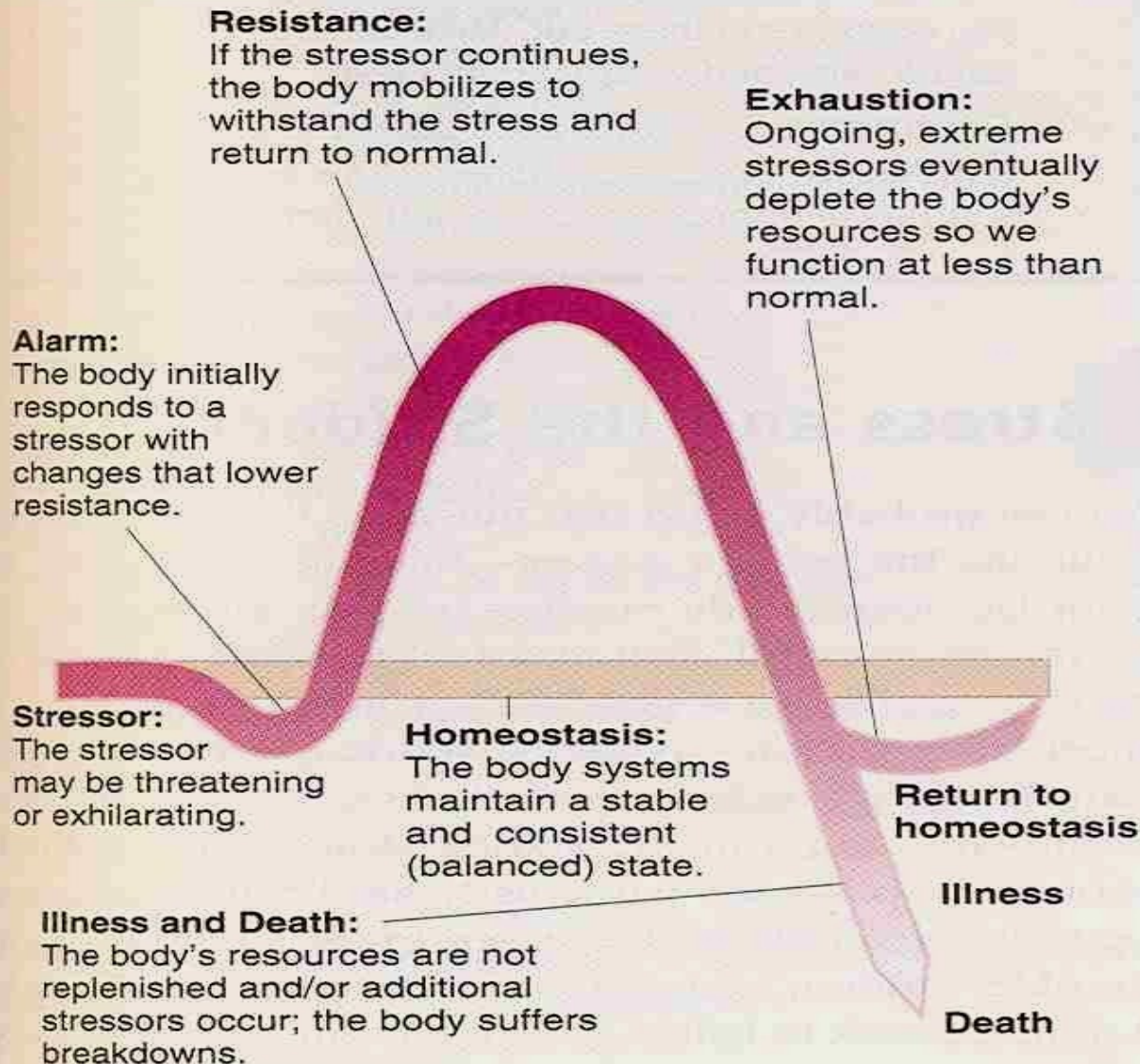


Figure 2-1 The three stages of Selye's General Adaptation Syndrome (GAS): Alarm, resistance, exhaustion.

Measuring Stress



- **Perceived Stress Scale (PSS)**
 - 10 questions inquiring, “In the last month, how often have you...”
 - Rated from never to very often (0-4)
 - Most common for measuring perceived stress
- **Social Avoidance and Distress Scale (SADS)**
 - 28 True/False questions
 - Developed to quantify social anxiety
 - Copyright of test held by the American Psychological Association

Measuring Stress (cont'd)



- **Trier Social Stress Test (TSST)**
 - Standardized protocol for inducing moderate psychosocial stress in a laboratory
 - Perform 5 minute speech and 5 minutes of mental arithmetic in front of an audience
- **Impact of Events Scale (IES)**
 - Questionnaire related to a specific stressful life-event
 - “How many times in the last 7 days have you...” had thoughts/memories about the event, from not at all to often

Studies Showing Relationship Between Stress and Cancer

Principle Researchers:	Stressor:	Results Found:
Ollonen et al., 2005.	Reviewed stressors of breast cancer patients and patients with benign breast disease over previous 10 years.	Higher incidence of breast cancer in those with more very stressful events and more losses.
Kruk & Aboul-Enein, 2004.	Women with major life events, stress of daily activity, and depression.	“3.7 times higher risk for BC, compared to those who did not experience such stress.”
Levav et al., 2000.	Parents of accident and war-victims	Increased risk of respiratory, uterine, and ovarian cancers

A Prospective Study of the Relationship Between Breast Cancer and Life Events, Type A Behavior Social Support and Coping Skills

-Cooper et al. 1986

- 2163 Women three groups
 - Diagnosed with breast cancer
 - Benign breast cysts
 - Normal breasts
- Women diagnosed with breast cancer
 - Experienced **fewer** stressful life events in total
 - Rated the events to be **more** stressful
 - Showed **fewer** coping skills

A Prospective Study of the Relationship Between Breast Cancer and Life Events, Type A Behavior Social Support and Coping Skills

A pink ribbon graphic is positioned in the upper right corner of the slide, symbolizing breast cancer awareness. The ribbon is tied in a loop and has a slight 3D effect with shadows.

-Cooper et al. 1986

- Women statistically treated for other variables like income, age, etc.
 - Larger proportions of widowed women in the cancer group relative to remaining groups
 - All loss and illness-related events were perceived as much more severe by the cancer group
 - Evidenced by coping skills and type A behavior scores
- According to the authors:
 - Clear mathematical relationship between stress and breast cancer
 - An even clearer link between breast cancer, perception of stress, and the ability of an individual to cope with stress

Allostatic Load



- Allostatic load:
 - Environmental challenges that cause an organism to begin efforts to maintain stability
 - Costs that the body's physiological systems make to maintain homeostasis during a stressor
- Allostatic load is typically determined using ten or more different physiological measures
- As stress increases so does the allostatic load

Hypothalamic-Pituitary-Adrenal Axis

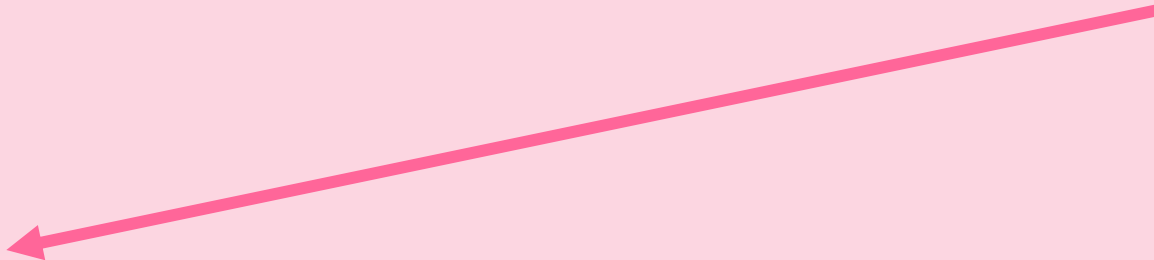
(wow that sounds scientific)



Stress triggers release of CRH from the hypothalamus in the brain



Blood stream to pituitary gland



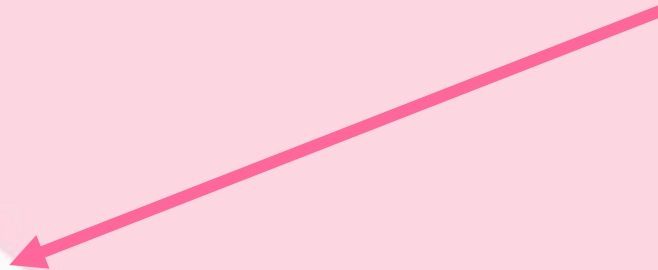
ACTH



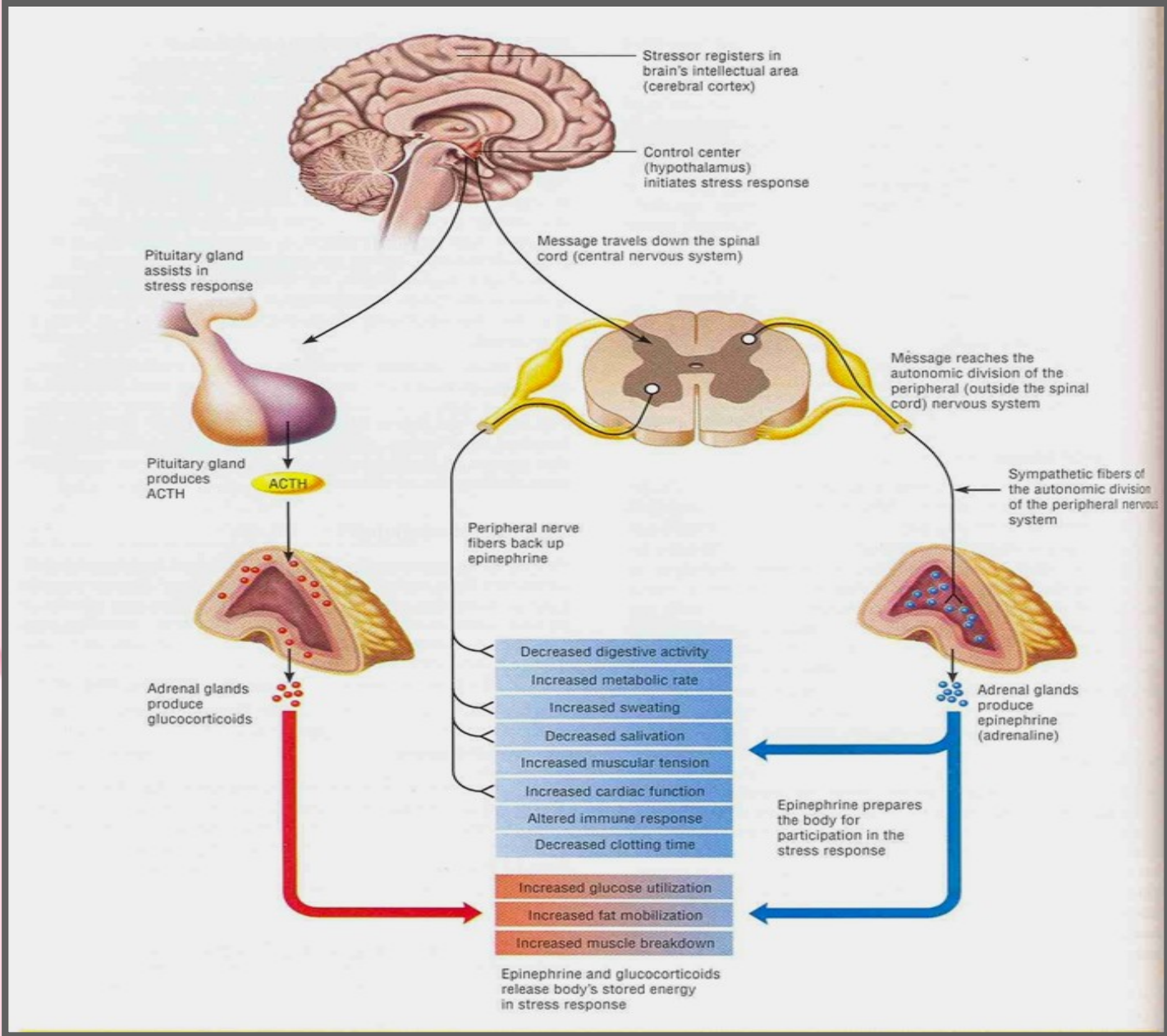
Bloodstream

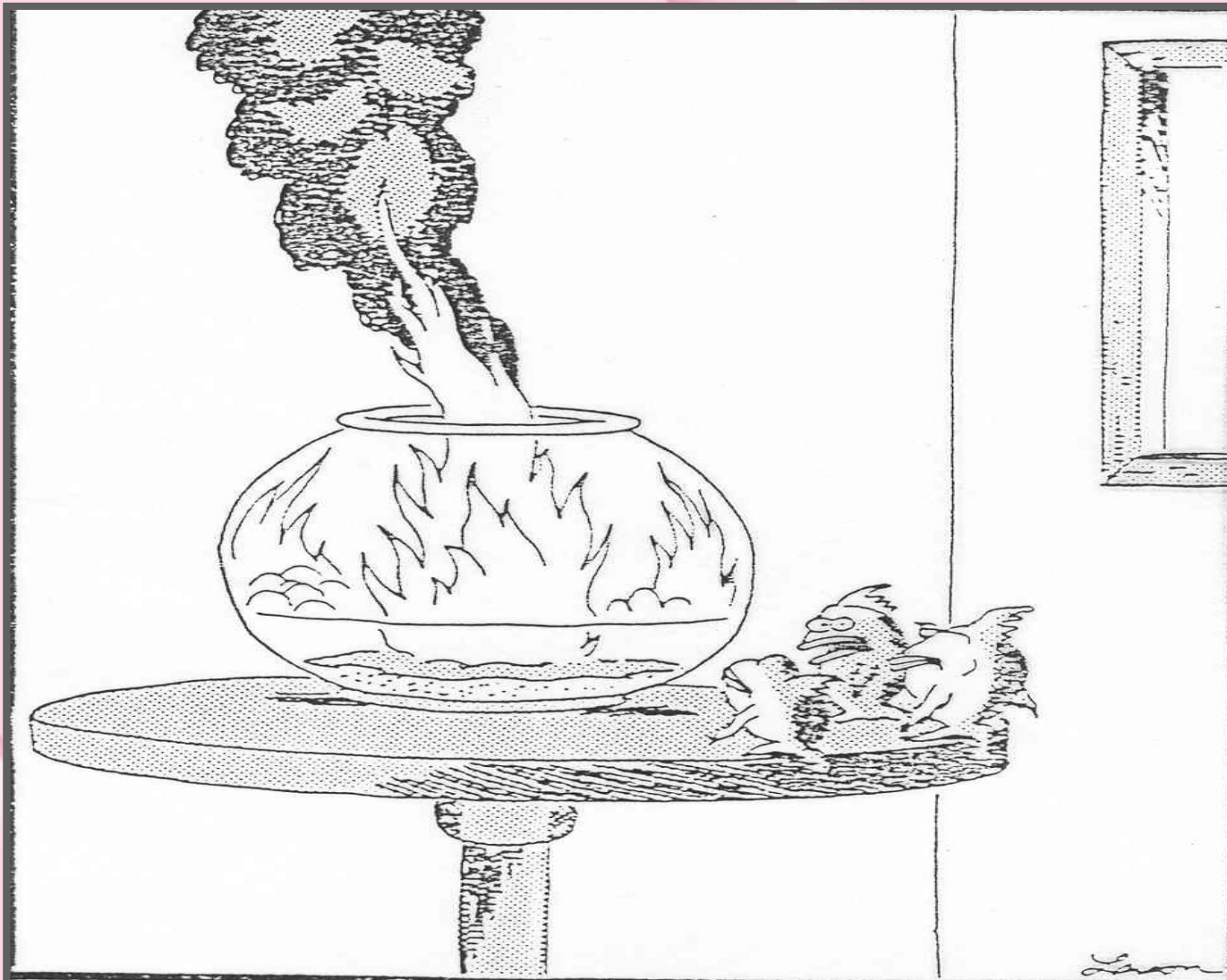


Adrenal glands



Releases cortisol





"Well, thank God we all made it out in time.
... 'Course, now we're equally screwed."



Stress Hormones



- Cortisol and Norepinephrine
- Measured as individual components of stress response or collectively to gauge activation at different levels along HPA axis
- Cortisol is easily accessible
 - Measured in urine, plasma, and saliva

Good Guy :

- Increases glucose levels
- Increases O₂ supply to skeletal muscles and heart
- Suppresses immune and digestive function to conserve energy
- Fights infection
- Wound healing

Bad Guy:



The Good Continues



- Cortisol limits inflammation via
 - Overproduction of anti-inflammatory cytokines
 - Shift between Th1 helper cell immunity and Th2 helper cell immunity
- Controlled inflammation is important because it:
 - Initiates healing of wounds
 - Reduces risk of infection
 - Prevents re-emergence of a latent virus
 - Creates hostile environment for developing tumor cells

Too Much of a Good Thing



- During stressful conditions
 - Overproduction of cortisol and norepinephrine
- Overproduction of stress hormones
 - Compromise the immune system's ability to eliminate everything from the common cold to a tumor cell

Effects of Stress

(caused or aggravated by)



- Cardiovascular disorders:
 - Raises blood serum levels
 - Coronary artery disease
 - High blood pressure
- Musculoskeletal disorders:
 - Back pain
 - Rheumatoid arthritis
 - Migraine headache

Effects of Stress (cont'd)



- Metabolic disorders:
 - Hyper/hypo thyroidism
 - Diabetes
- Impairs immune system resistance to viral-linked disorders
- Obesity
 - Leptin produced in fat cells

Tumor Progression and Relapse

A pink ribbon symbol, commonly used for breast cancer awareness, is positioned in the upper right corner of the slide. The background features abstract, flowing pink and white ribbons.

- No definitive evidence showing that stress initiates cancer
 - Evidence demonstrating stress increases the progression of tumors

(McKenna MC, Zevon MA, Corn B, et al. 1999; Glaser et al. 2005)

- Stress has also been indicated in higher incidences of relapse in breast cancer patients

(Ramirez AJ, Craig TK, Watson JP, et al. 1989; Spiegel and Sephton 2001)

Brief Review



Overproduction of cortisol and other stress hormones

1. Related to autoimmune abnormalities
2. Causes downregulation of the immune system's response to cortisol
 - Causes general, non-specific inflammation to remain unchecked and promote tumorigenesis

Immune System Abnormalities

A pink ribbon symbol is located in the top right corner of the slide, set against a background of soft, flowing pink and white ribbons.

- Overproduction of cortisol can:
 - Slow proliferation and maturation of T and B lymphocytes
 - Decrease number and cytotoxicity of natural killer (NK) cells
 - Both T and B lymphocytes and NK cells are effective at eliminating tumor cells
- Negative effects on cellular immunity limit the ability to remove newly developed tumors

Immune System Abnormalities (cont'd)



- Certain latent viruses are able to alter cell DNA and therefore able to generate tumor cells

(Marketon and Glaser 2008; Yang et al. 2010; Glaser and Kiecolt-Glaser 2005)

- Immunosuppression includes
 - Compromised effectiveness (decreased cytotoxicity)
 - Decreased cell numbers
 - Increasing the number of mutations that can occur
 - Increasing the chance of a tumor cell developing

(Fox 1988; Chrousos 2000; de Visser et al. 2006)

If stress is inevitable...
what can be done?



First: Exercise

Second: Exercise

Third: Exercise

Physiological Effects of Exercise



- The physiological effects of an exercise program have been well documented
- These benefits include:
 - Increased cardio function
 - Decreased blood pressure
 - Better blood lipid profile
 - Increased muscular strength and endurance
 - Increased fat-free mass

Cancer and Exercise



- Cancer is disease of mind, body and spirit, but a proactive and positive experience will help
- Strong immune system = cancer cells destroyed and prevented from multiplying and forming a tumor
 - Immune system improved by exercise
 - Normal disposal of damaged or unneeded cells
- Cancer cells cannot thrive in an oxygenated environment
 - Exercising daily helps to get more oxygen down to the cellular level

Obesity and Cancer



- According to the National Cancer Institute, obesity and physical inactivity may account for 25 to 30% of several major cancers, including:
 - Colon
 - Breast (postmenopausal)
 - Endometrial
 - Kidney
 - Esophagus

Obesity and Cancer (cont'd)



- Preventing weight gain can reduce the risk of many cancers
- Experts recommend that people establish habits of healthy eating and physical activity early in life
 - Prevent overweight and obesity
- Even a weight loss of only 5 to 10 percent of total weight can provide health benefits

How much Exercise?



Relatively low levels of aerobic exercise can protect your immune system.

20 to 30 minutes of brisk walking five days per week is an ideal training program for maintaining a healthy immune response.

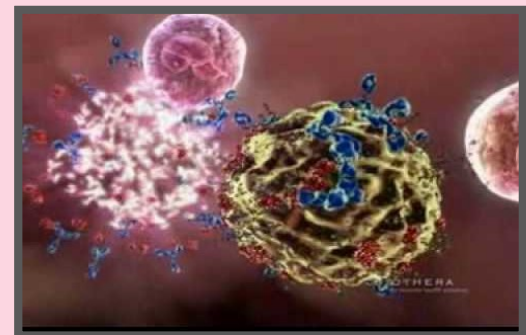


“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”

Exercise Effects on the Immune System



- Moderate exercise has been linked to a positive immune system response
 - Circulation is quicker
 - Better able to kill bacteria and viruses
 - Increased antibody response
 - Increased natural killer (T cell) response.



Exercise Effects on Mental Health



- Several mental health benefits associated with exercise:
 - Improved self-esteem, self-efficacy, and body image
 - Behaviors associated with stress (alcohol)
- Less documented effect of exercise on selected cognitive function:
 - Executive function
 - Working memory

Exercises to Lower Stress




- Aerobic exercise
 - Light to moderate walking, jogging/running
 - Cycling
- Stretching and low impact exercise
 - T'ai Chi
 - Yoga
 - Pilates
- Strength training/resistive exercises

Our Study - Women with Breast Cancer



“Can Aggressive Intervention Improve
Quality of Life Among Cancer
Patients”

A pink ribbon symbol is located in the upper right corner of the slide. The background features a light pink color with several large, flowing, ribbon-like shapes in shades of pink and white that create a sense of movement and depth.

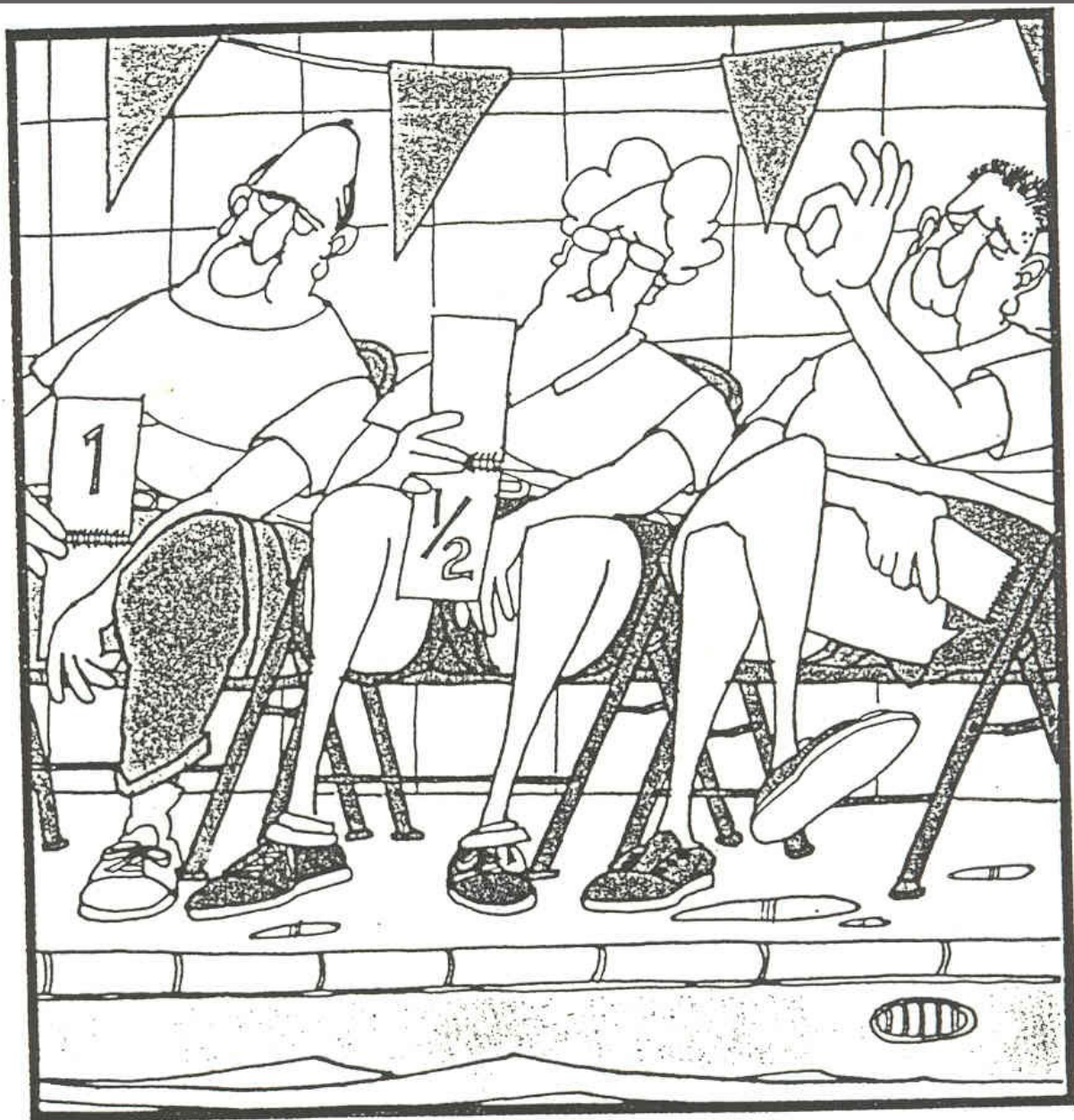
More than 50% of cancer patients experience signs of weight gain as a side effect of chemotherapy.

Although it seems that aerobic and stretching exercises have the greatest benefits, resistive exercises have positive benefits as well.

Variables



- Bone mineral content
- Cognitive functions
- Self-efficacy
- Comparing aerobic and resistive exercises



The judges remain unimpressed.



My Thanks



- Human Performance Lab
- Isaac Cook
- Casey Jo Magee
- Denton Thompson