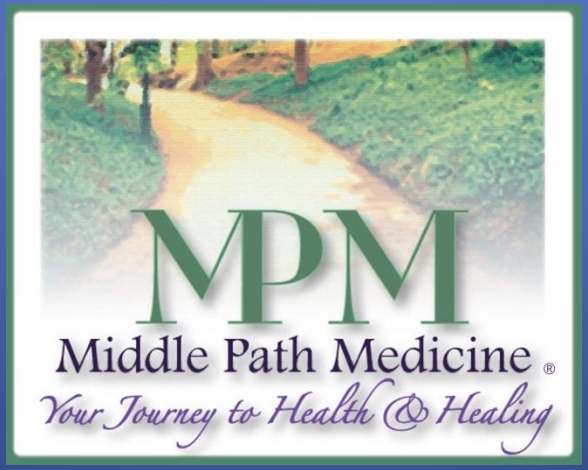
Integrative Oncology

Integrative Cancer Therapies

Gary E. Foresman, MD

July 2014



"In 2010, about 600,000 Americans, and more than 7 million humans around the world, will die of cancer.

In the United States, 1 in 3 women and 1 in 2 men will develop cancer during their lifetime.

A quarter of all American deaths, and about 15% of all deaths worldwide, will be attributed to cancer.

In some nations, cancer will surpass heart disease to become the most common cause of death."

The Emperor of All Maladies, 2010

"Diseases desperate grown
By desperate appliance are relieved,
Or not at all."

-William Shakespeare, *Hamlet*

The Emperor of All Maladies, 2010

"Cancer begins and ends with people. In the midst of scientific abstraction, it is sometimes possible to forget this one basic fact…Doctors treat diseases, but they also treat people, and this precondition of their professional existence sometimes pulls them in two directions at once."

-June Goodfield

The Emperor of All Maladies, 2010

Cancer: A Pathological Definition

"A malignant growth or tumor caused by abnormal and uncontrolled cell division"

- Often near - synonyms include: "**neoplasia**"—novel, inexplicable distorted growth and "**pathological hyperplasia**"—where cells acquire an autonomous will to divide.
- These definitions are old and incomplete.

“Cancer does not grow too much; it dies too little.”

-Robert Nagourney, MD

from

Customized Cancer Treatment

By Ralph W. Moss, PhD 2010

Cancer: A New Definition

- Since the Nobel Prize winning work of three professors, Sydney Brenner (Salk Institute), John Sulston (Wellcome Trust), and Robert Horvitz (MIT), in 2002, cancer is now recognized as a disease of tissues that don't necessarily have excessive proliferation, but lack the ability to perform a normal cellular function known as **Programmed Cell Death (PCD).**

- In the average human adult, between 50 and 70 billion cells die each day due to PCD. In the course of a year, this adds up to cells that equal the weight of the individual.

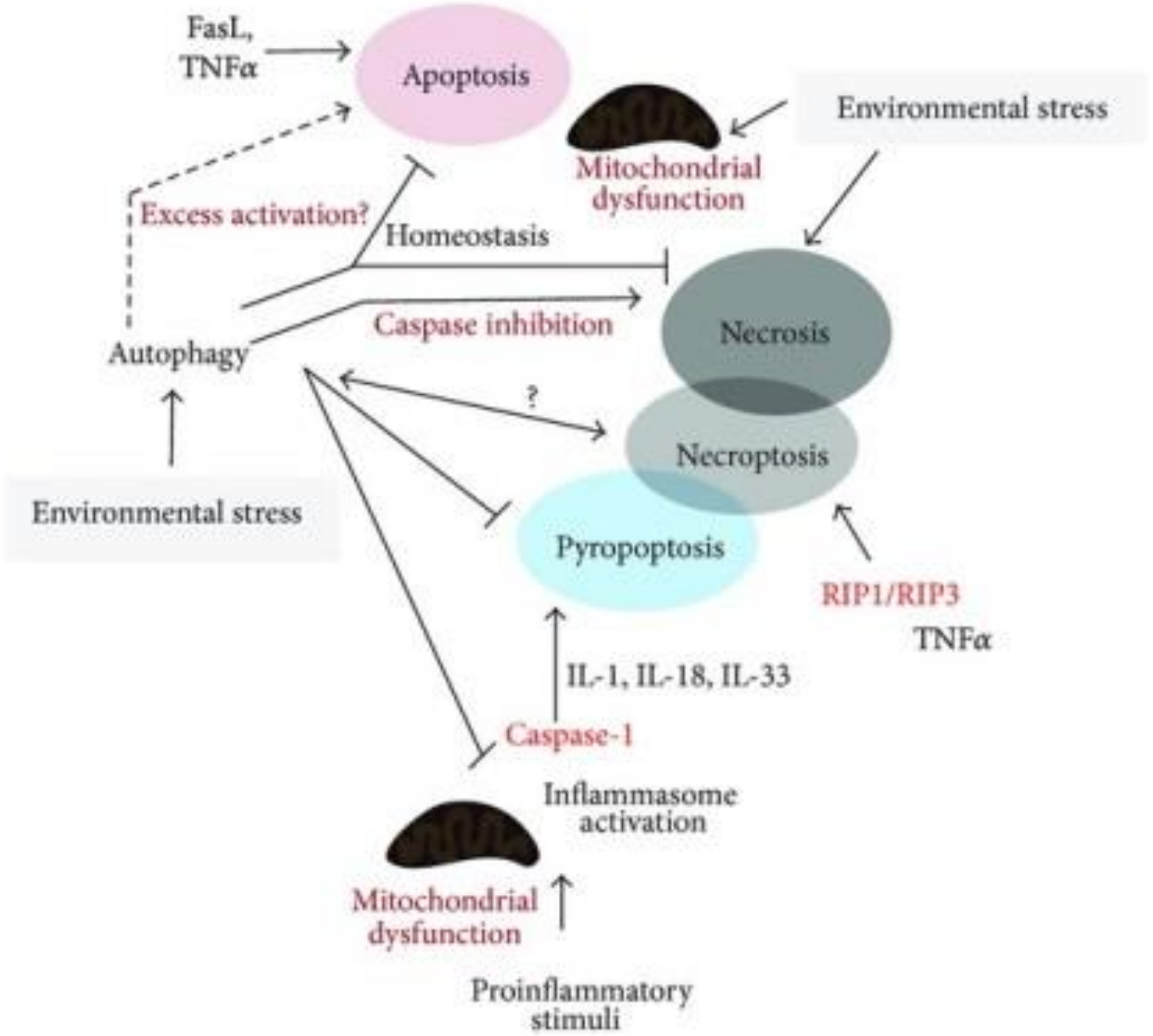
Cancer: A New Definition

- One mechanism of PCD, apoptosis, is derived from an ancient Greek word denoting the natural process by which leaves fall from trees in autumn.
- Apoptosis is a mechanism of active self-destruction, of which there are many others that combine to become PCD.
- This shift in understanding of cancer from unregulated cell growth to dysregulated PCD still confounds most of our thinking about cancer.

The Impact of Autophagy on Cell Death Modalities

Stefan W. Ryter, [1,2,*] Kenji Mizumura, [1,2] and Augustine M. K. Choi [2]

PMID: 24639873


FasL,
TNFα
Apoptosis
Mitochondrial dysfunction
Environmental stress
Excess activation?
Homeostasis
Caspase inhibition
Necrosis
Autophagy
?
Necroptosis
Environmental stress
Pyropoptosis
RIP1/RIP3
TNFα
IL-1, IL-18, IL-33
Caspase-1
Inflammasome activation
Mitochondrial dysfunction
Proinflammatory stimuli

Autophagy has a complex relationship with various modes of cell death, including regulated (e.g., apoptosis, pyroptosis, and necroptosis) and catastrophic (e.g., necrosis) types of cell death. Autophagy has been implicated in association with caspase-independent cell death in apoptosis-compromised cells leading to necrosis and necroptosis.

Furthermore, autophagy has been implicated as an inhibitor of both apoptosis and necrosis by preserving cellular functions, removing toxic debris, and maintaining cellular energy charge. Nevertheless, proapoptotic roles of autophagy have also been reported.

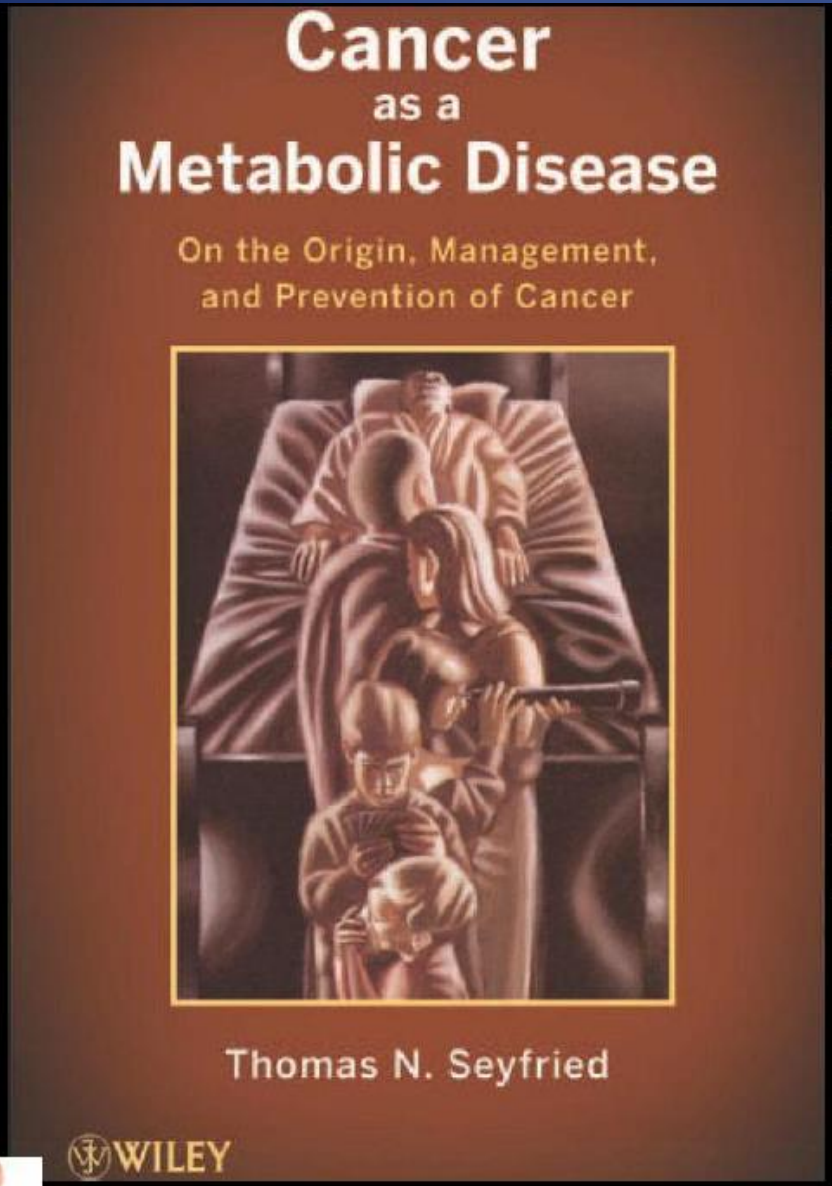
Proinflammatory stimuli can activate inflammasome-dependent caspase-1 activation leading to proinflammatory cytokines maturation. Excess activation of this pathway can lead to pyroptotic cell death. Mitochondrial dysfunction plays a key role in both apoptosis signaling and the activation of the inflammasome pathway. Autophagy can influence these pathways through modulation of the mitochondrial pool.

The relationships between autophagy and necroptosis or pyroptosis require further elucidation.

"Say . . . what's a mountain goat doing
way up here in a cloud bank?"

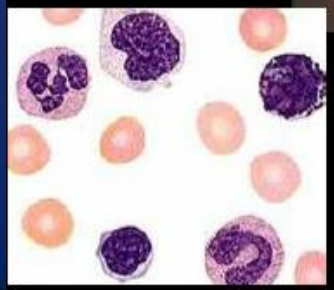
The Hallmarks of Cancer

1. Self-sufficiency in growth signals: an autonomous drive to proliferate. Activation of proto-oncogenes.
2. Insensitivity to growth-inhibitory signals: cancer cells inactivate tumor suppressor genes.
3. Evasion of programmed cell death.
4. Limitless replicative potential: immortality.
5. Sustained angiogenesis: cancer cells acquire the ability to develop their own blood supply.
6. Tissue invasion and metastasis: cancer cells acquire the capacity to migrate, invade, and colonize other organs.



This book expands upon Otto Warburg's well-known theory that all cancer is a disease of energy metabolism. However, Warburg did not link his theory to the "hallmarks of cancer" and thus his theory was discredited. This book aims to provide evidence, through case studies, that cancer is primarily a metabolic disease requiring metabolic solutions for its management and prevention. Support for this position is derived from critical assessment of current cancer theories.

- **ISBN-10:** 0470584920
- **ISBN-13:** 978-0470584927

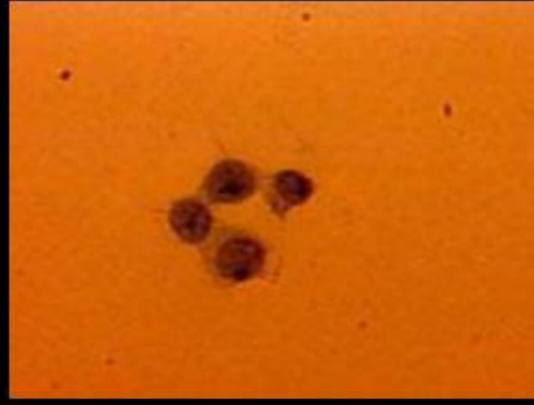


Tumor Biology

- There are over 100 identified proto-oncogenes and tumor suppressor genes.
- Each cancer has between 50 to 80 mutated genes.
- One breast cancer sample from a 43 year old woman had 127 genetic mutations.
- There are between 11 and 15 important cancer signaling pathways present within each cancer.

Max Wicha, M.D.

Distinguished Professor of Oncology
Director, University of Michigan
Comprehensive Cancer Center



PMID:
21685
479

- **ANN ARBOR, Mich. -** Of all the neoplastic cells in human breast cancers, only a small minority - perhaps as few as one in 100 - appear to be capable of forming new malignant tumors, according to just-published research by scientists in the University of Michigan Comprehensive Cancer Center. ....."These tumor-inducing cells have many of the properties of stem cells,"

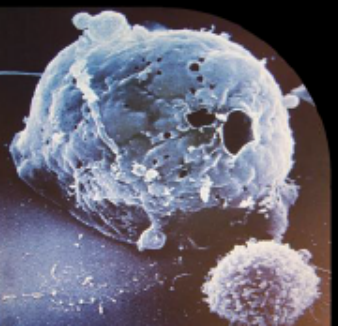
- "The problem is, when we treat cancer cells with chemotherapy, the cancer stem cells are being stimulated to grow too."

..treatment is a problem

- Dr. Wicha's lab has found that inflammatory molecules secreted by **dying tumor cells can hook up with the stem cells** and cause them in effect to come out of hibernation.

- Chemo and radiation kill off the fastest-growing cells in the body, which applies to most cancer cells, but **the cancer stem cells** that create those rapidly dividing tumor cells actually grow much more slowly themselves, and **are less susceptible** to those therapies, he said.

- The treatment results in an IL-8 ("SOS") signal to be sent out to muster reinforcements from the mesenchymal stem cells which increase the number and virulence of cancer stem cells.



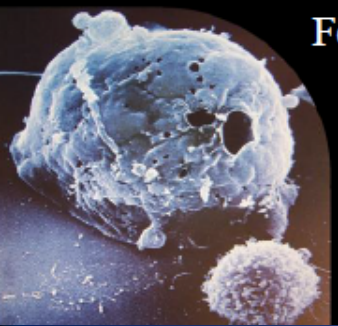
"Considerable evidence suggests **that tumors contain only a minority of cells which are capable of regrowing the tumor (ie. tumor stem cells).**

99.1% - 99.6% of the tumor cells are NOT dangerous (aside from obstructive factors).

"Similarly, usually less than 1% of primary tumor cells cultured *in vitro* can give rise to colonies."

Diehn, M Therapeutic Implications of the Cancer Stem Cell Hypothesis *Semin Radiat Oncol.* 2009 April; 19(2): 78–86. PMID:19249645

Hill RP The proportion of stem cells in murine tumors. Int J Radiat Oncol Biol Phys. 1989 Feb;16(2):513-8.



Oncology: The Definition

- *Onkos* is the Greek term for a mass or a load, or more commonly a burden; cancer was imagined as a burden carried by the body.
- The study of this burden on the human organism defines oncology.
- When cancer spreads from one site to another, we call it **metastasis** (from Latin- beyond stillness).
- "The image of cancer as our desperate, malevolent, contemporary doppelganger is so haunting because it is at least partly true."

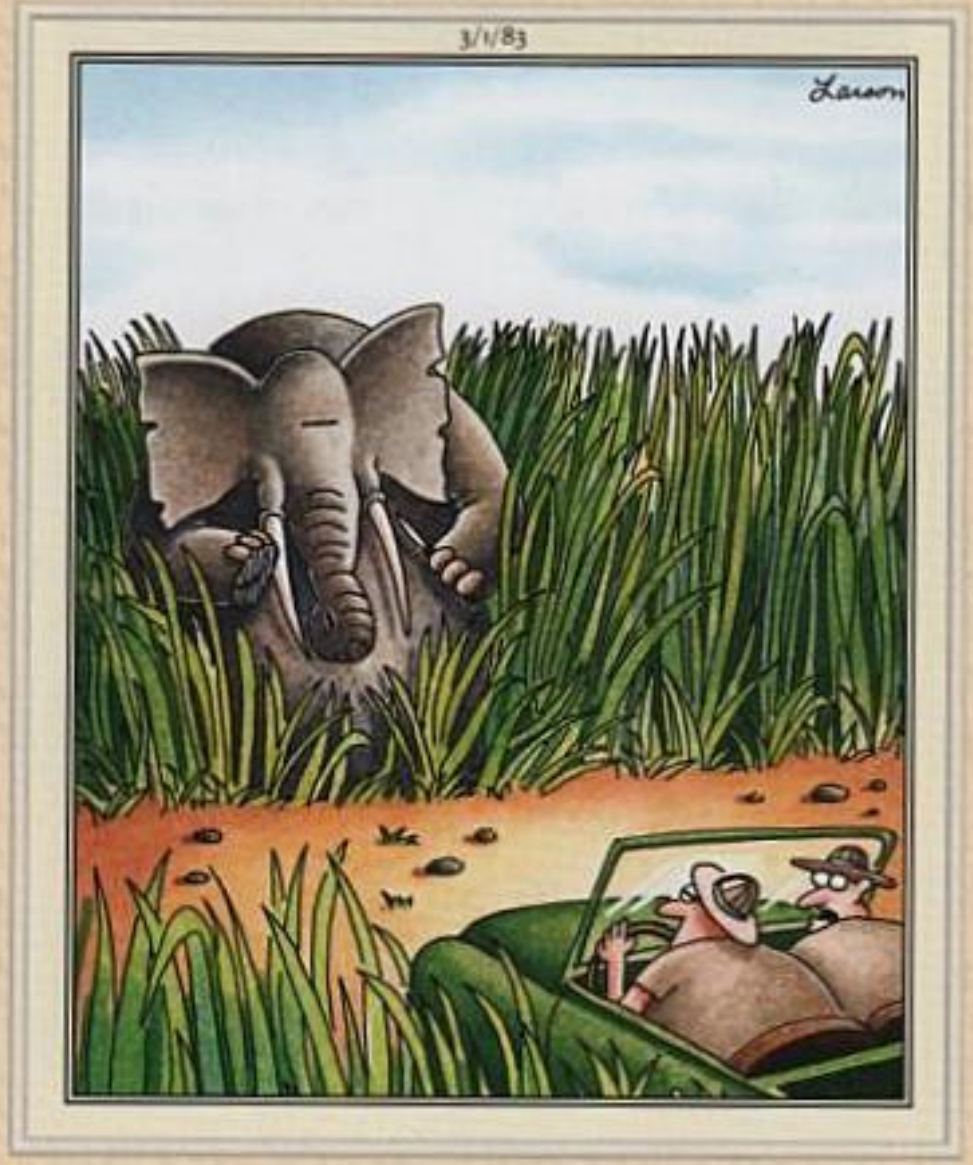
-The Emperor of All Maladies, 2010

WINNER OF THE PULITZER PRIZE

THE EMPEROR OF ALL MALADIES

A BIOGRAPHY OF CANCER

SIDDHARTHA MUKHERJEE



"Not too close, Higgins. ... This one's got a knife."

Definitions

- Surgical Oncologist: the specialist in surgical approaches to oncology only.
- William Stewart Halsted, born in 1852 in New York, moved to Johns Hopkins (Baltimore) in 1889 becoming the mentor of American surgical approaches.
- Founder of the “radical mastectomy”, using the word *radical* from the Latin word meaning ‘root’.
- As a man with oscillating addictions between cocaine and morphine, he shepherded the surgical profession into the world of a super human initiation that emphasized heroism, self-denial, diligence, and tirelessness.

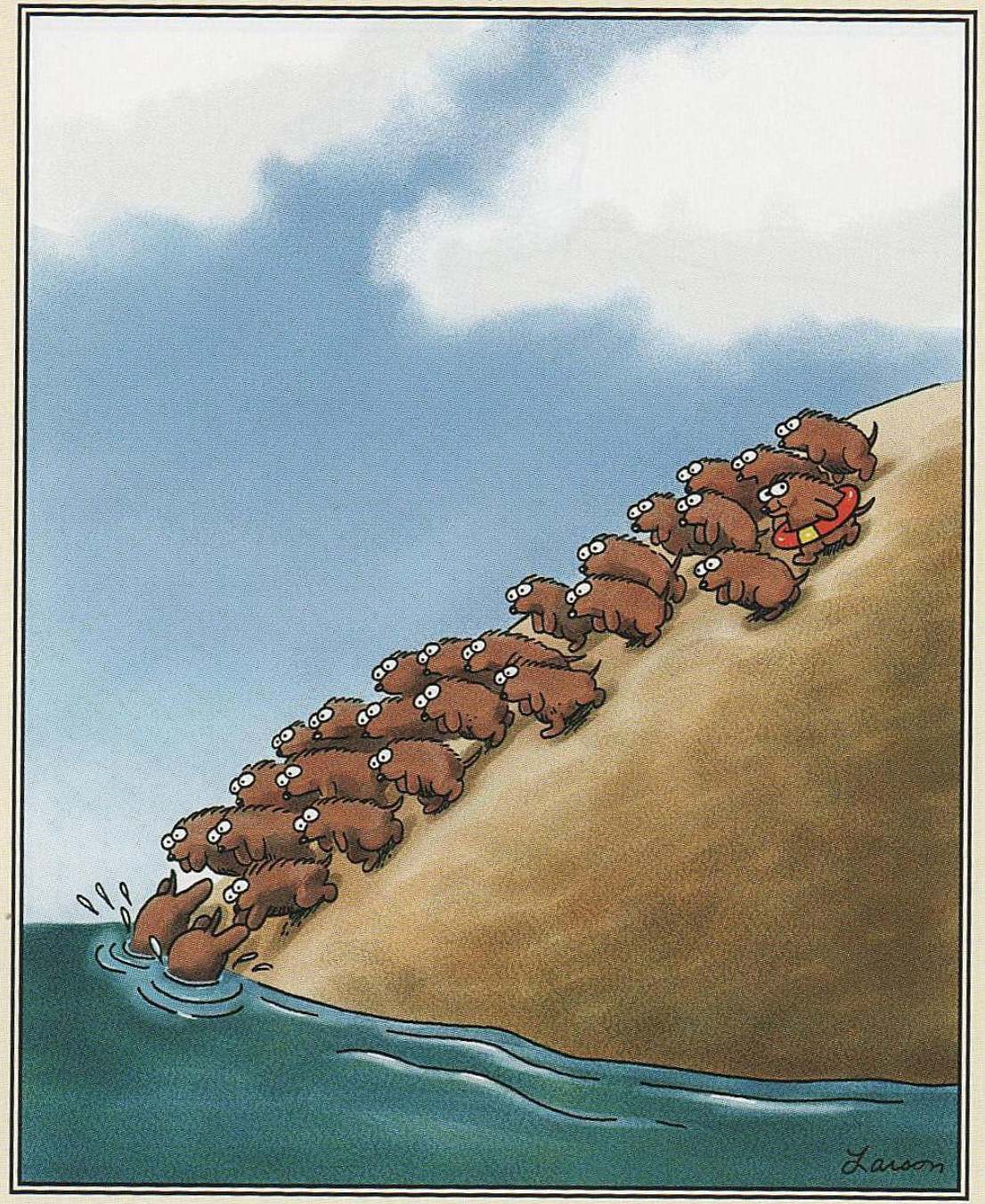
Definitions

- Performing radical mastectomies from 1891 to 1907, his own data proved that his more radical surgery could not cure patients who had cancer in the lymph nodes.
- Dr. Halsted encouraged surgeons to continue finding more radical ways of up-rooting cancer surgically from the human body.
- Finally in 1981, a multi-center trial proved radical surgery no more effective than simple surgery (in the treatment of breast cancer).
- Despite never a shred of credible evidence, the surgical oncologist subjected over 500,000 women to unnecessary, life-threatening surgery.

Definitions

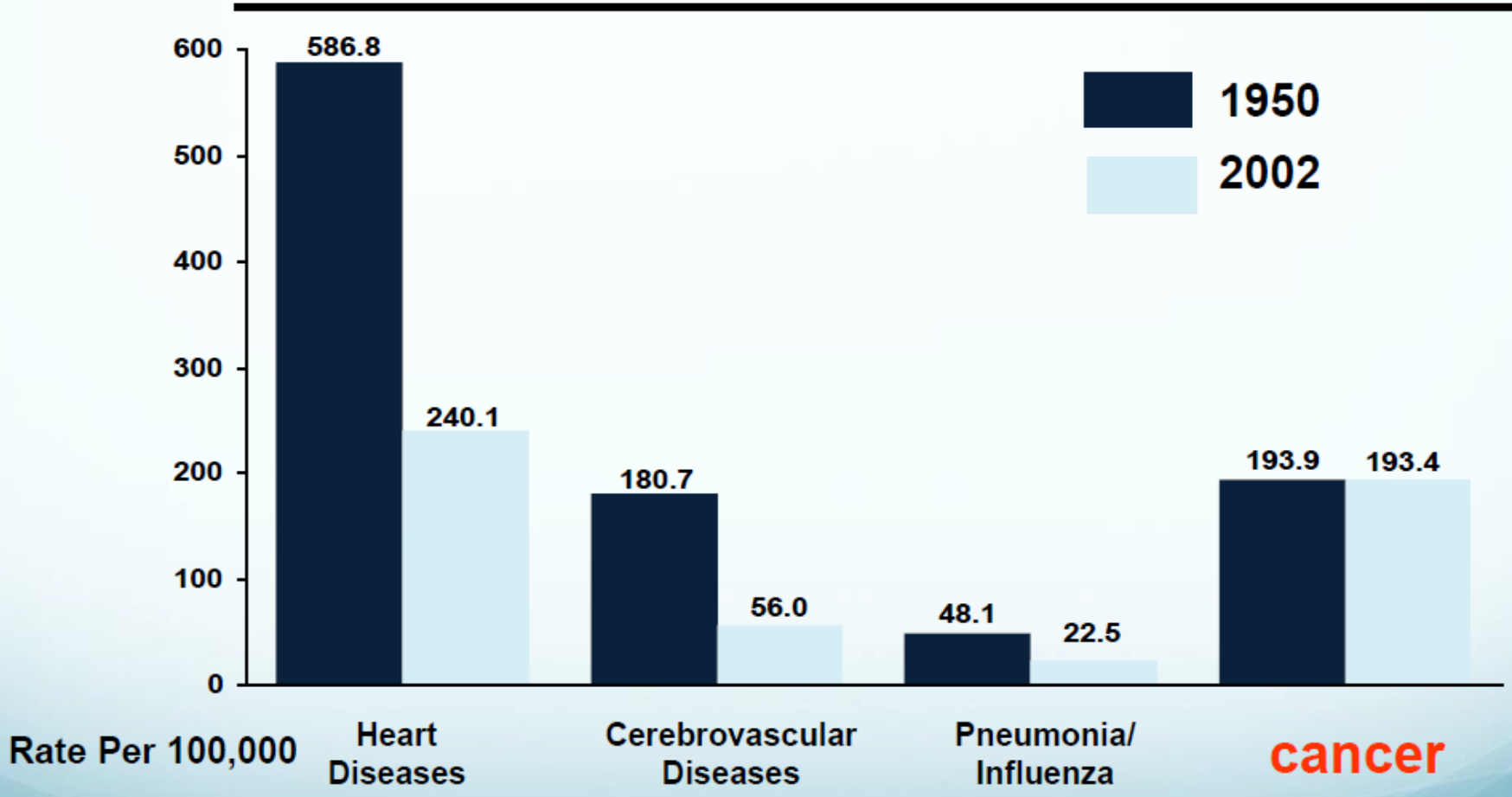
- Medical Oncologist: the specialist in the Western chemotherapeutic approach to oncology only.
- Dramatic benefits in the treatment of leukemias, lymphomas, testicular cancer, and choriocarcinoma due to combination chemotherapy which has made sometimes incurable diseases into curable ones.
- However, treatment of most solid tumors has added mere months of survival in the 65 year history of chemotherapy.
- Between 1991 and 1999, 40 thousand women around the world underwent marrow transplantation (after high-dose chemotherapy) for breast cancer at an estimated cost of $4 billion despite no credible evidence that it improved survival.
- The influence of the pharmaceutical industry on physician practice…

12/15/80



Change in the US Death Rates* by Cause, 1950 & 2002

(A 2005 Presentation From the American Cancer Society)

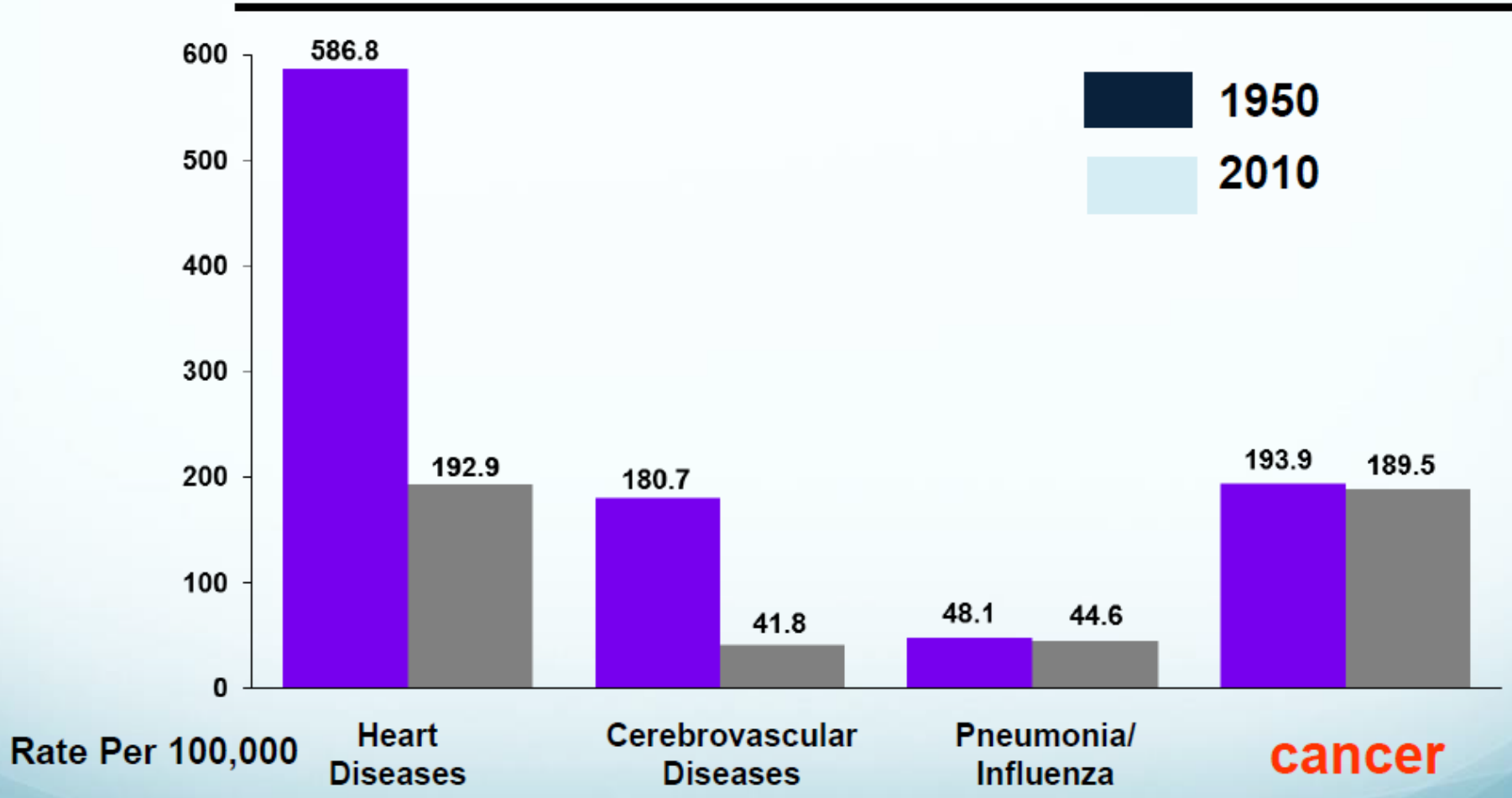


* Age-adjusted to 2000 US standard population.

Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
2002 Mortality Data: US Mortality Public Use Data Tape, 2002, NCHS, Centers for Disease Control and Prevention, 2004

Change in the US Death Rates* by Cause, 1950 & 2010

(A 2005 Presentation From the American Cancer Society plus 2010 Data from the CDC)



* Age-adjusted to 2010 US standard population.

Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
2010 Mortality Data: US Mortality Public Use Data Tape, 2002, NCHS, Centers for Disease Control and Prevention, 2011

Problems with Conventional Chemotherapy

FACT: ~2% of all cancers respond to chemotherapy.
FACT: Conventional Chemotherapy hurts more than it helps.

OPINION: ***"The overall contribution of curative and adjuvant cytotoxic chemotherapy to 5-year survival in adults was estimated to be 2.3% in Australia and 2.1% in the USA . . . chemotherapy only makes a minor contribution to cancer survival. To justify the continued funding and availability of drugs used in cytotoxic chemotherapy, a rigorous evaluation of the cost-effectiveness and impact on quality of life is urgently required."***

Morgan G, Ward R, Barton M. in his article:
The contribution of cytotoxic chemotherapy to 5-year survival in adult malignancies.
See *Clin Oncol* (R Coll Radiol). 2004 Dec;16(8):549-60.)

Definitions

- Radiation Oncologist: the specialist in the radiation medicine approach to oncology only.
- Used in conjunction with lumpectomy, radiation therapy spares unnecessary radical surgical approaches.
- Can be used as part of total brain irradiation in leukemia and small cell lung cancer.
- Can be used to treat painful metastases.

Definitions

- Integrative Oncologist: the specialist in the treatment of both the cancer as well as the person who has the cancer. Teams with Western Specialists for providing the best therapeutic options in that individual's cancer care. The expert on the team who prescribes Nutrition, Stress Management, Exercise, and Orthomolecular as well as non-traditional drug treatment options.

The Role of the Integrative Oncologist

- Truly primary care for the cancer patient.

- Due to the fear that a diagnosis of cancer brings, and the severe limitations in the Western medical approach to cancer, people are going to the internet for answers which should be provided by their primary care physician.

General Treatment Principals

- All Senses For Healing

  As your patient and their family is in so much of a fear-based state, never has there been a more important time for wholism and 'center-stage' principals.

  – **Visual**: discuss all videos/TV/news programs that they watch. Focus on time in nature, home beauty, Feng Shui

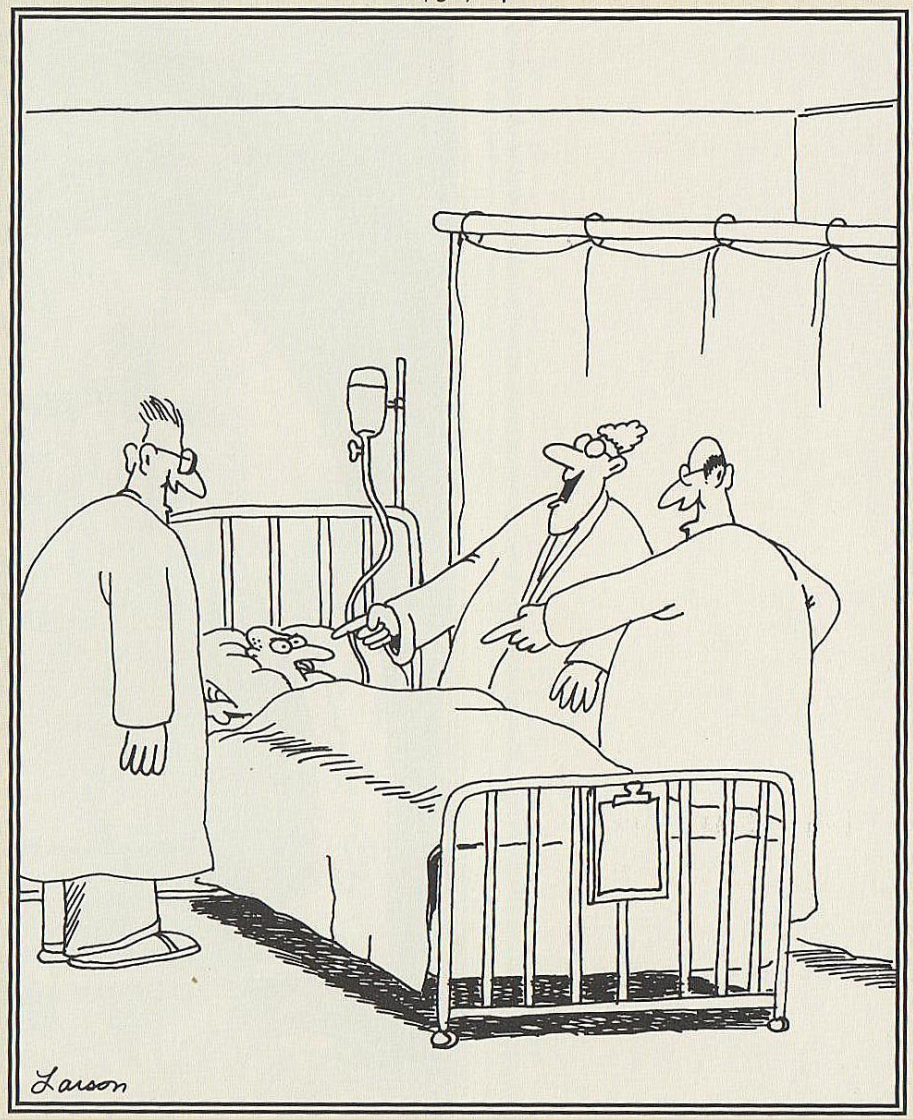
  – **Auditory**: music as medicine, singing bowls, the non-local effects of harmony

General Treatment Principals

- **Laughter**: the audio-visual continuum
- **Smell**: Essential Oils/aromatherapy, the power of personal experience
- **Taste**: the conscious use of spices; healthy shopping and cooking
- **Touch**: how touch deficiency exists whereas chemotherapy deficiency does not. All organic skin care and home care products.

The life –transforming power of cancer to heal.

6/30/84



Testing whether laughter *is* the best medicine.

General Treatment Principals

- Meditation/Stress-Reduction/Self-Realization

  Perceived stress has been linked to almost every tumor type and more aggressive tumors. Every study on stress-reduction shows improved quality of life and some show improved survival as well.

  – **Techniques**:
    - Transcendental Meditation (TM) www.tm.org
    - Primordial Sound Meditation (PSM) www.chopra.com/meditation
    - HearthMath-Biofeedback technology: www.heartmath.com
    - Middle Path Medicine: Stress Management Series: http://www.middlepathmedicine.com/Articles_and_Slides/Newsletters/Stress_Management.html

Biofeedback

Breast Cancer and Stress

- Sapolsky/Spiegel(Stanford)

  Metastatic Breast Cancer Patients

  Assess Cortisol Pattern(salivary)

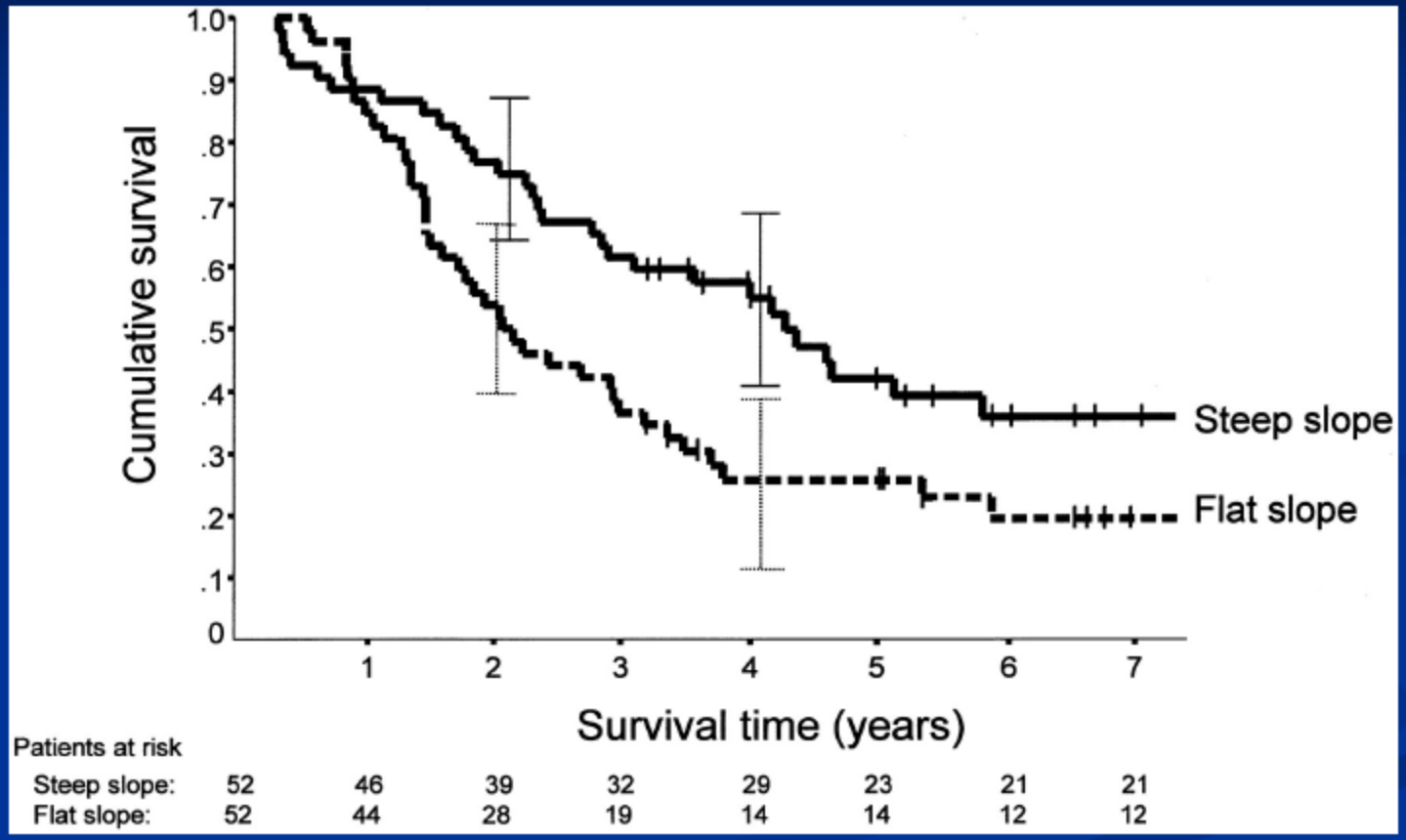
  Pts. with flattened cortisol profiles

  Independent & significant predictor of decreased survival.

- Stress-related HPA dysregulation

  Poor prognostic factor in Breast Ca

Survival Curves for patients split into two equal groups at the median diurnal cortisol slope



Sephton, S. E. et al. J Natl Cancer Inst 2000;92:994-1000

General Treatment Principals

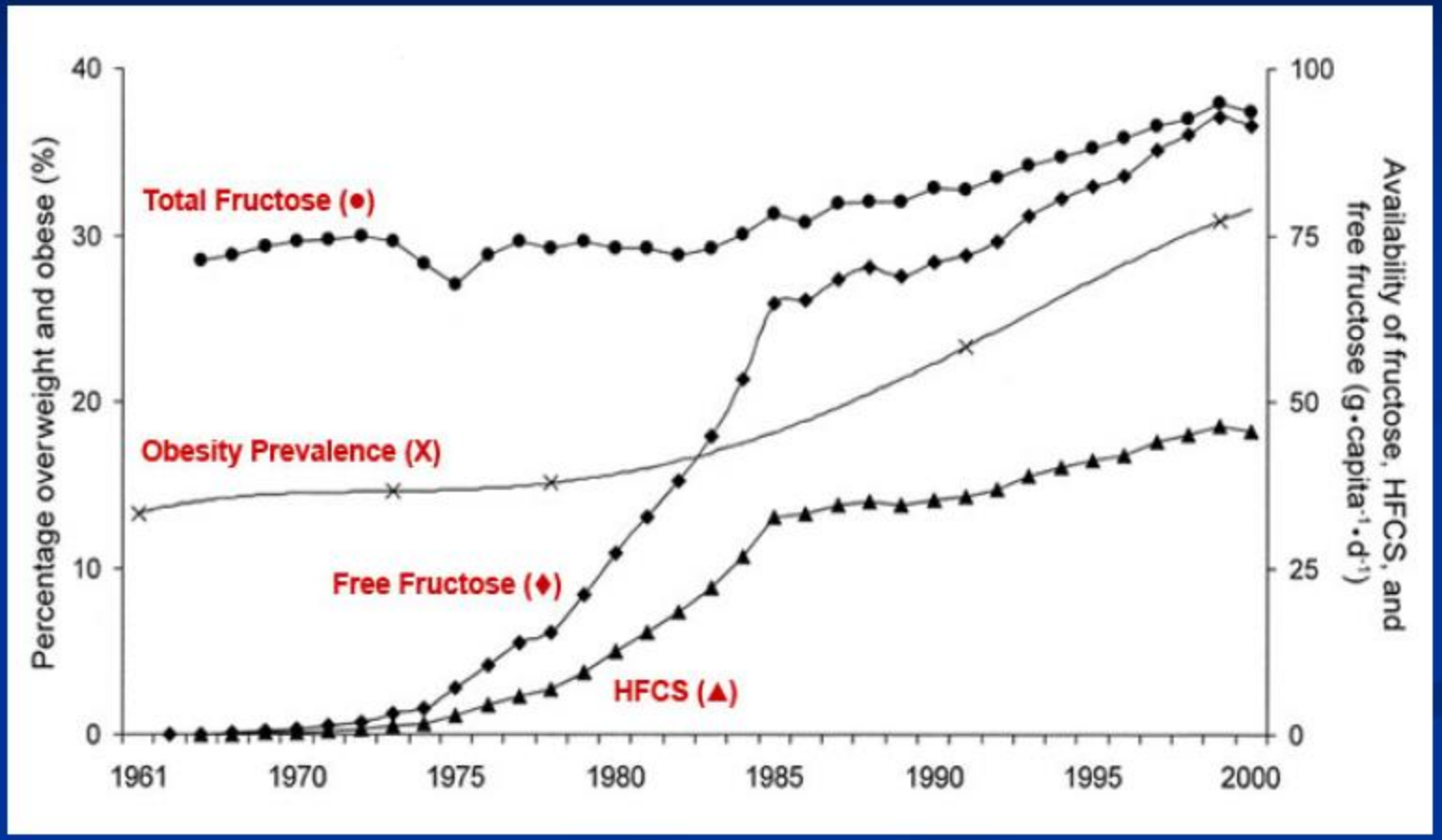
- Nutrition:
  - Medical oncologists are under tremendous pressure to treat with medicines that are often ineffective. They are routinely taught to ignore information within their own literature which proves that good nutrition improves outcomes better than many chemotherapy regimens.
  - On the other hand, many nutritionally oriented practitioners overstate the benefits of their particular belief system about nutrition.
  - This leaves the patient confused and disempowered.


I'LL HAVE THE HALF-POUND DOUBLE-DELUXE BACON STEERBURGER, PLEASE...
YOU WANT CHEMOTHERAPY WITH THAT?

General Treatment Principals

- Nutrition:
  - A “Paleo” organic, whole-food diet emphasizing vegetables, fruits, nuts, wild-caught fish, and organic lean proteins is preferred.
  - Most patients need to lose weight and repair the high-glycemic and pro-inflammatory diet that partially caused and is currently feeding their cancer.
  - Nutrition treats the person who has cancer, not cancer itself
  - A word on ketogenic diets
  - A word on biologic dentistry

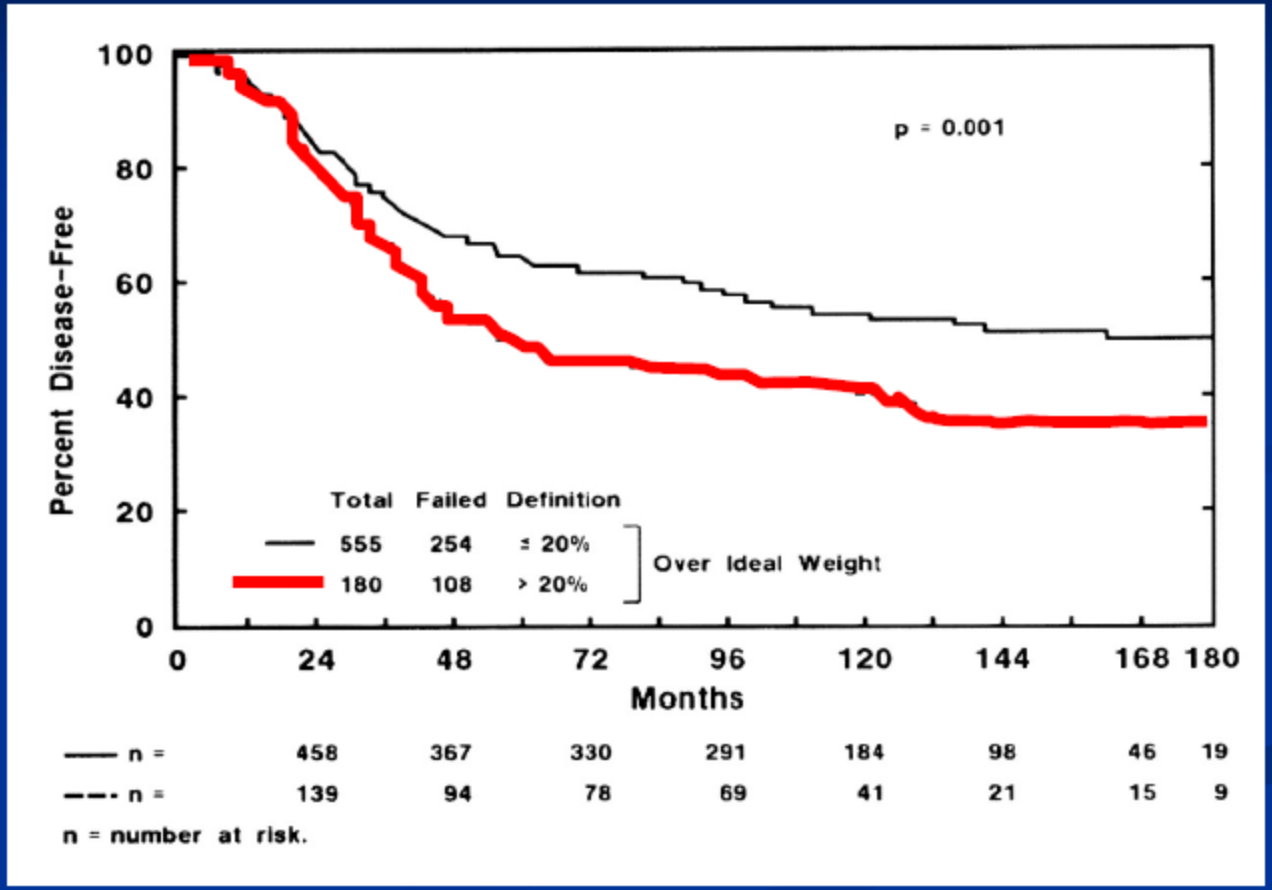
Increased FBCS correlates with Rising Obesity



Obesity Reduces Breast Cancer Survival

BREAST CANCER PROGNOSIS

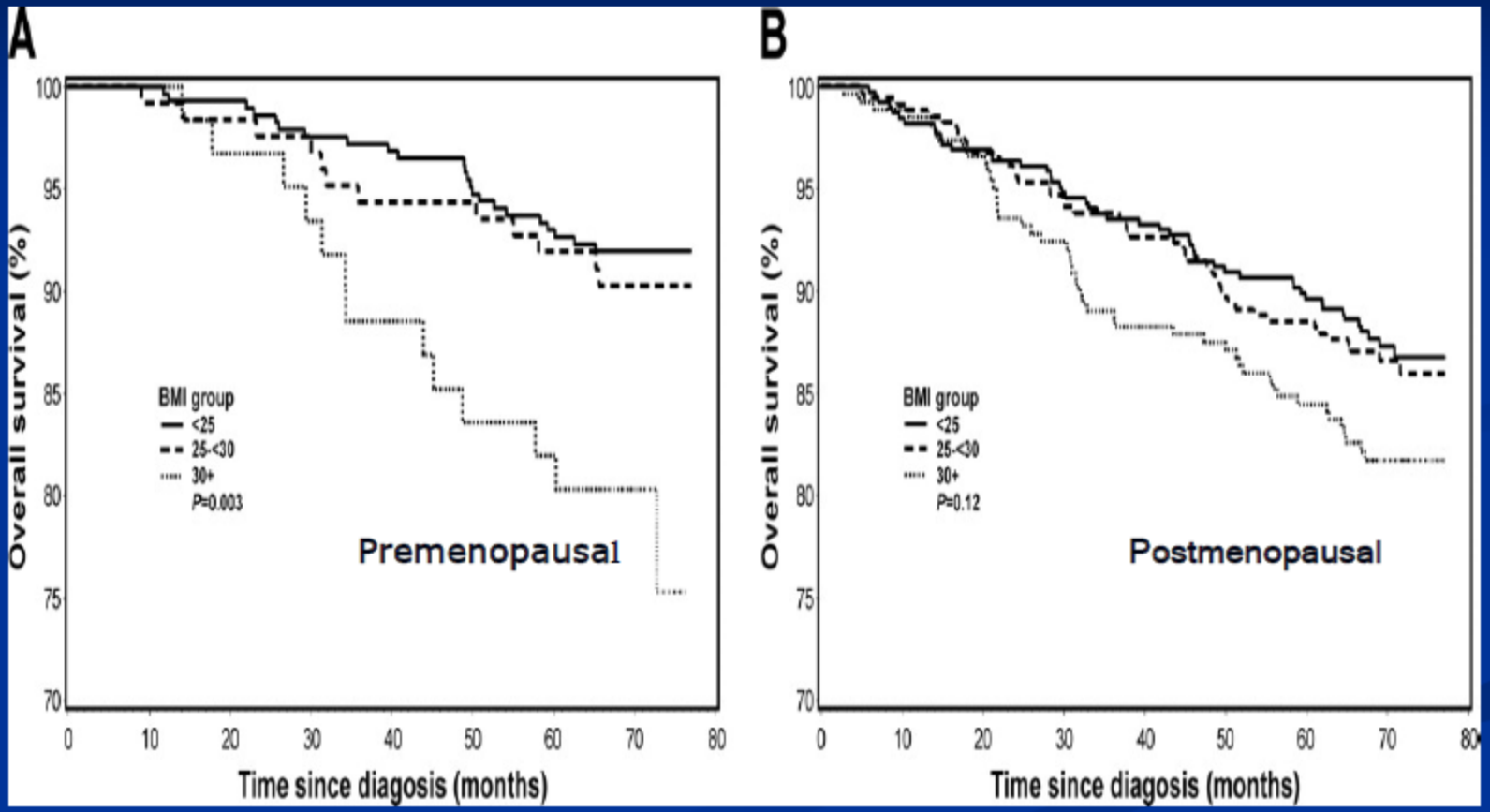
- GENERAL
- **NEW CONCEPTS**



Disease-Free Survival, Post-Adjuvant Chemotherapy Breast Cancer

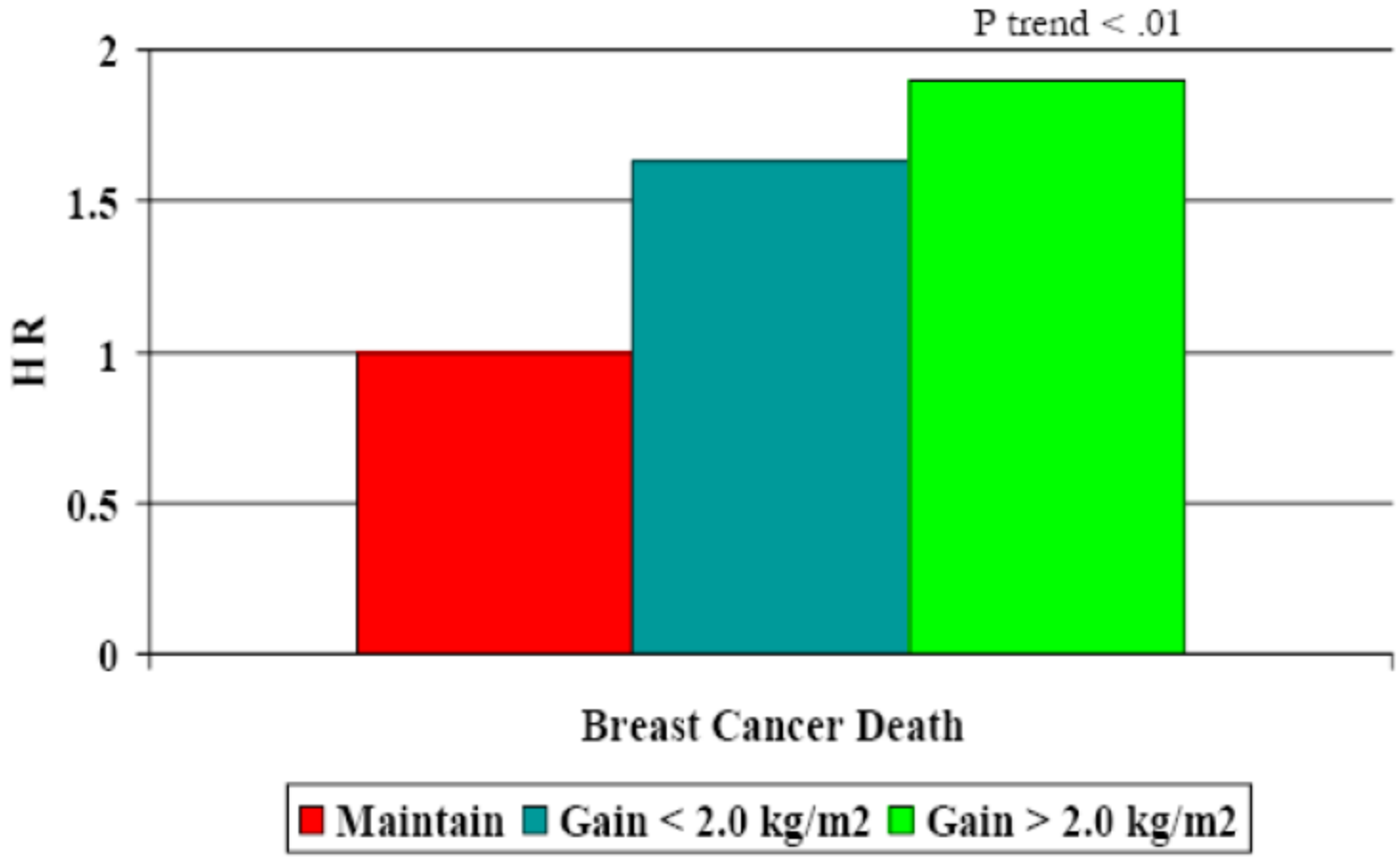
by +/- Obesity Hortobagyi,G. Ann Int Med.120:18-25,1994

Mortality due to all causes after breast cancer diagnosis, by BMI

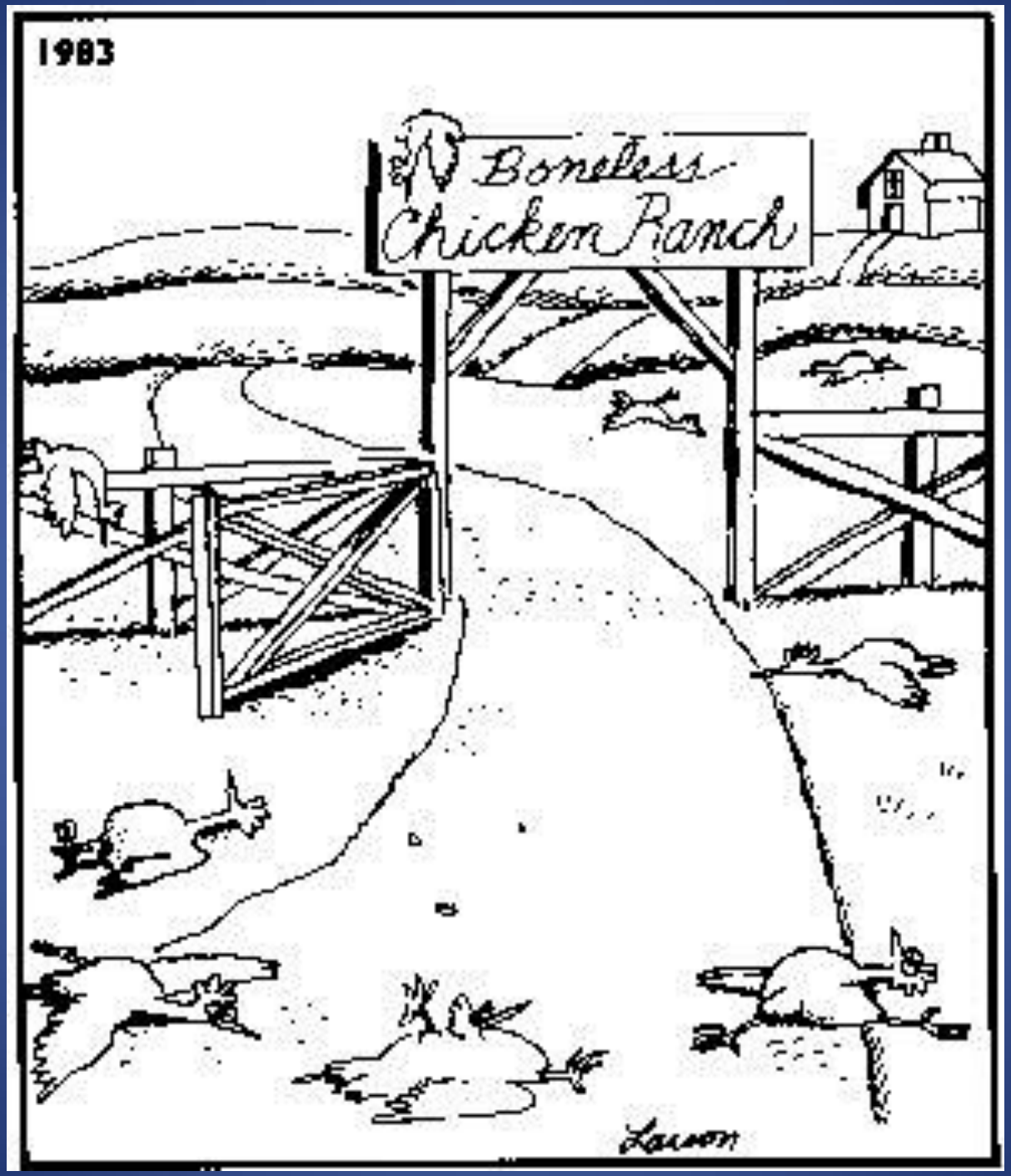


Cleveland, R. J. et al. Cancer Epidemiol Biomarkers Prev 2007;16:1803-1811

Post-Diagnosis Weight Gain and Breast Cancer Death in Women with BMI < 25 at diagnosis



Kroenke C JCO 2005


1983
Boneless
Chicken Ranch
Lauson

General Treatment Principals

- Exercise:
  - This might be more important than prescribing appropriate nutrition.
  - Every trial shows that even a modest exercise regime when compared to sedentary lifestyle improves quality of life, and occasionally survival, often more than chemotherapy.
  - All levels of fitness are important.
    1. "Yogic" fitness—flexibility, core, balance
    2. Aerobic fitness—this is not the time, however, for high-intensity interval training.
    3. Resistance fitness—maintenance of lean body mass is critical.
    4. Skill set – improves compliance and enjoyment

J Natl Cancer Inst. 2012 May 8. [Epub ahead of print]

Physical Activity, Biomarkers, and Disease Outcomes in Cancer Survivors: A Systematic Review.

Ballard-Barbash R, Friedenreich CM, Courneya KS, Siddiqi SM, McTiernan A, Alfano CM.

Source

Affiliations of authors: Applied Research Program (RB-B, SMS) and Office of Cancer Survivorship (CMA), Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Bethesda, MD; Department of Health and Human Services, National Cancer Institute, National Institutes of Health, Bethesda, MD (RB-B, SMS, CMA); Faculty of Physical Education and Recreation, University of Alberta, Edmonton, AB, Canada (KSC); Department of Population Health Research, Alberta Health Services-Cancer Care, Calgary, AB, Canada (CMF); Program in Epidemiology, Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA (AM).

Abstract

Background

Cancer survivors often seek information about how lifestyle factors, such as physical activity, may influence their prognosis. We systematically reviewed studies that examined relationships between physical activity and mortality (cancer-specific and all-cause) and/or cancer biomarkers.

J Natl Cancer Inst. 2012 May 8. [Epub ahead of print]

Physical Activity, Biomarkers, and Disease Outcomes in Cancer Survivors: A Systematic Review.

Ballard-Barbash R, Friedenreich CM, Courneya KS, Siddiqi SM, McTiernan A, Alfano CM.

Methods

We identified 45 articles published from January 1950 to August 2011 through MEDLINE database searches that were related to physical activity, cancer survival, and biomarkers potentially relevant to cancer survival. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement to guide this review. Study characteristics, mortality outcomes, and biomarker-relevant and subgroup results were abstracted for each article that met the inclusion criteria (i.e., research articles that included participants with a cancer diagnosis, mortality outcomes, and an assessment of physical activity).

Results

There was consistent evidence from 27 observational studies that physical activity is associated with reduced all-cause, breast cancer-specific, and colon cancer-specific mortality. There is currently insufficient evidence regarding the association between physical activity and mortality for survivors of other cancers. Randomized controlled trials of exercise that included biomarker endpoints suggest that exercise may result in beneficial changes in the circulating level of insulin, insulin-related pathways, inflammation, and, possibly, immunity; however, the evidence is still preliminary.

J Natl Cancer Inst. 2012 May 8. [Epub ahead of print]

Physical Activity, Biomarkers, and Disease Outcomes in Cancer Survivors: A Systematic Review.

Ballard-Barbash R, Friedenreich CM, Courneya KS, Siddiqi SM, McTiernan A, Alfano CM.

Conclusions

Future research directions identified include the need for more observational studies on additional types of cancer with larger sample sizes; the need to examine whether the association between physical activity and mortality varies by tumor, clinical, or risk factor characteristics; and the need for research on the biological mechanisms involved in the association between physical activity and survival after a cancer diagnosis. Future randomized controlled trials of exercise with biomarker and cancer-specific disease endpoints, such as recurrence, new primary cancers, and cancer-specific mortality in cancer survivors, are warranted.

Physical Activity and Breast Cancer Prognosis

	Physical Activity Category After Diagnosis, MET-h/wk					
	<3 (n=959)	3-8.9 (n=862)	9-14.9 (n=335)	15-23.9 (n=428)	≥24 (n=403)	*P* trend
Total Deaths	1.00	0.71 (0.56-0.89)	0.59 (0.41-0.84)	0.56 (0.41-0.77)	0.65 (0.48-0.88)	.003
Breast Cancer Deaths	1.00	0.80 (0.60-1.06)	0.50 (0.31-0.82)	0.56 (0.38-0.84)	0.60 (0.40-0.89)	.004
Recurrence	1.00	0.83 (0.64-1.08)	0.57 (0.38-0.85)	0.66 (0.47-0.93)	0.74 (0.53-1.04)	.05

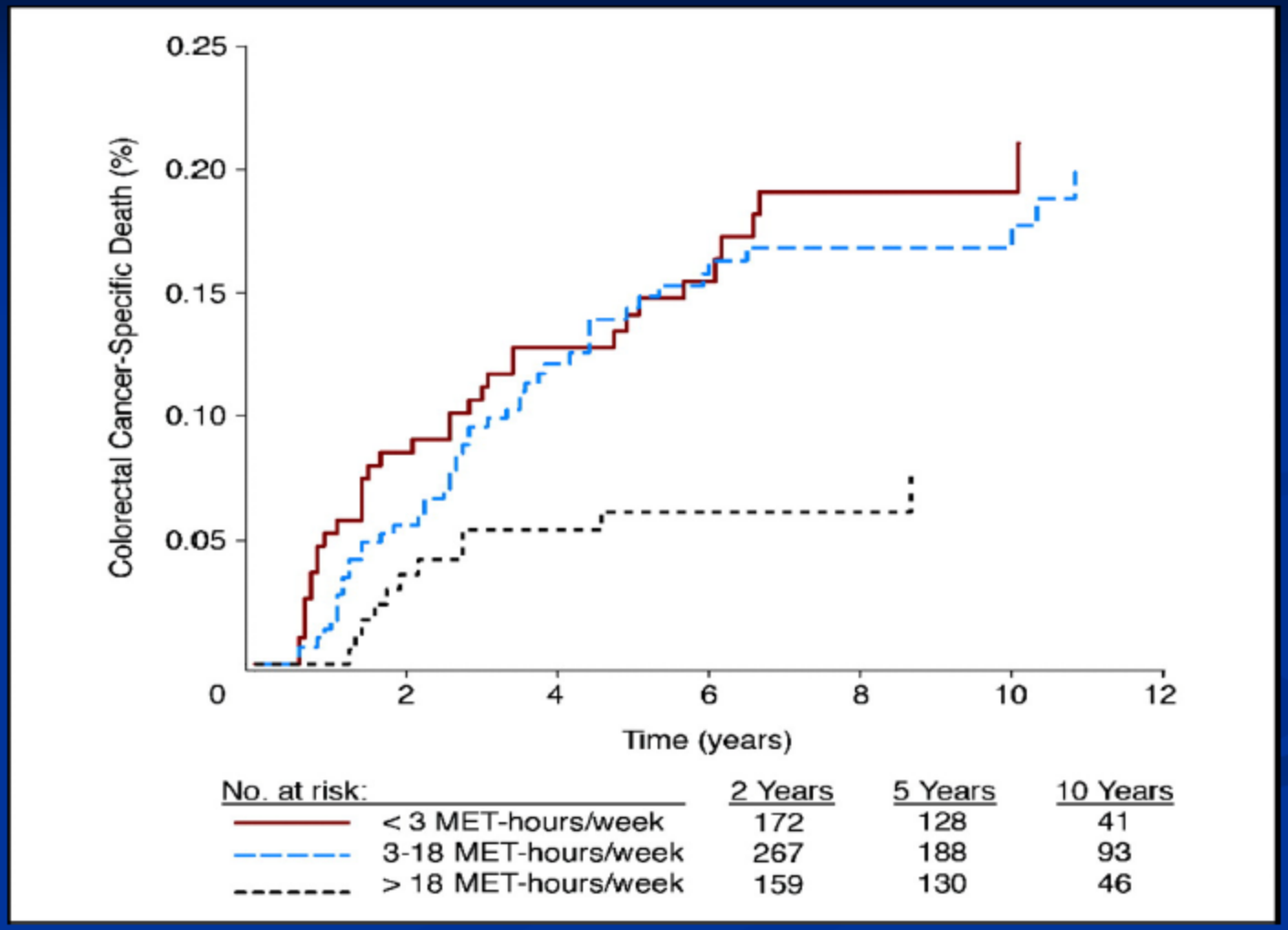
*Adjusted for age, screening, risk factors, and treatment

Source: Holmes MD, et al. JAMA 293:2479-2486, 2005

A MET or metabolic equivalent is the amount of energy used by the body to perform a physical activity or daily task. At rest, the average person has an oxygen consumption of 1 MET (or 3.5 ml/kg-min). MET values increase as more activity is performed.

Physical Activity	MET
Light Intensity Activities	**< 3**
sleeping	0.9
watching television	1.0
writing, desk work, typing	1.8
walking, 1.7 mph (2.7 km/h), level ground, strolling, very slow	2.3
walking, 2.5 mph (4 km/h)	2.9
Moderate Intensity Activities	**3 to 6**
bicycling, stationary, 50 watts, very light effort	3.0
walking 3.0 mph (4.8 km/h)	3.3
calisthenics, home exercise, light or moderate effort, general	3.5
walking 3.4 mph (5.5 km/h)	3.6
bicycling, <10 mph (16 km/h), leisure, to work or for pleasure	4.0
bicycling, stationary, 100 watts, light effort	5.5
Vigorous Intensity Activities	**> 6**
jogging, general	7.0
calisthenics (e.g. pushups, situps, pullups,jumping jacks), heavy, vigorous effort	8.0
running jogging, in place	8.0
rope jumping	10.0

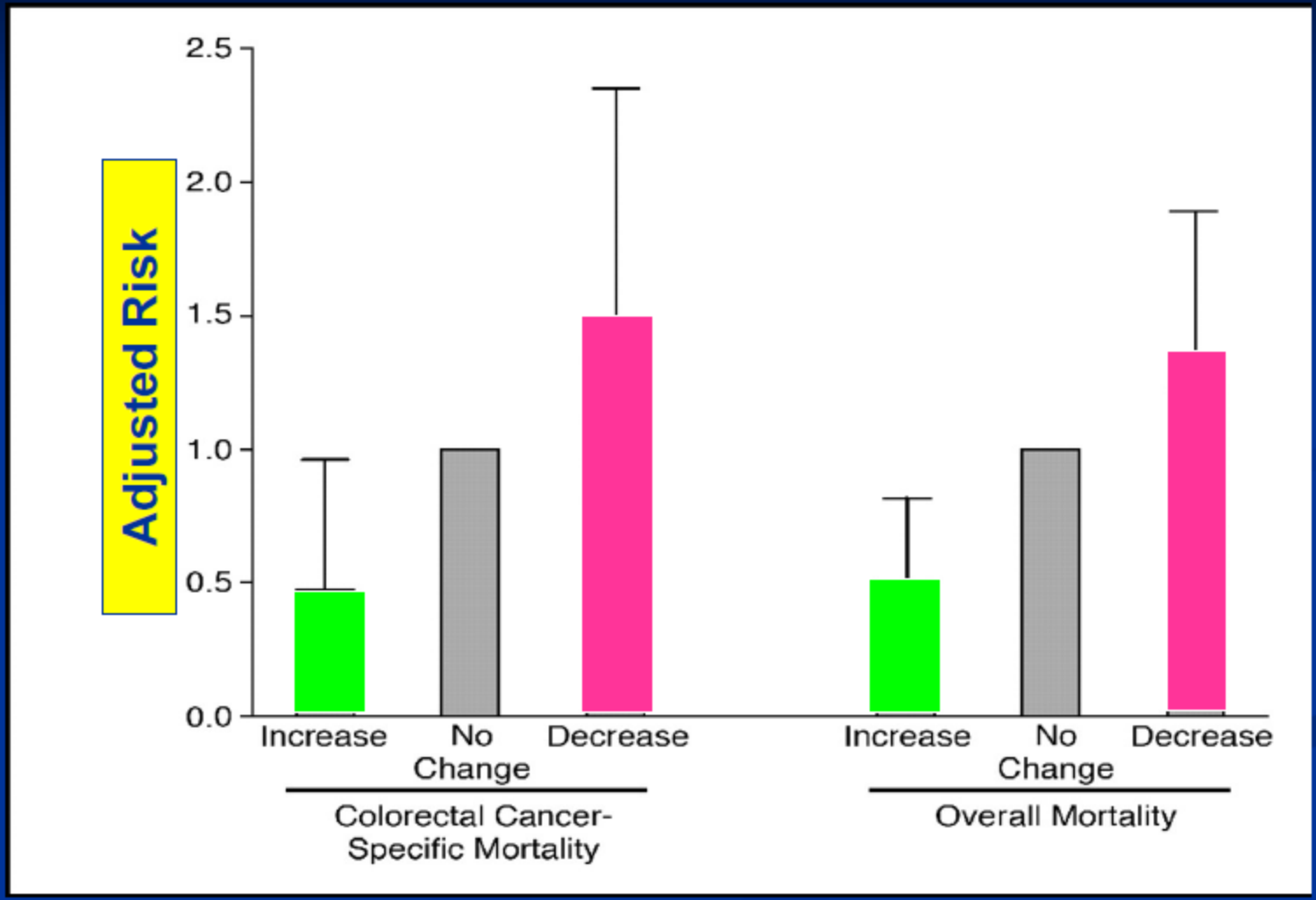
Exercise (18 met-hrs) Reduces Colorectal Mortality



No. at risk:	2 Years	5 Years	10 Years
< 3 MET-hours/week	172	128	41
3-18 MET-hours/week	267	188	93
> 18 MET-hours/week	159	130	46

Meyerhardt, J. A. et al. J Clin Oncol; 24:3527-3534 2006

Physical Activity Begun *After* Colon Cancer Diagnosis Reduces Risk >50%

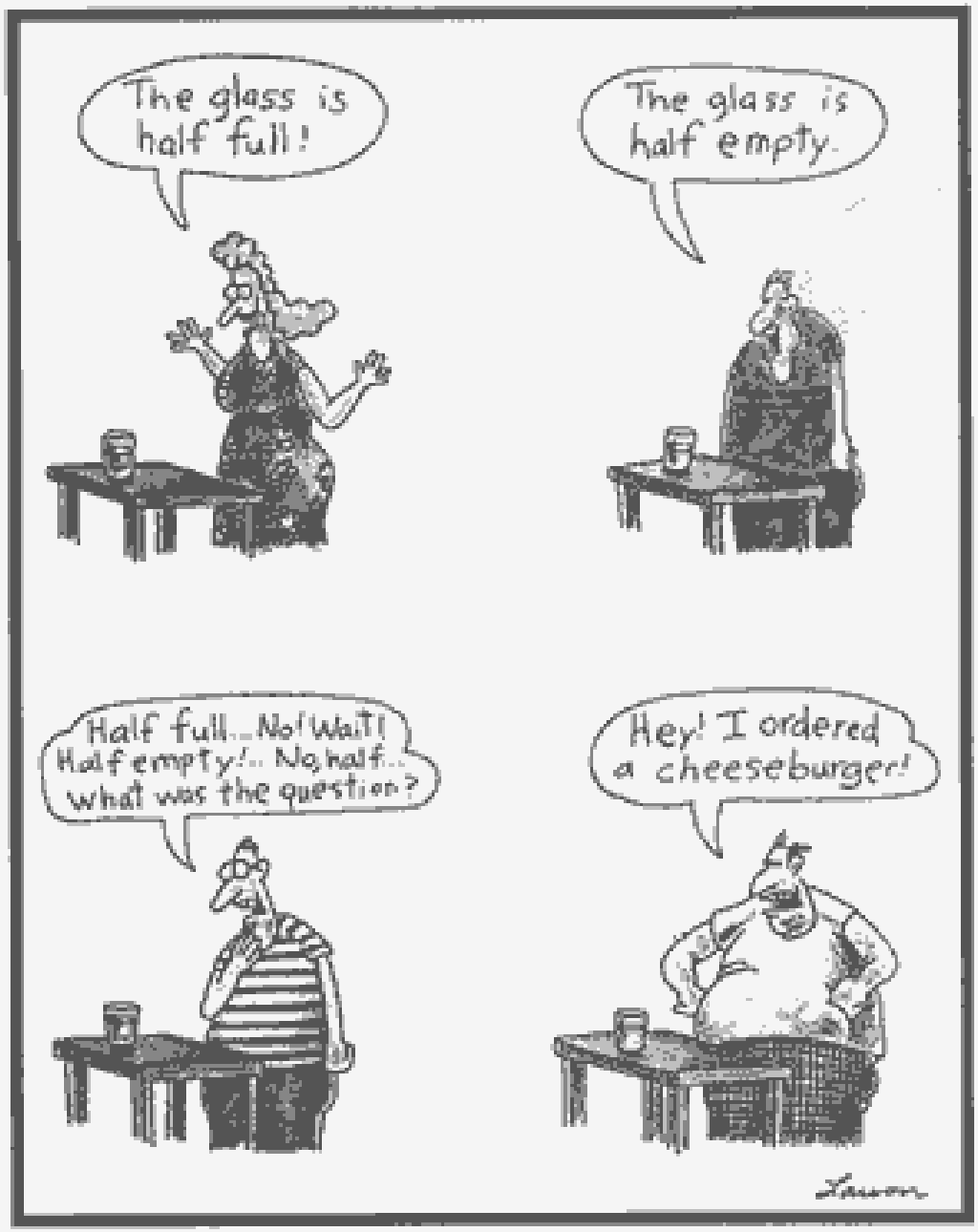


Meyerhardt, J. A. et al. J Clin Oncol; 24:3527-3534 2006

"The available evidence already urges medical oncologists to incorporate dietary habits and lifestyle attitudes as a prominent component of their breast cancer adjuvant treatment strategy."

"A not-only-drug approach to the science and practice of medical oncology has come of age"

Puntoni M et al J Clin Oncol 27: 323-325, 2009



The four basic personality types

Supplements

- Always Heal the GI Tract FIRST
  - 4R Program utilizing your personal favorites.
  - http://www.middlepathmedicine.com/Articles_and_Slides/Powerpoints_and_Audio/Digestive_Difficulties.pdf
  - Remember that many cancer patients are suffering from leaky gut and food allergies; consider ALCAT (or other food sensitivty testing) testing in all of your patients to help individualize your nutrition prescription.

Antioxidants in Oncology

- 19 trials, Randomized, Concurrent with Chemo Tx
- Survival or response reported
- Glutathione, Melatonin, Vit A, Vit C, Vit E, NAC, Ellagic Acid, Mixture
- None reported decrease in efficacy
- Many reported:
  - ✓Increased survival time
  - ✓Tumor response
  - ✓Fewer toxicities
- Larger studies with more statistical power are needed

Block et al. Cancer Treatment Reviews. 2007;33:407-18
PMID 17367938

Cancer Chemother Pharmacol. 2012 Jan 24.

The efficacy and safety of melatonin in concurrent chemotherapy or radiotherapy for solid tumors: a meta-analysis of randomized controlled trials.

Wang YM, Jin BZ, Ai F, Duan CH, Lu YZ, Dong TF, Fu QL.

Source

Department of Pharmacy, The First Affiliated Hospital of Xinxiang Medical University, 88 Jiankang Road, The City of Weihui, Xinxiang, Henan Province, China.

Abstract

BACKGROUND:

Recently, melatonin has been associated with cancer both in vitro and in vivo. However, the value of melatonin in the treatment of cancer remains disputable. Hence, we performed a systematic review of randomized controlled trials (RCTs) of melatonin in solid tumor cancer patients and observed its effect on tumor remission, 1-year survival, and side effects due to radiochemotherapy.

METHODS:

An electronic search was conducted using the databases Pubmed, Medline, EMBASE, Cochrane library, and CNKI, from inception to November 2011. Trials using melatonin as adjunct treatment concurrent with chemotherapy or radiotherapy for cancer were included. Pooled relative risk (RR) for the tumor remission, 1-year survival, and radiochemotherapy-related side effects were calculated using the software Revman 5.0.

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RESULTS:

The search strategy identified 8 eligible RCTs (n = 761), all of which studied solid tumor cancers. The dosage of melatonin used in the 8 included RCTs was 20 mg orally, once a day. Melatonin significantly improved the complete and partial remission (16.5 vs. 32.6%; RR = 1.95, 95% CI, 1.49-2.54; P < 0.00001) as well as 1-year survival rate (28.4 vs. 52.2%; RR = 1.90; 95% CI, 1.28-2.83; P = 0.001), and dramatically decreased radiochemotherapy-related side effects including thrombocytopenia (19.7 vs. 2.2%; RR = 0.13; 95% CI, 0.06-0.28; P < 0.00001), neurotoxicity (15.2 vs. 2.5%; RR = 0.19; 95% CI, 0.09-0.40; P < 0.0001), and fatigue (49.1 vs. 17.2%; RR = 0.37; 95% CI, 0.28-0.48; P < 0.00001). Effects were consistent across different types of cancer. No severe adverse events were reported.

CONCLUSIONS:

Melatonin as an adjuvant therapy for cancer led to substantial improvements in tumor remission, 1-year survival, and alleviation of radiochemotherapy-related side effects.

Low Dose Naltrexone

- www.lowdosenaltrexone.org
- Nighttime dosage of this narcotic antagonist leads to a brief suppression and subsequent dramatic increase in endorphins and enkephalins with subsequent improvement in cell regulation and apoptosis/ PCD.
- Contraindicated in patients on narcotics (morphine = love of death).
- My anecdotal experience.

Ascorbate and Cancer

- Induction of apoptosis
- Suppression of Hypoxia Inducible Factor, synergistic with HBOT
- Reduction of IGF
- Inhibition of COX-2

Ascorbate and Cancer:
Selective Toxicity of Ascorbate to Cancer Cells

Unique Aspects to Cancer Cell Metabolism:

- Dependent on glycolysis
- More glut receptors
- Deficient in catalases
- With high-dose IVC, ascorbate enters neoplastic cells at higher concentrations. Due to deficient catalase, H_2O_2 accumulates, damaging the cell.

Nutrients to Augment Vitamin C Efficacy

Alpha Lipoic Acid

- Improves intracellular ascorbic acid (AA) levels
- Complex absorption
- Although R-Lipoic Acid is the active enantiomer, S-Lipoic Acid may prevent polymerization of R-Lipoic Acid and therefore enhance overall bioavailability.
- Direct and indirect antioxidant mechanisms with no effect on hydrogen peroxide.
- Dosage: Alpha Lipoic Acid TR 300mg two times per day

Nutrients to Augment Vitamin C Efficacy

Acetyl-L-Carnitine

- Derivative of amino acids lysine and methionine
- Boosts glutathione levels, synergistic with Lipoic Acid and CoQ10
- Documented improvements in quality of life, increased tolerance of chemotherapy, facilitation of aerobic respiration leading to re-differentiation or apoptosis
- Dosage: 1,000mg three times a day

Nutrients to Augment Vitamin C Efficacy

Quercetin

- Well documented antiproliferative and apoptosis-inducing properties
- Works directly with the multidrug resistance (MDR) site
- As an MDR modulator, quercetin works as a unique chemosensitizer
- Dosage: 1,000mg three times per day

Antioxidants in Oncology

Summary:

- Novel regimens combining HDIVC with chemotherapy, botanicals, and other orthomolecular supplements unique to each tumor type will be necessary.
- HDIVC is only contraindicated with chemotherapy regimens including methotrexate or Bortezomib (Velcade), and TRAIL ligand.

GCMAF

- GCMAF.EU
- Nagalase (alpha-N-acetylgalactosaminidase) Nagalase is an extracellular matrix-degrading enzyme that is (increased) secreted by cancerous cells in the process of tumor invasion. It also is an intrinsic component of the envelope protein of various virions, such as HIV, Epstein-Barr virus (EBV), herpes zoster and the influenza virus. Thus, it is also secreted from virus-infected cells. http://www.europeanlaboratory.nl/

GCMAF

- Measuring nagalase and subsequent treatment with GCMAF and salicinium has dramatically affected my integrative oncology practice.
- Dose range of GOleic from 0.25 cc Q wk to 0.5 cc BIW (in my practice) others have used up t0 2 cc QD without side effects. Obvious cost limitations exist. PMID 23857228

Salicinium

- www.salicinium.com
- My first approach to overcoming nagalase has been GCMAF, but have found adding this agent orally or IV to be necessary for refractory cases.

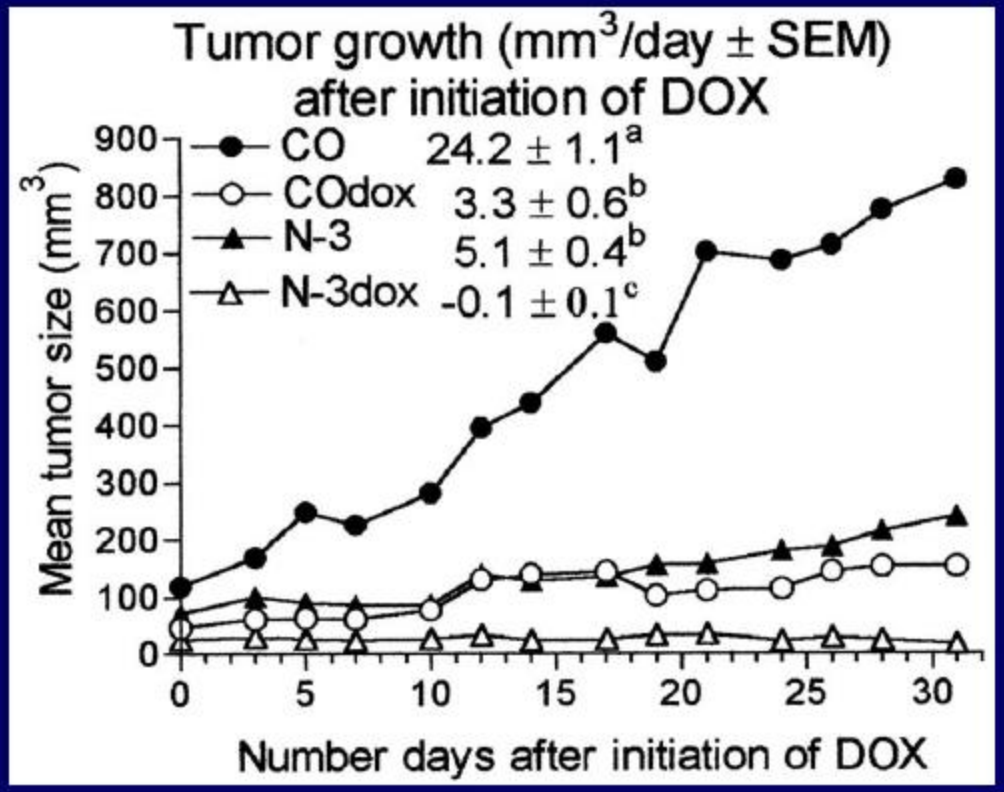
Palladium-Lipoic Complex

- www.polymva.com
- Both orally and IV this agent synergizes with our oncology protocols.
- I primarily use this agent in those refractory to HDIVC.

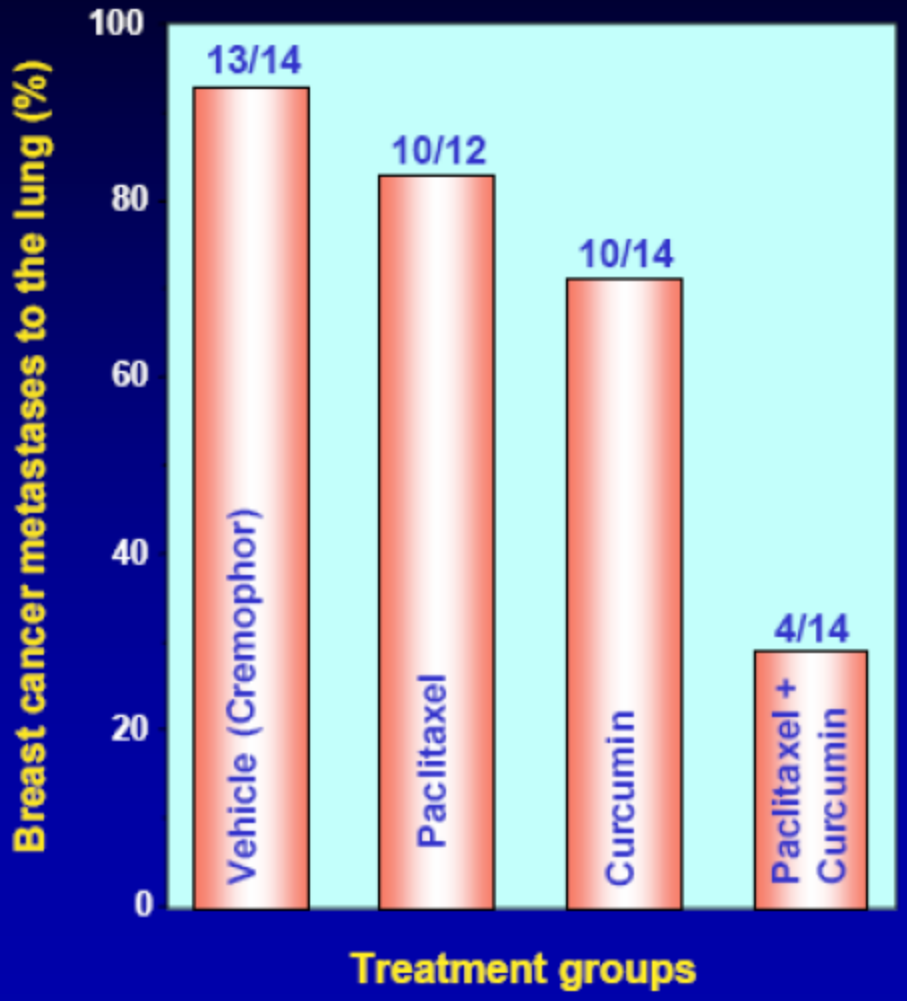
Supplements

- Supplements to Avoid:
  - Folate, methionine, and B-12 are all considered tumor promoters, a controversial subject.
  - Beta-carotene (when taken alone)- not mixed carotenoids- also considered a tumor promoter.
  - St. John's Wort- too many drug interactions
  - Controversial Supplements: NAC, glutathione, and tangeretin—as these supplements have mixed effects in different cancers and with different chemotherapy routines.

Breast Cancer Tumor Growth Doxorubicin + Diet N-3FA vs Corn Oil



Curcumin potentiates the effect of paclitaxel by suppressing the metastasis of the human breast cancer to the lung in mouse xenograft model



"We should write that spot down."