

OBESITY NUTRITION AND CANCER

You are what you eat

**Heart Attack Grill
Nathan's Hotdogs
Sneaky Pete**

Recommended Daily Calories



WESTERN DIET — LOTS OF PROCESSED FOODS, MEAT, ADDED FAT, SUGAR AND REFINED GRAINS — “INVARIABLY SUFFER FROM HIGH RATES OF THE SO-CALLED WESTERN DISEASES: OBESITY, TYPE 2 DIABETES, CARDIOVASCULAR DISEASE AND CANCER.” INDEED, 4 OF THE TOP 10 KILLERS OF AMERICANS ARE LINKED TO THIS DIET.



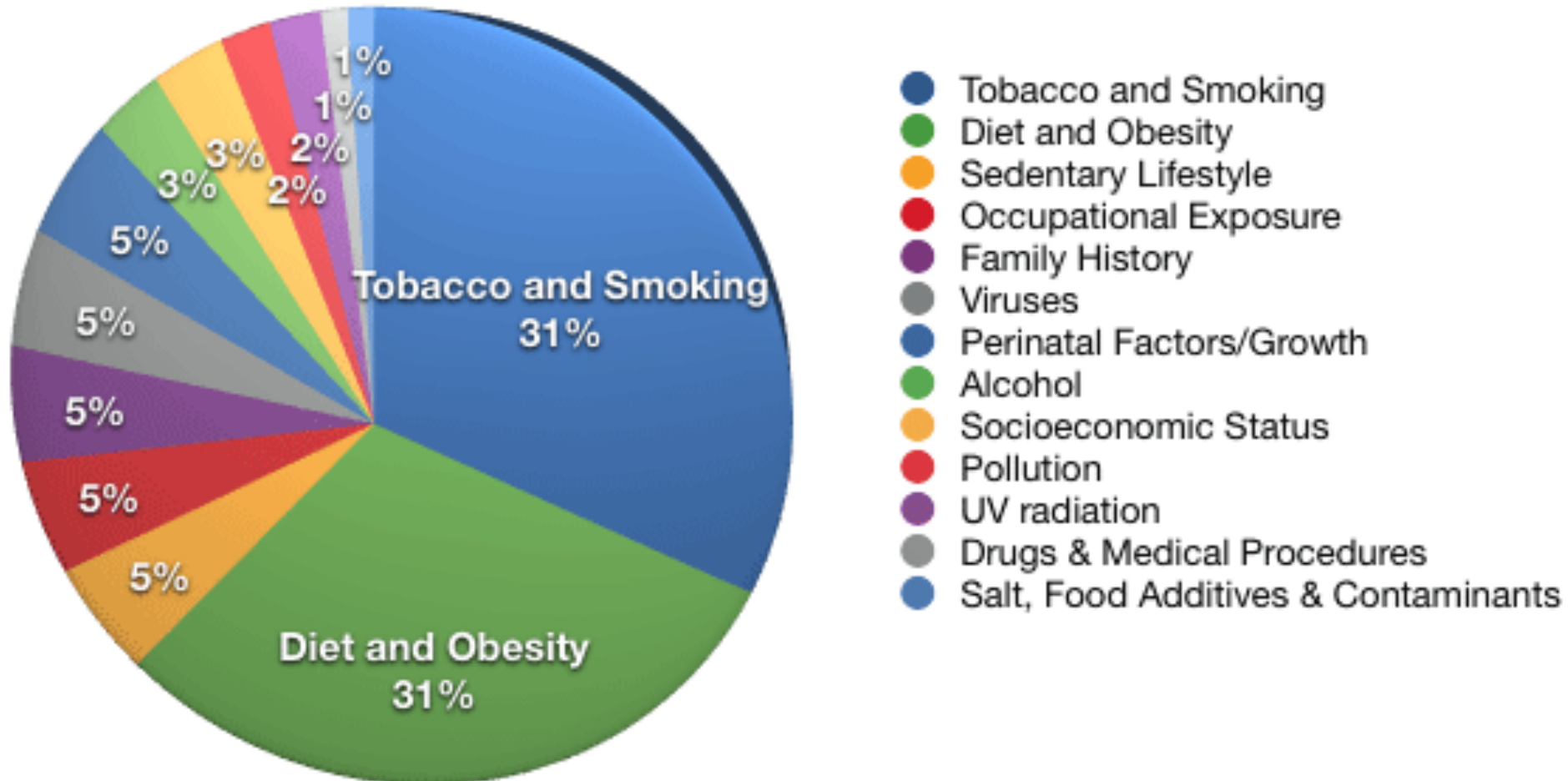
FOOD, CALORIES AND CANCER RISK

- ❑ MOST CHEMICALS ENCOUNTERED DAILY THROUGH INGESTION FROM FOODS **ORGANIC FOOD LOWERS CANCER RISK**
- ❑ CANCER RISK IS RELATED TO BOTH FOODS THAT INCREASE OR DECREASE
- ❑ DIETS RICH IN SATURATED FATS (ESP. RED MEATS) HAVE BEEN LINKED TO SEVERAL TYPES OF CANCERS (COLON, BREAST, PROSTATE)
- ❑ APPARENT LINKAGE IS BECAUSE FATS HAVE A HIGHER CALORIE CONTENT THAN OTHER NUTRIENTS



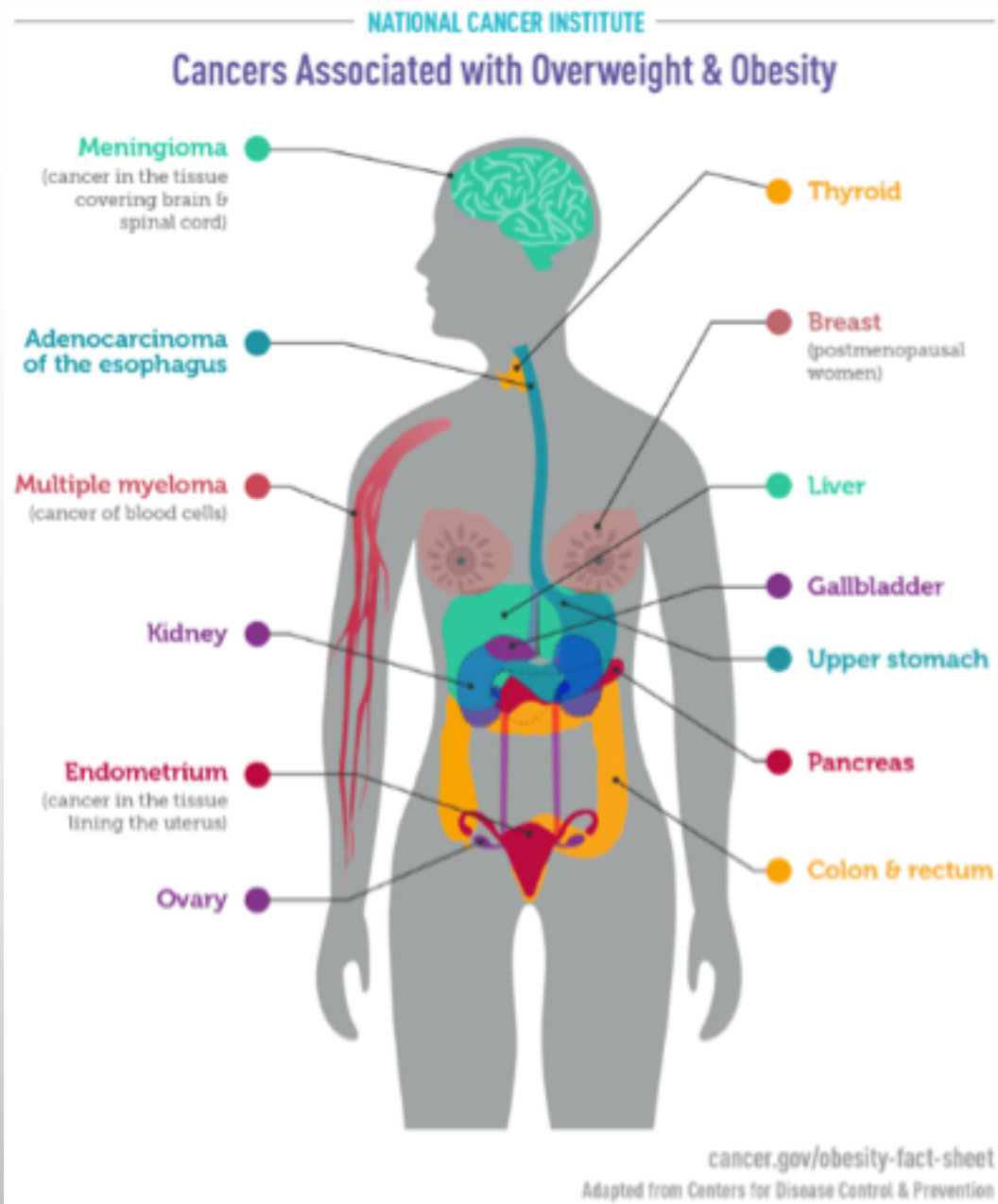
ESTIMATE OF CANCER DEATHS ATTRIBUTABLE TO DIFFERENT CAUSES

Risk Factors for Cancer

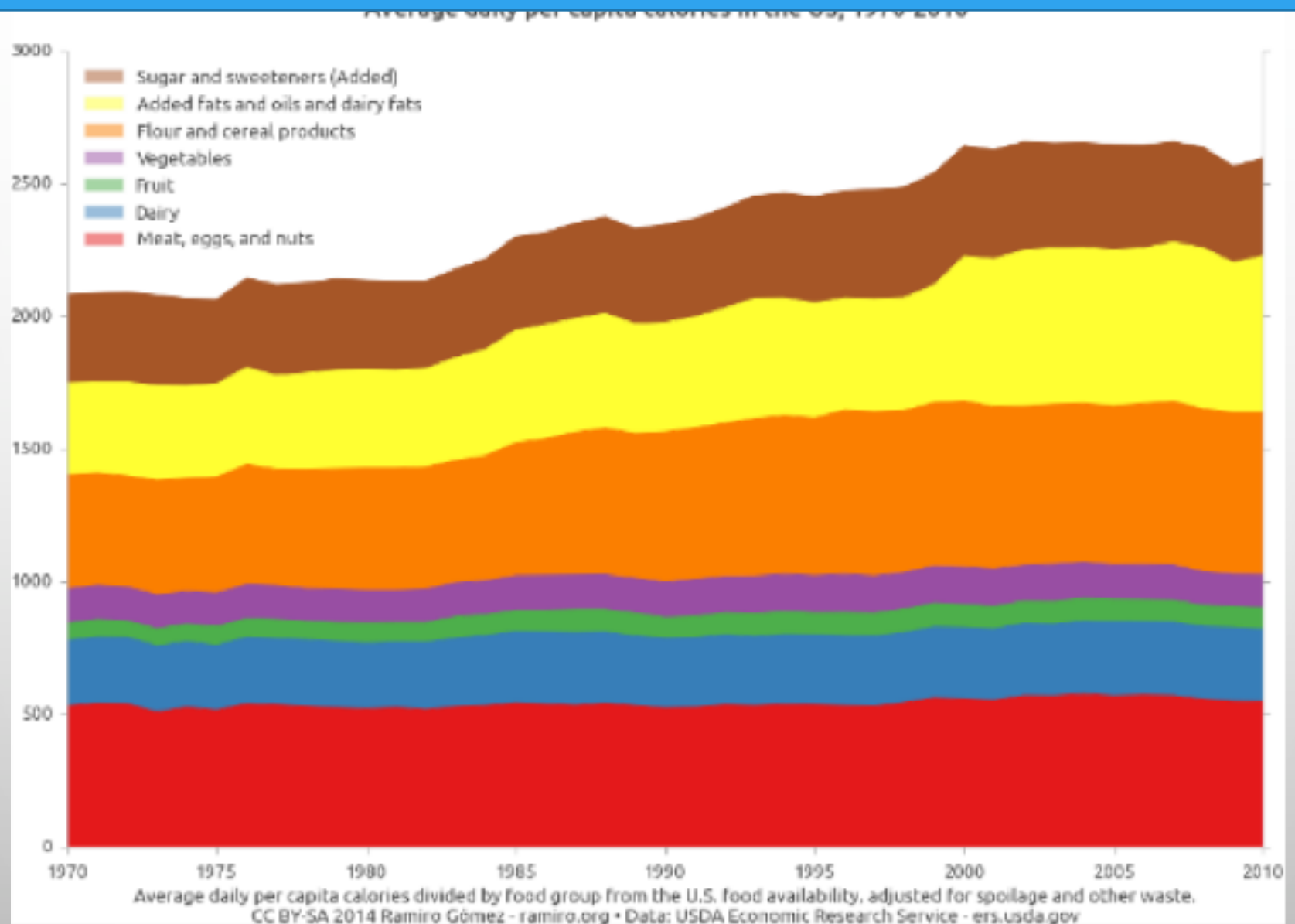


Source: World Cancer Research Fund, American Institute for Cancer Research, Food Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective

OBSERVATIONAL STUDIES LINK OBESITY TO A VARIETY OF CANCER TYPES



Changes Western Diet, Standard American Diet

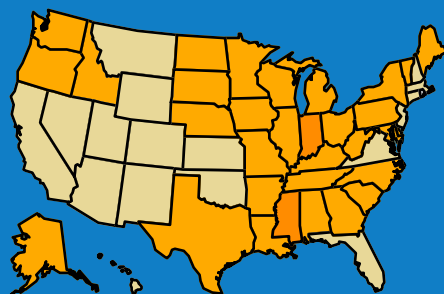




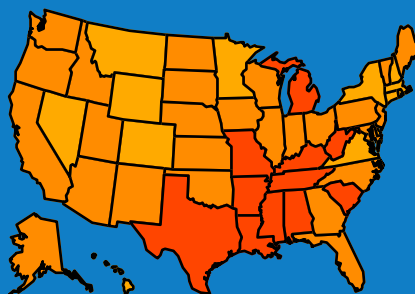
Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

Obesity (BMI ≥ 30 kg/m²)

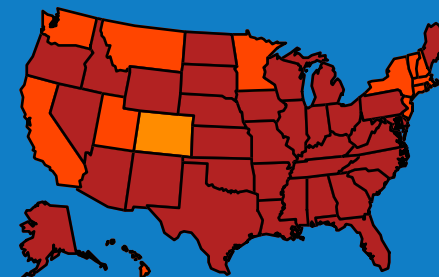
1994



2000



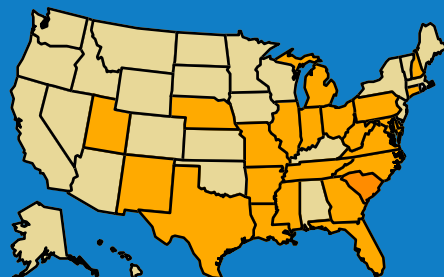
2015



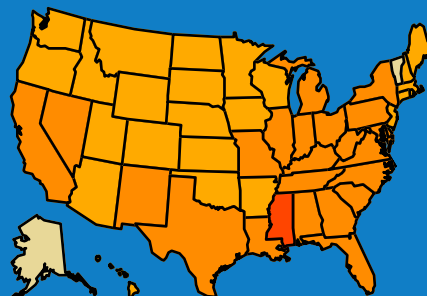
□ No Data <14.0% 14.0%–17.9% 18.0%–21.9% 22.0%–25.9% $\geq 26.0\%$

Diabetes

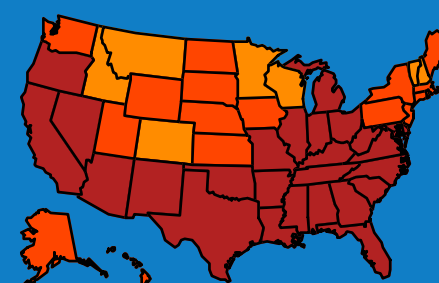
1994



2000



2015

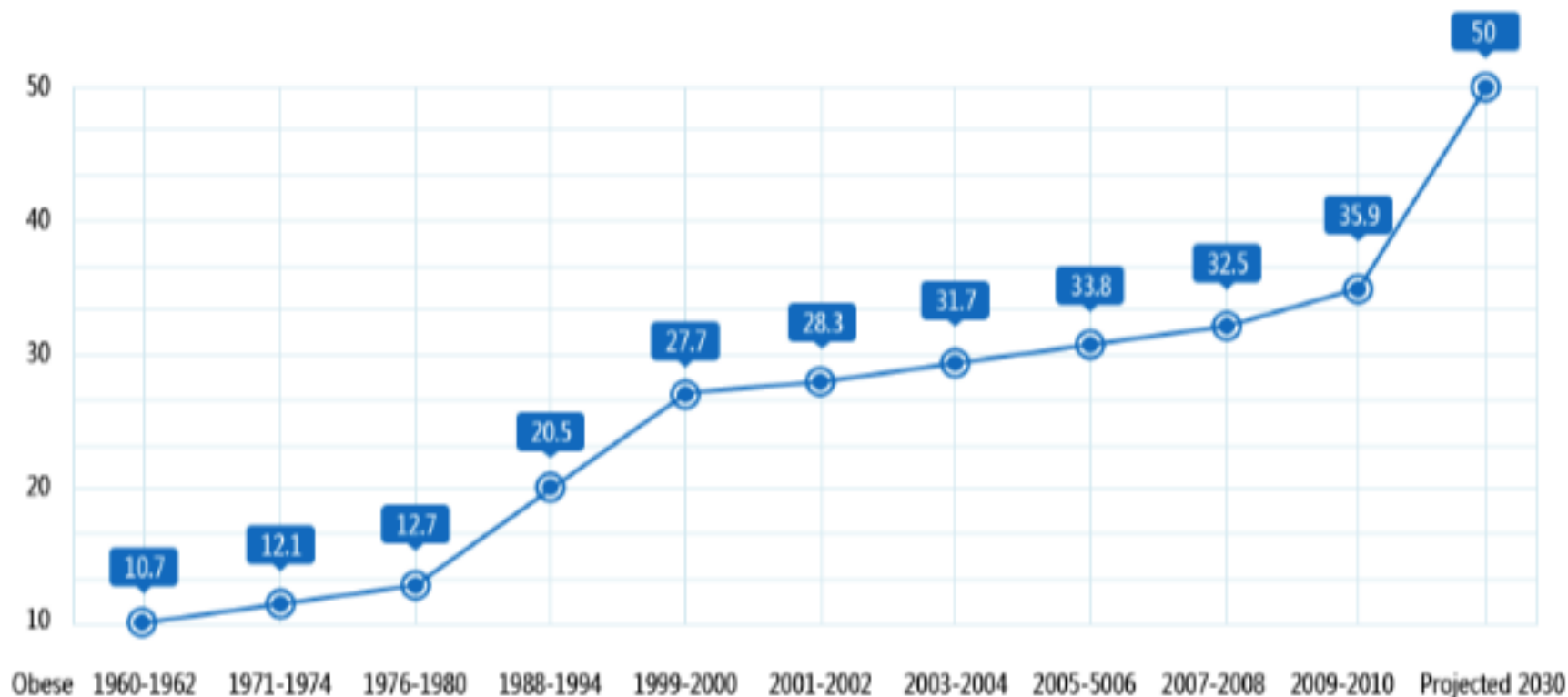


□ No Data <4.5% 4.5%–5.9% 6.0%–7.4% 7.5%–8.9% $\geq 9.0\%$

CDC's Division of Diabetes Translation. United States Surveillance System available at <http://www.cdc.gov/diabetes/data>



Prevalence of Obesity Among U.S. Adults Aged 20-74



Derived from NHANES data (http://www.cdc.gov/nchs/data/hestat/obesity_adult_09_10/obesity_adult_09_10.html#table1)

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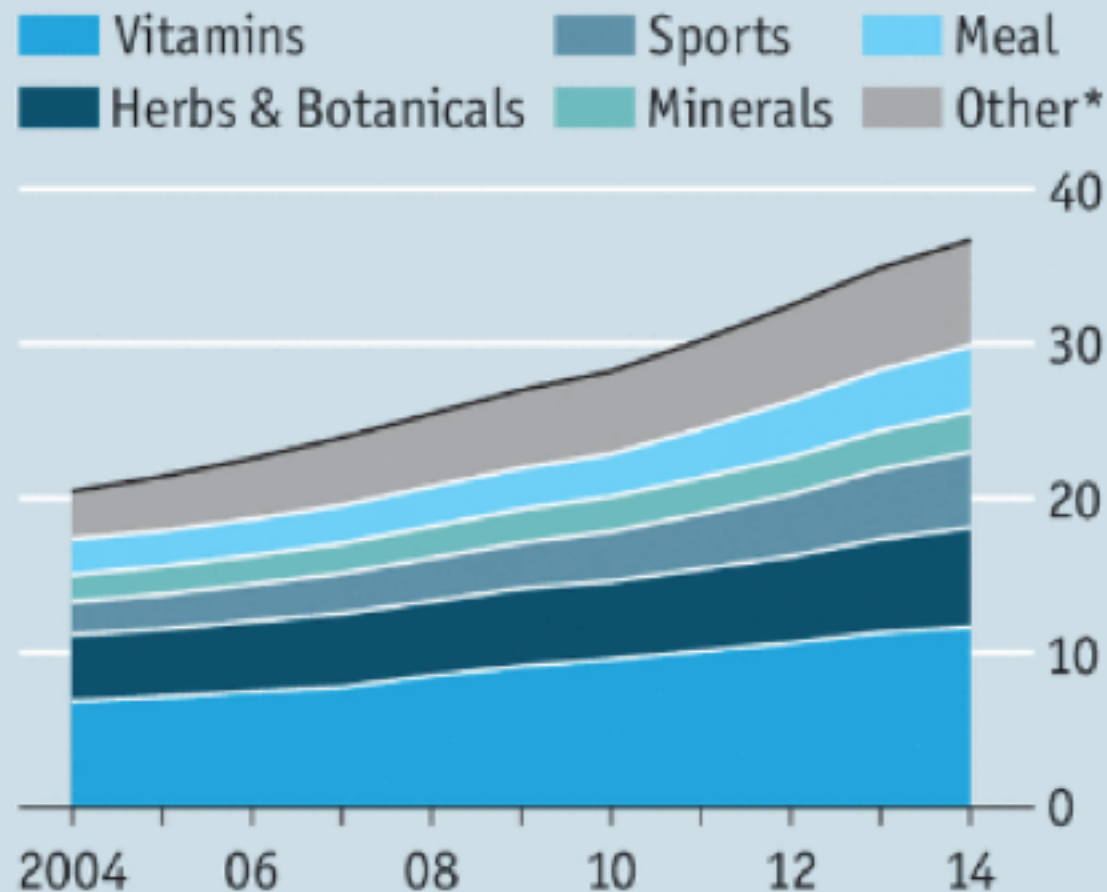
Enough Is Enough: Stop Wasting Money on Vitamin and Mineral Supplements VIEW

Despite sobering evidence of no benefit or possible harm, use of multivitamin supplements increased among U.S. adults from 30% between 1988 to 1994 to 39% between 2003 to 2006, while overall use of dietary supplements increased from 42% to 53% (9). Longitudinal and secular trends show a steady increase in multivitamin supplement use and a decline in use of some individual supplements, such as β -carotene and vitamin E. The decline in use of β -carotene and vitamin E supplements followed reports of adverse outcomes in lung cancer and all-cause mortality,

In conclusion, β -carotene, vitamin E, and possibly high doses of vitamin A supplements are harmful. Other antioxidants, folic acid and B vitamins, and multivitamin and mineral supplements are ineffective for preventing mortality or morbidity due to major chronic diseases. Although available evidence does not rule out small benefits or harms or large benefits or harms in a small subgroup of the population, we believe that the case is closed— supplementing the diet of well-nourished adults with (most) mineral or vitamin supplements has no clear benefit and might even be harmful. These vitamins should not be used for chronic disease prevention. Enough is enough.

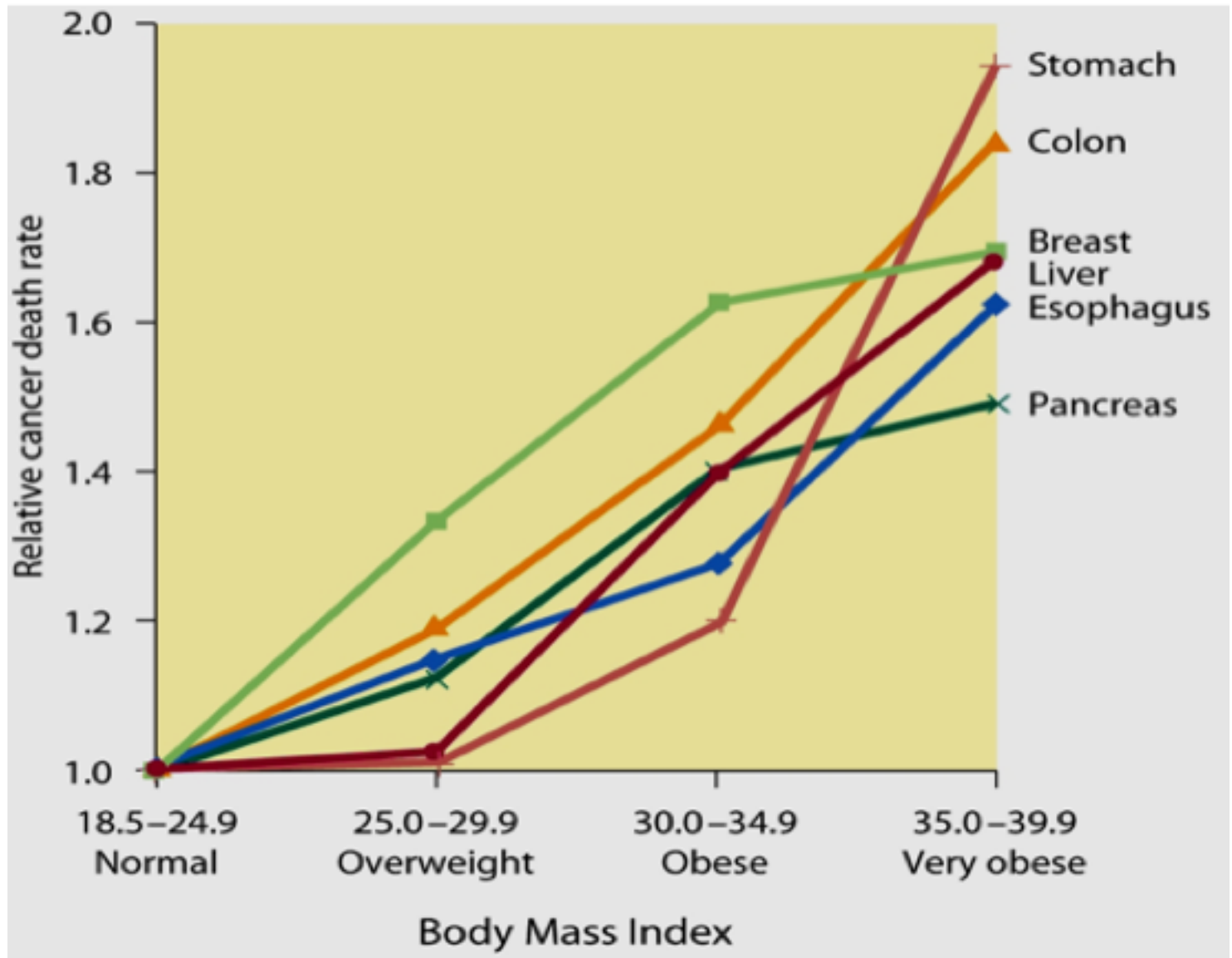
Eye-popping pill-popping

Supplements sales in US, \$bn



Source: Nutrition Business Journal *Fish oil and probiotics

BODY MASS INDEX AND CANCER



From L. J. Kleinsmith, *Principles of Cancer Biology*. Copyright (c) 2006 Pearson Benjamin Cummings.

Obesity's Link to Cancer

"Obesity is on its way to replacing tobacco as the number one preventable cause of cancer. We need to confront this growing problem and develop all the necessary tools to limit its impact." - Clifford Hudis, MD, 2013-2014 ASCO President

Obesity Increases Cancer Risk

Cancers Linked to Obesity

Men

Head/neck
Esophagus
Pancreas
Kidney
Colon
Rectum
Prostate



Women

Head/neck
Esophagus
Breast
Pancreas
Kidney
Colon
Rectum
Endometrium



In 2007, more than **84,000** new cancer cases were due to obesity.

The percentage of cancer cases attributed to obesity varies, but is as high as **40%** for some cancers, particularly esophageal and endometrial.



Overweight/obesity contributes to as many as **1 in 5** cancer-related deaths.

Mechanisms Linking Obesity and Cancer



Obese people often have increased levels of **insulin** and insulin-like growth factor-1 (IGF-1) in their blood, which may promote the development of certain tumors.



Fat tissue produces higher amounts of **estrogen**, which may drive development of certain obesity-related cancers, including estrogen-sensitive breast cancers and endometrial cancer.

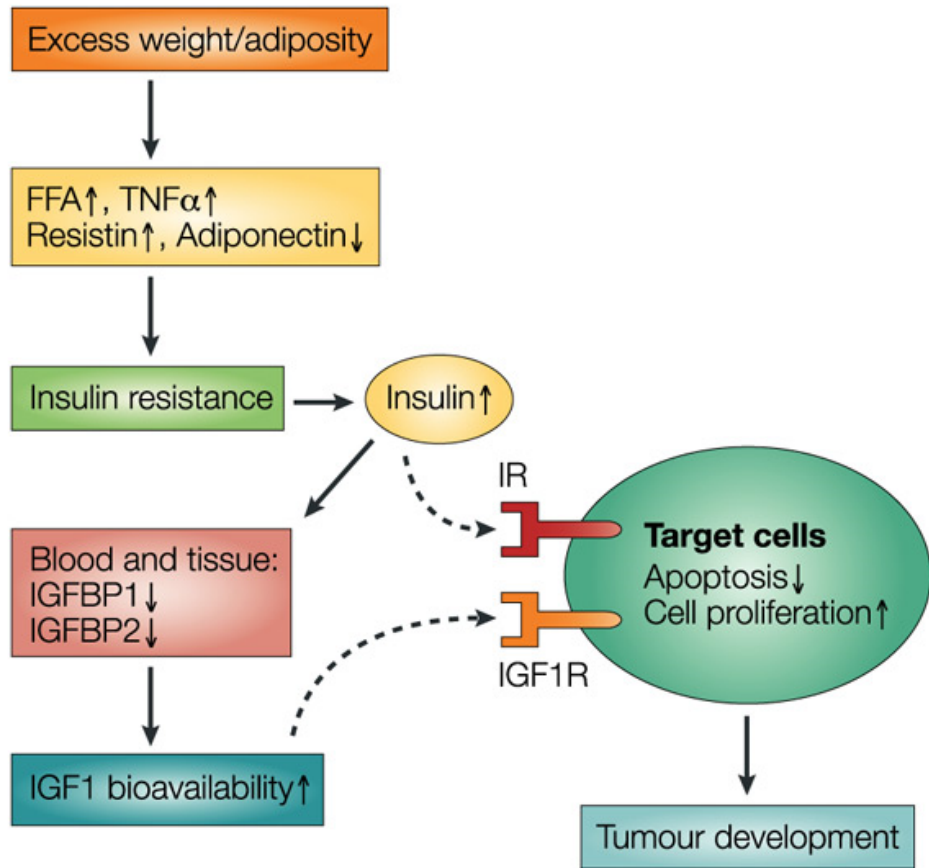


Obese people often have chronic low-level, or "subacute," **inflammation**, which has been associated with increased cancer risk.

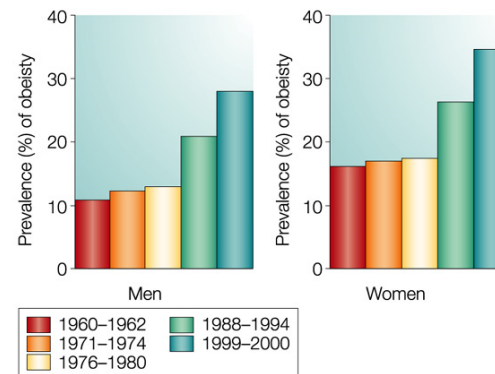
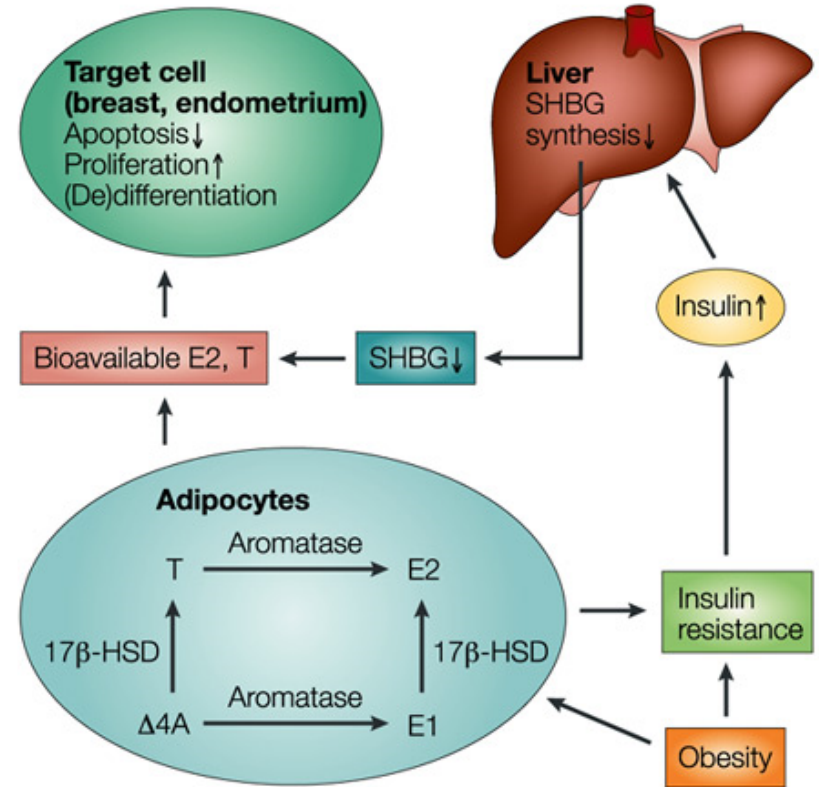


Fat cells (adipocytes) may also have effects on certain tumor growth regulators.

PROPOSED MECHANISM OF OBESITY & CANCER



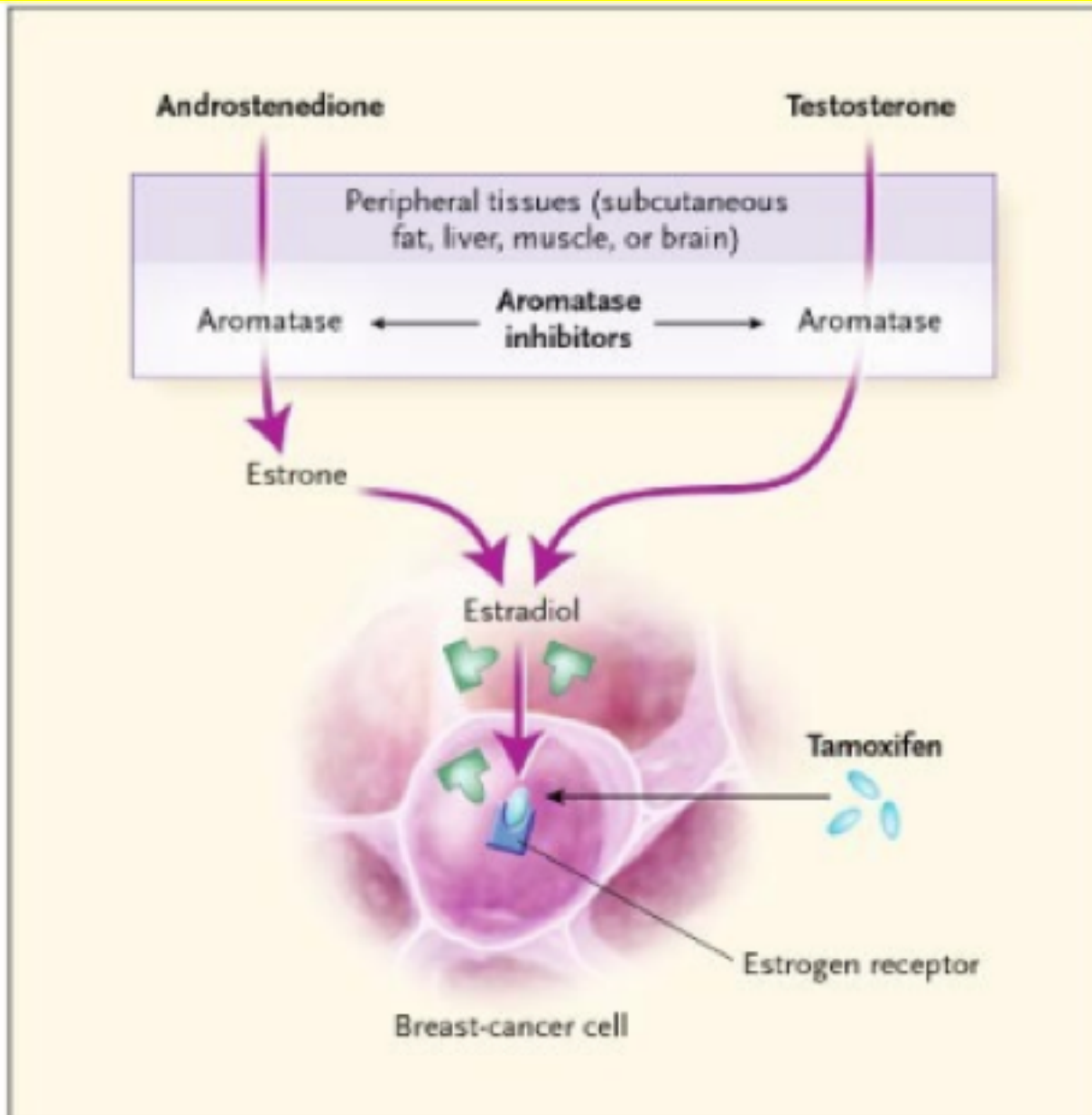
Nature Reviews | Cancer



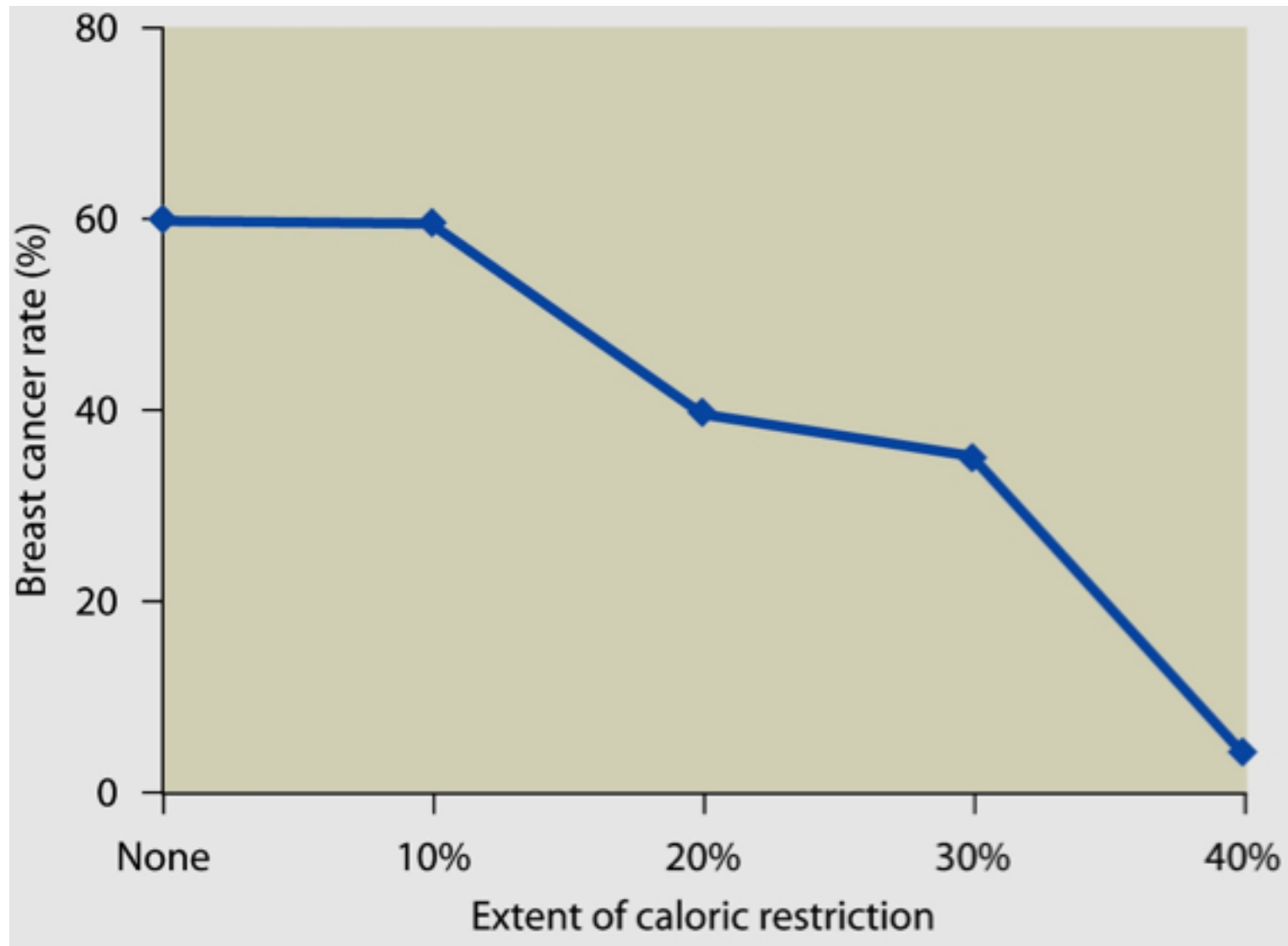
Nature Reviews | Cancer

Nature Reviews | Cancer

Hormone Therapy for postmenopausal ER+ Breast Cancer



INFLUENCE OF CALORIC INTAKE ON CANCER RISK



From L. J. Kleinsmith, *Principles of Cancer Biology*. Copyright (c) 2006 Pearson Benjamin Cummings.

CALORIE RESTRICTION, DIET AND AGING



Jeff Miller/University of Wisconsin-Madison

Canto, left, a 27-year-old rhesus monkey, is on a restricted diet, while Owen, 29, is not. The two monkeys are part of a study of the links between diet and aging.

By ROGER COHEN

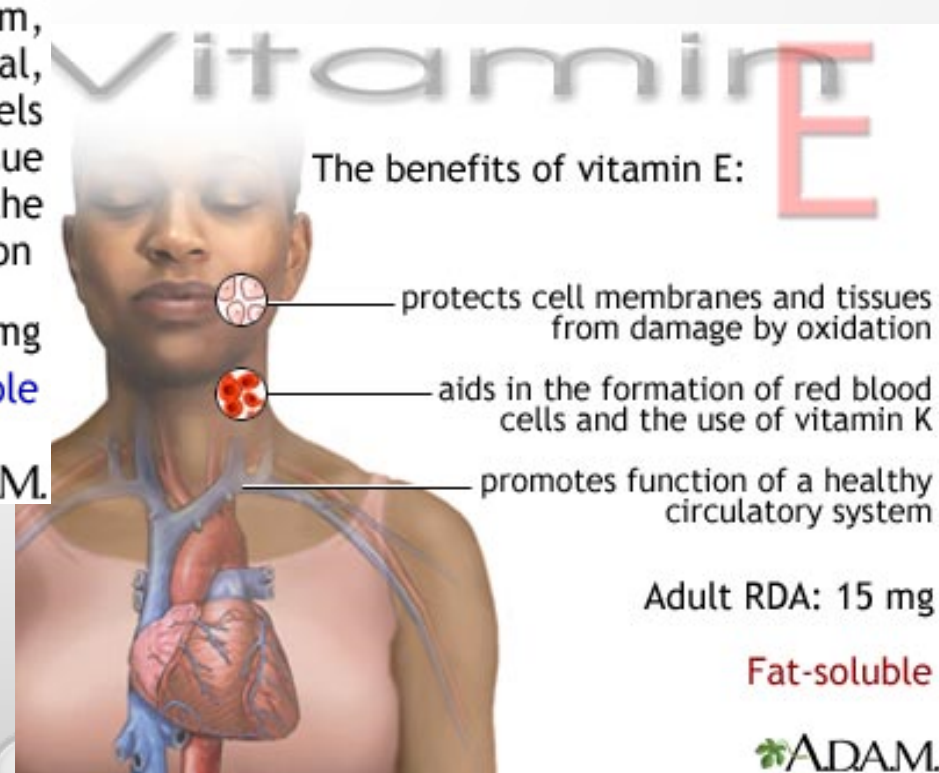
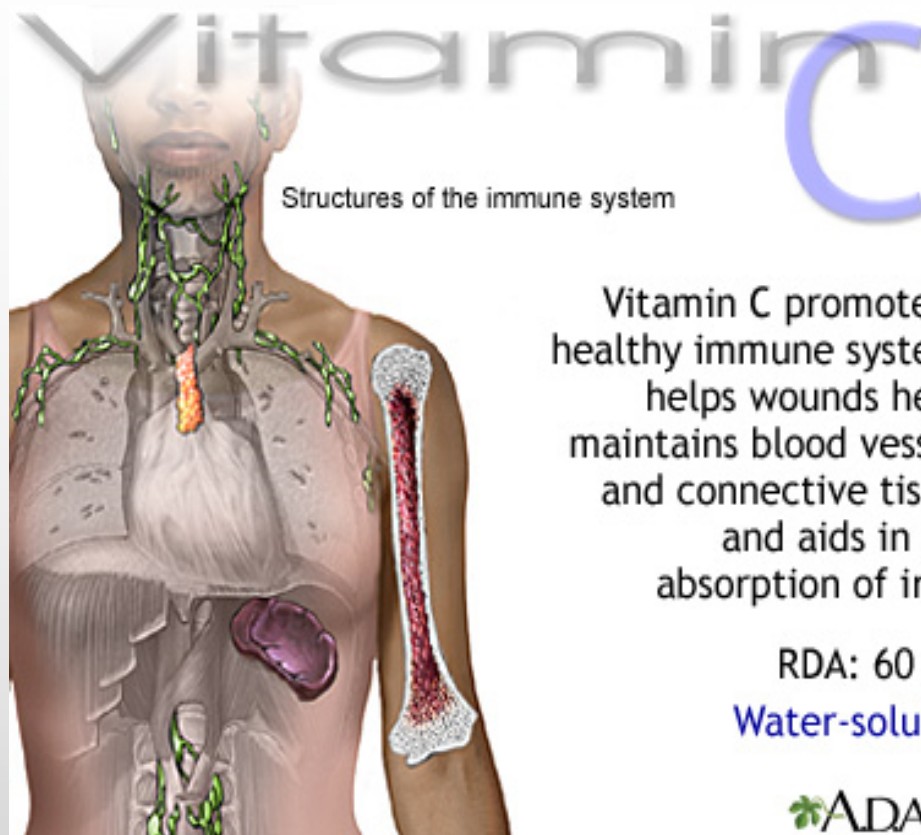
Published: July 15, 2009

 TWITTER

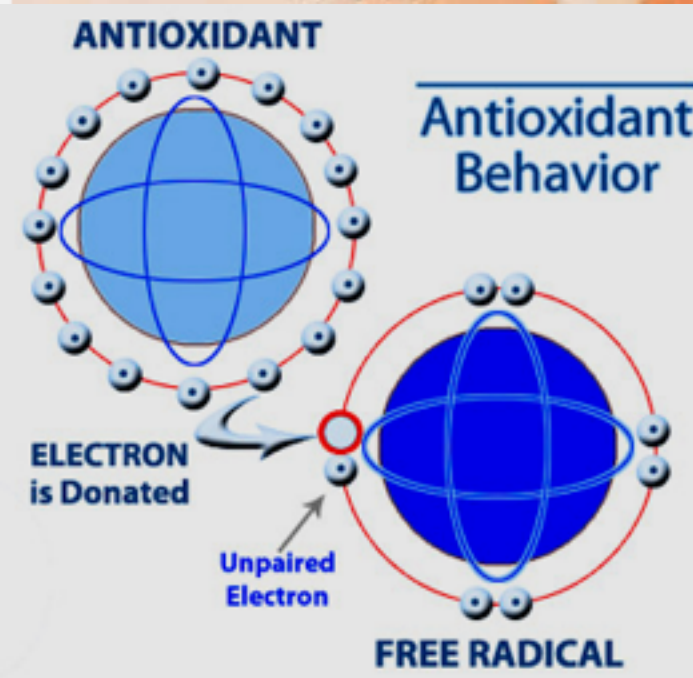
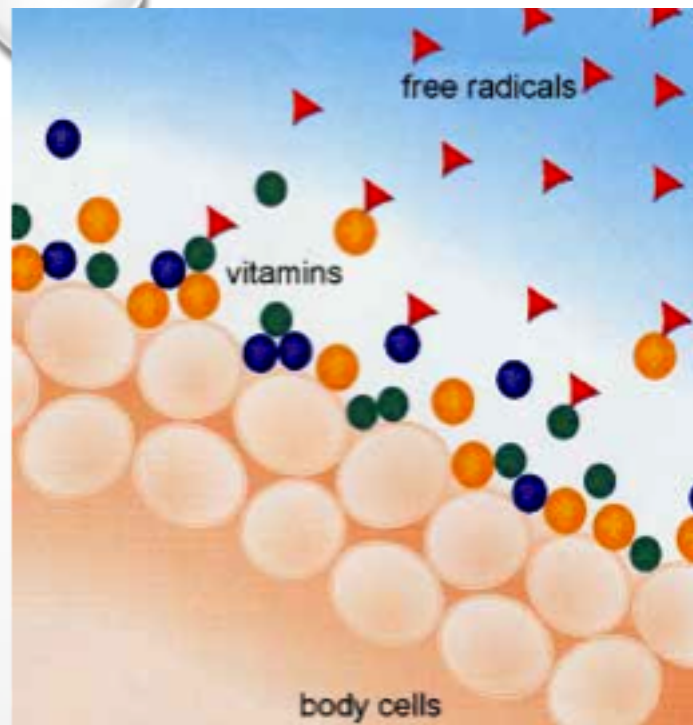
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BENEFITS OF SOME VITAMINS WITH ANTIOXIDANT PROPERTIES

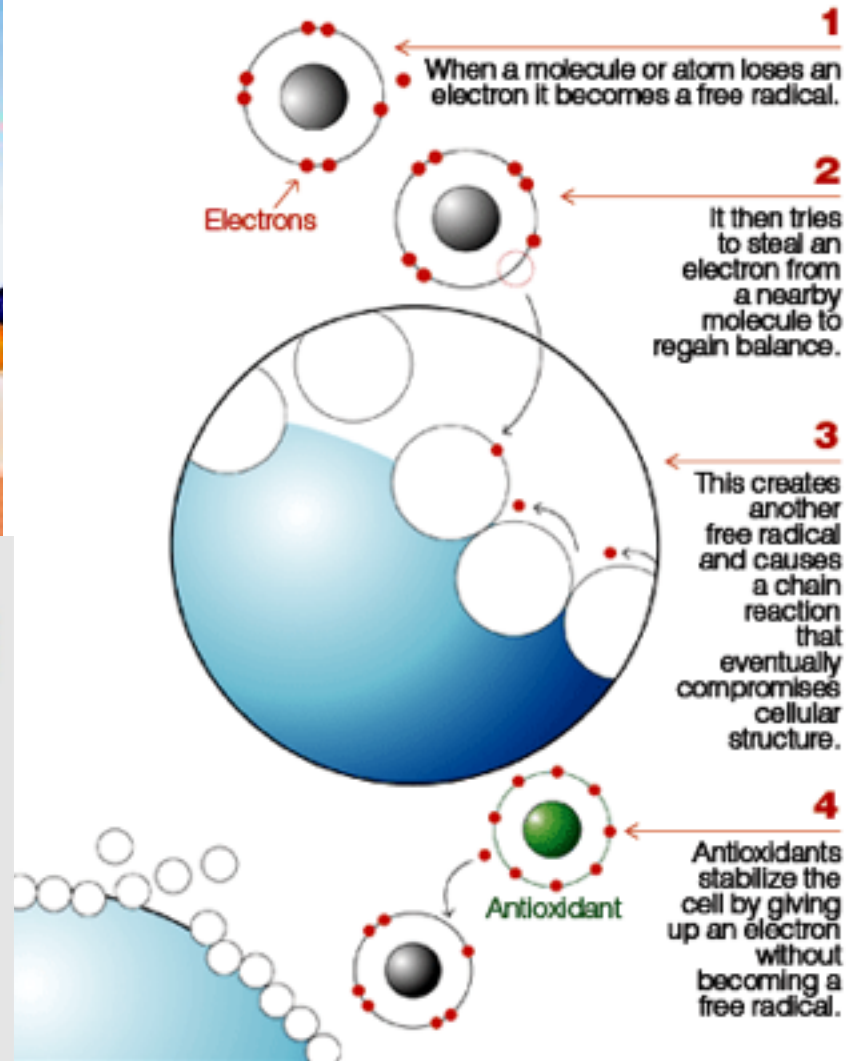


Counteracting Free Radicals with Antioxidants



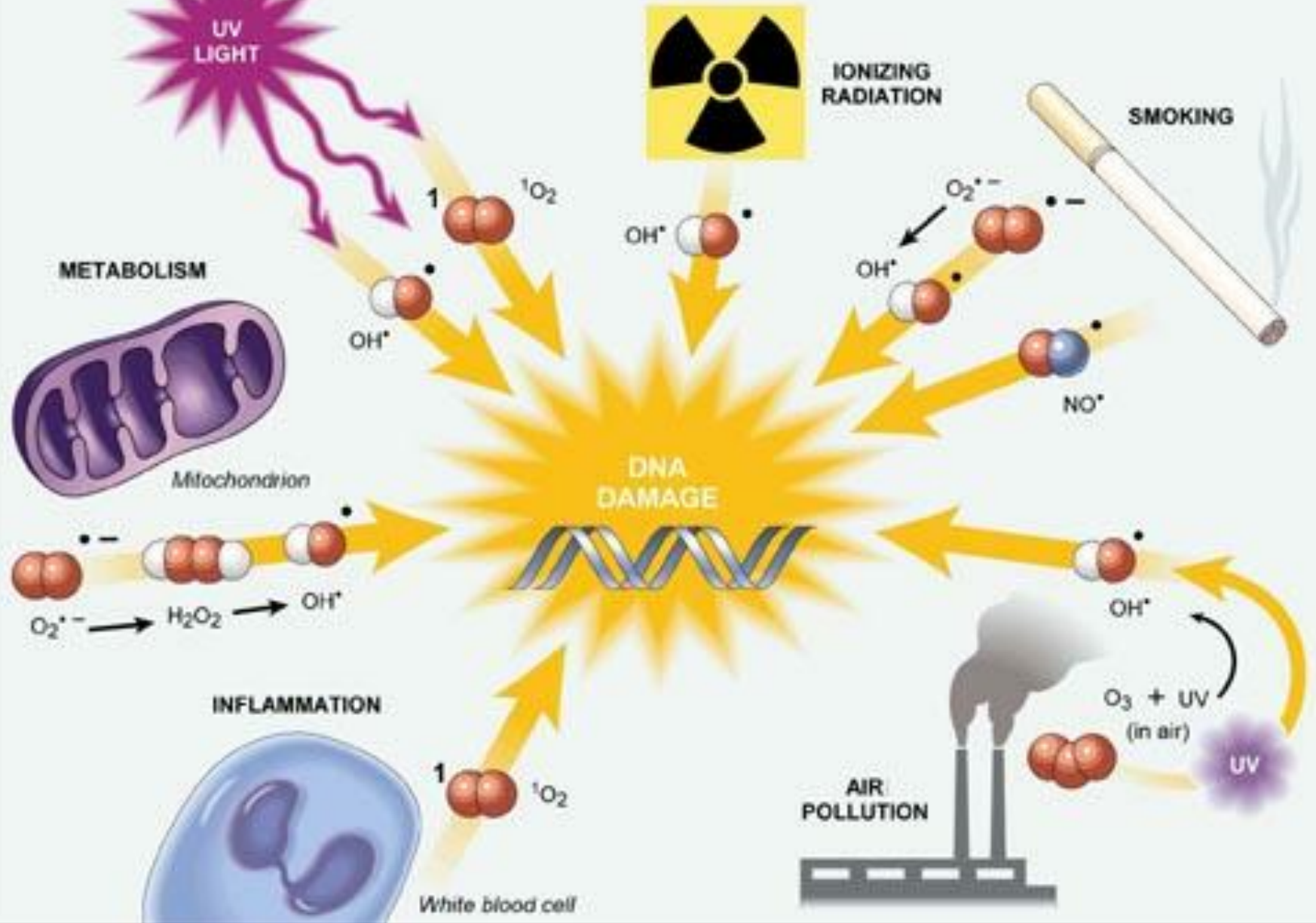
WHAT IS A FREE RADICAL?

Every time your body undergoes stress - from sunburn to scotch - you produce renegade molecules called free radicals

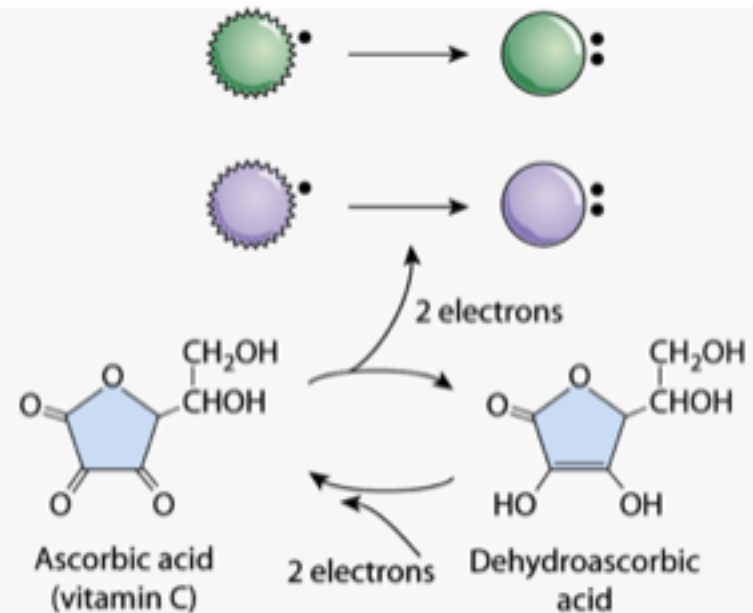
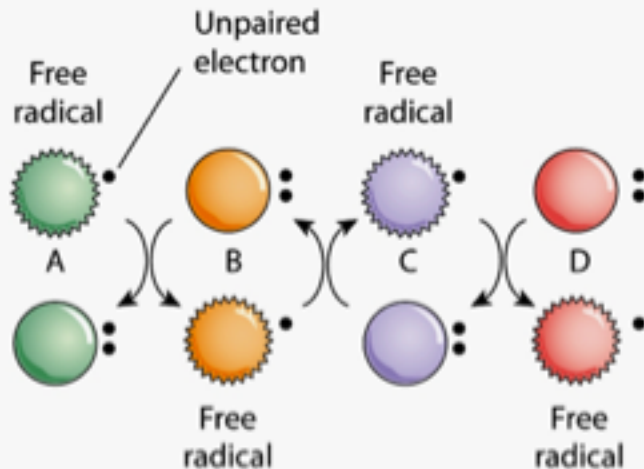


Producing too many free radicals can damage your cells, tissues, and organs. You can protect your cells from free radical damage by eating foods that are high in antioxidants, such as colorful fruits and vegetables.

FORMATION OF FREE RADICALS



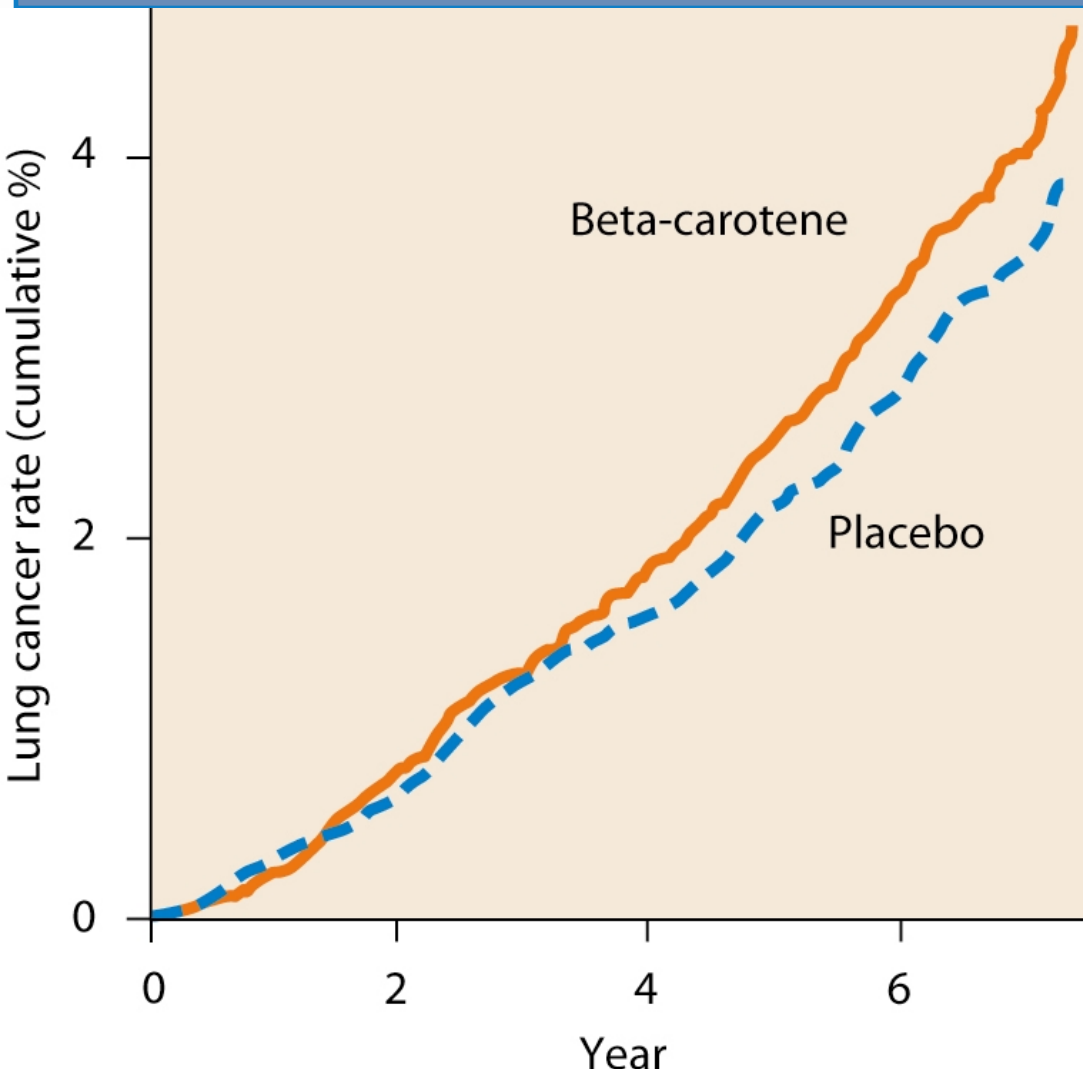
FREE RADICALS AND ANTIOXIDANTS



(a) Free radical cascade. A free radical (A) is a highly unstable substance that quickly attacks another nearby molecule (B), taking an electron that it needs to gain stability. Upon losing an electron, the second molecule also becomes a free radical and removes an electron from a third molecule (C), creating a chain reaction that can cause considerable damage within a cell, including DNA mutations.

(b) Example of an antioxidant. Antioxidants halt free radical reactions by donating their own electrons to free radicals without becoming unstable in the process. Shown here is ascorbic acid (vitamin C), which donates electrons to free radicals and undergoes oxidation to dehydroascorbic acid in the process. Dehydroascorbic acid is then converted back to ascorbic acid through a simple metabolic reaction and the process is repeated again.

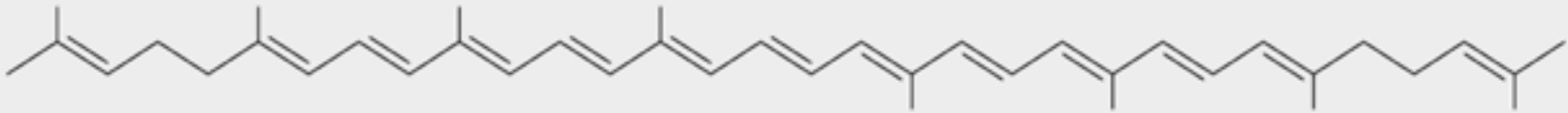
EFFECT OF VITAMIN A ON LUNG CANCER RATES IN MALE SMOKERS



☐ **C**ONSUMING VEGETABLES AND FRUITS THAT CONTAIN BETA-CAROTENE MAY BE HELPFUL, BUT HIGH-DOSE BETA-CAROTENE SUPPLEMENTS MAY ACTUALLY BE HARMFUL, ESPECIALLY FOR CIGARETTE SMOKERS

**More is not better
Hawkeye**

Tomatoes



Lycopene

Inhibit tumor formation; enhance detoxification

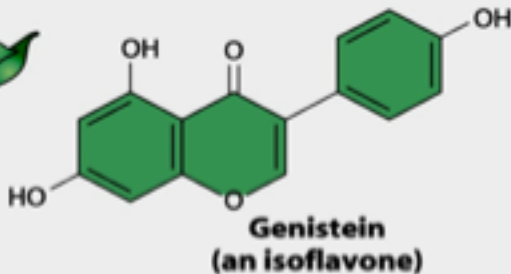
Broccoli

CS(=O)CCCCN=C=S

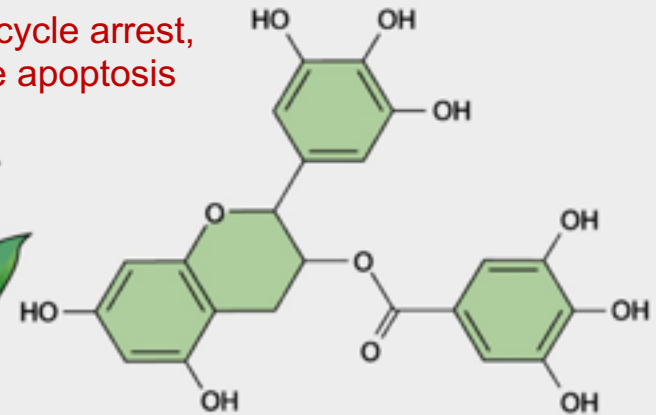
Sulforaphane
(an isothiocyanate)

Anti-estrogen at high conc. Phytoestrogen at low conc.

Soybeans



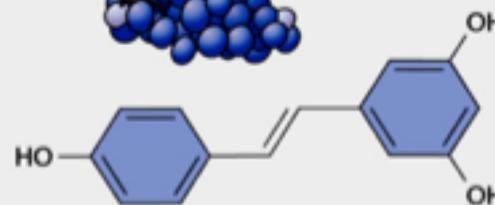
Green tea



Epigallocatechin gallate (EGCG)

Antioxidant, inhibit inflammation,
DNA mutation, cell growth

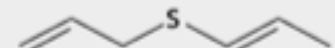
Grapes



Resveratrol

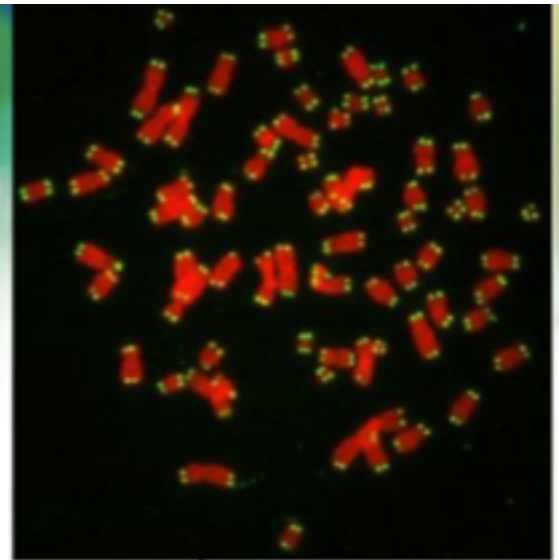
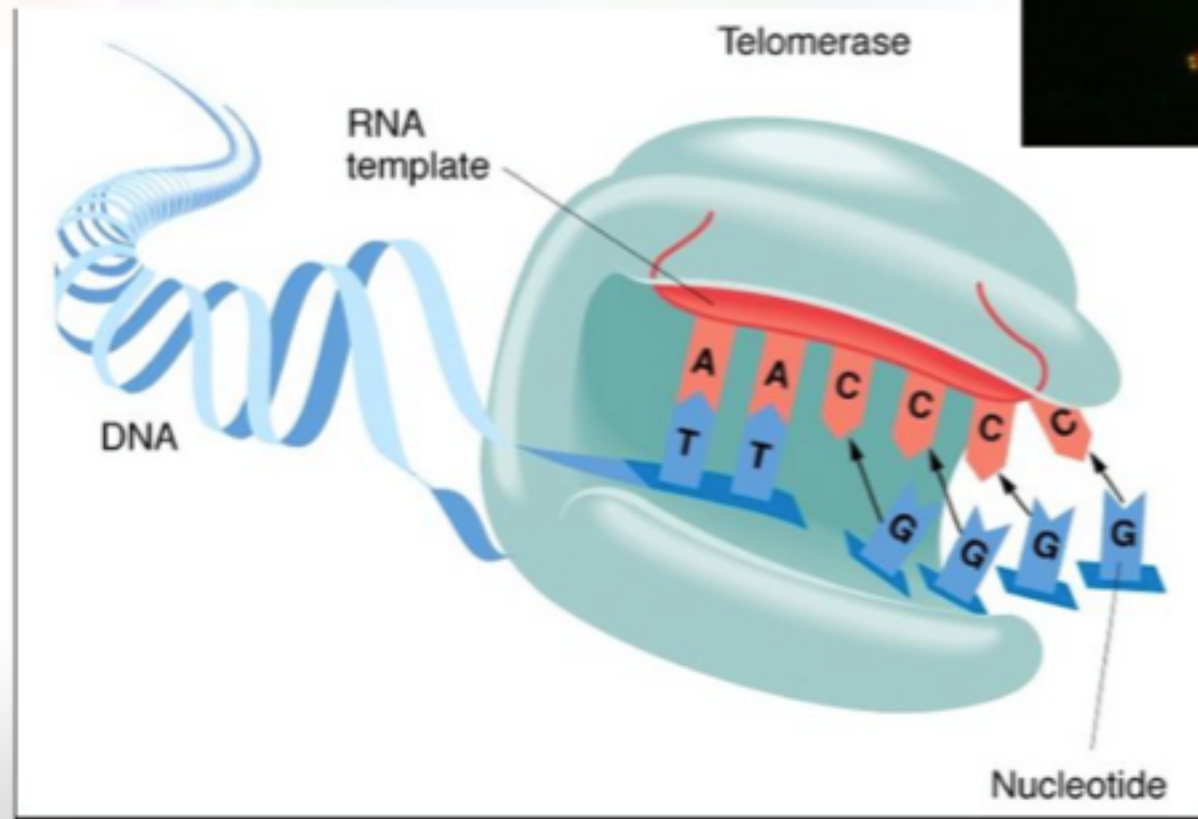
Reduce stomach, colon & prostate cancers

Garlic



Diallyl sulfide

Telomeres and telomerase



Selective death of cancer cells by preferential induction of reactive oxygen species in response to (-)-epigallocatechin-3-gallate.

Min NY, Kim JH, Choi JH, Liang W, Ko YJ, Rhee S, Bang H, Ham SW, Park AJ, Lee KH.

Department of Life Science, College of Natural Science, Chung-Ang University, Seoul 156-756, Republic of Korea.

Abstract

(-)-Epigallocatechin-3-gallate (EGCG) induces apoptosis in cancer cells without adversely affecting normal cells. Understanding the cancer-specific cytotoxic activity of EGCG is very important in defining the mechanism of tumorigenesis and identifying superb chemotherapeutic agents against cancer. We comparatively assayed human telomerase reverse transcriptase (hTERT)-mediated apoptosis by EGCG-induced reactive oxygen species (ROS) in normal cells and cancer cells. EGCG showed differential levels of ROS induction between the cell types; ROS, especially hydrogen peroxide, was highly induced in cancer cells, while it was not in normal cells. In addition, the higher level of ROS down-regulated hTERT via binding of CCCTC binding factor (CTCF) to the core promoter region of hTERT, which repressed hTERT expression. CTCF binding was epigenetically controlled by the demethylation of the previously hypermethylated site for CTCF, which was induced by down-regulation of DNA methyltransferase 1 (DNMT1). In contrast, hTERT down-regulation was not observed in normal cells. These results suggest that preferential death of cancer cells by EGCG could be caused by the cancer-specific induction of ROS and epigenetic modulation of expression of apoptosis-related genes, such as hTERT.

- EGCG from green tea
- Cancer magic bullet
- Telomerase induced apoptosis short telomeres

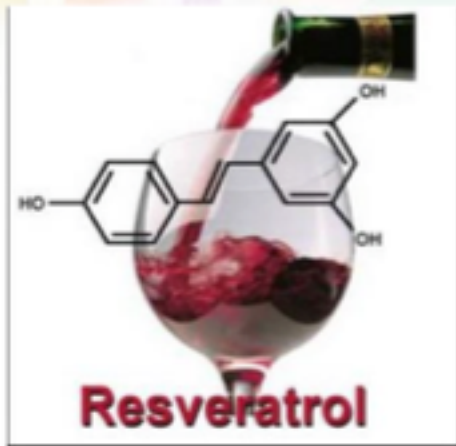
Green Tea Extract Cost Man His Liver, Atty Claims as Trial Opens ...

CVN News (blog) - Mar 28, 2019

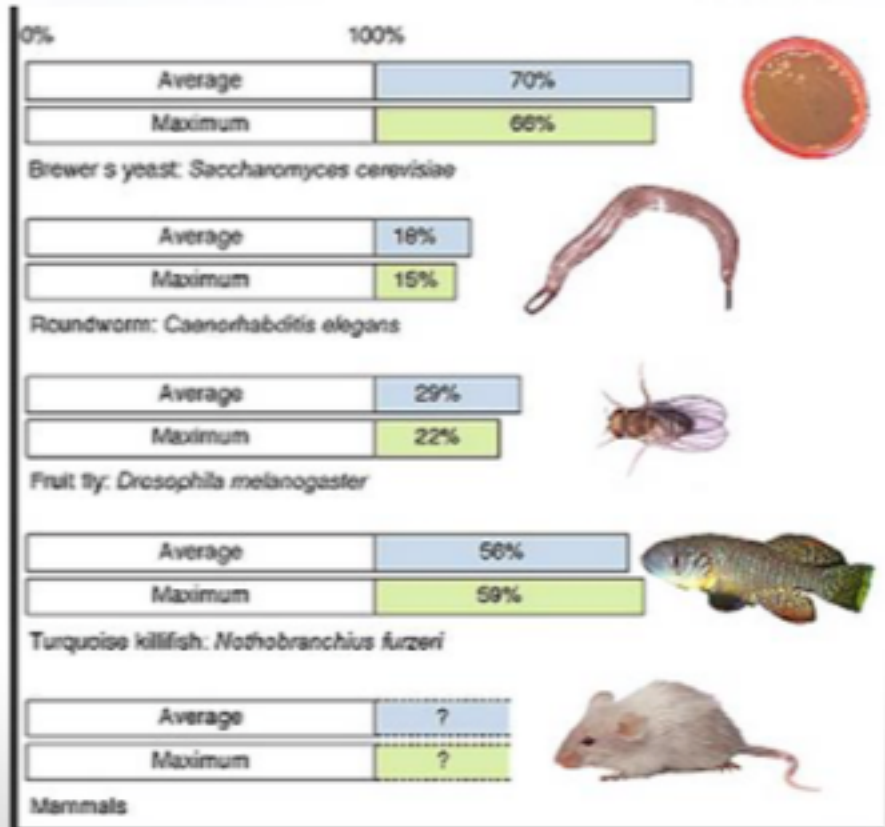
James McCants, then 50, was forced to undergo a liver transplant in July 2014, months after he began taking **green tea extract supplements** ...



Wine is good !

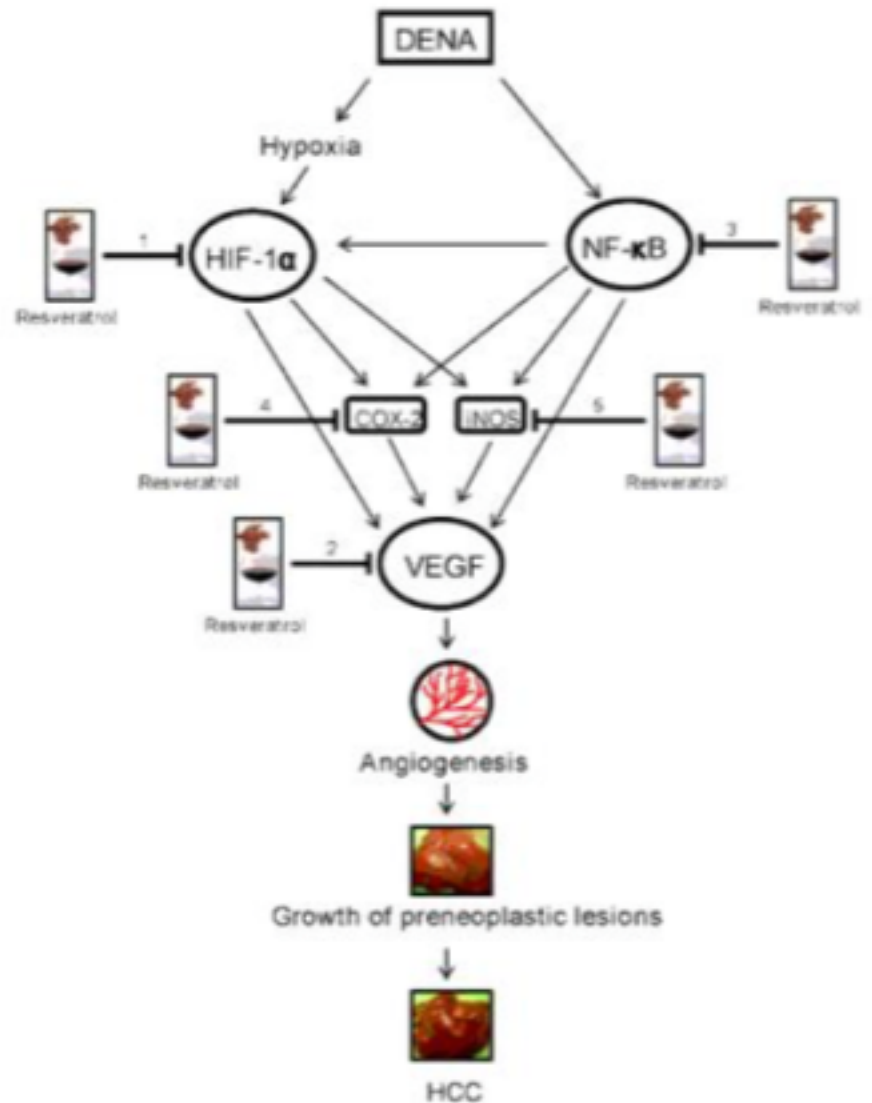


- Found in grapes and other fruits and nuts
- Purified



Resveratrol Potential mechanism

- Bioavailability
- Animal models
- Cell lines
- ? Humans?



Too Good To Be True? Anti-Aging Proteins Not So Potent After All

But in a new report in *Nature*, scientists at the Institute of Health Ageing at the University College London say the foundational work connecting sirtuins to longer life in animals was flawed. The main problem, the authors write, is that the experiments didn't take into account the effects of other genes that might have influenced longevity. And some of these effects, they say, might differ between lab-bred animals and their naturally occurring, or 'wild' counterparts.

When the authors of the *Nature* paper, led by David Gems, reproduced the early studies in worms and flies and accounted for other genetic factors that could impact longevity, the effect of sirtuins disappeared.

The researchers also tested whether fruit fly sirtuin could be activated by resveratrol — with no luck. And they concluded that the life-extending effect of calorie restriction was not in fact due to sirtuins.

"Studies on yeast lifespan were the first to cast doubt on the role of sirtuins in longevity," noted the authors of an accompanying commentary in *Nature*, **reported** the AFP. The new study "puts a final nail in the coffin."

OBESITY CANCER LINKS

Several possible mechanisms have been suggested to explain the association of obesity with increased risk of certain cancers:

- Fat tissue produces excess amounts of estrogen, high levels of which have been associated with the risk of breast, endometrial, and some other cancers.
- Obese people often have increased levels of insulin and insulin-like growth factor-1 (IGF-1) in their blood (a condition known as hyperinsulinemia or insulin resistance), which may promote the development of certain tumors.
- Fat cells produce hormones, called adipokines, that may stimulate or inhibit cell growth. For example, leptin, which is more abundant in obese people, seems to promote cell proliferation, whereas adiponectin, which is less abundant in obese people, may have antiproliferative effects.
- Fat cells may also have direct and indirect effects on other tumor growth regulators, including mammalian target of rapamycin (mTOR) and AMP-activated protein kinase.
- Obese people often have chronic low-level, or "subacute," inflammation, which has been associated with increased cancer risk.