Putting Cancer Risks from Food in Perspective

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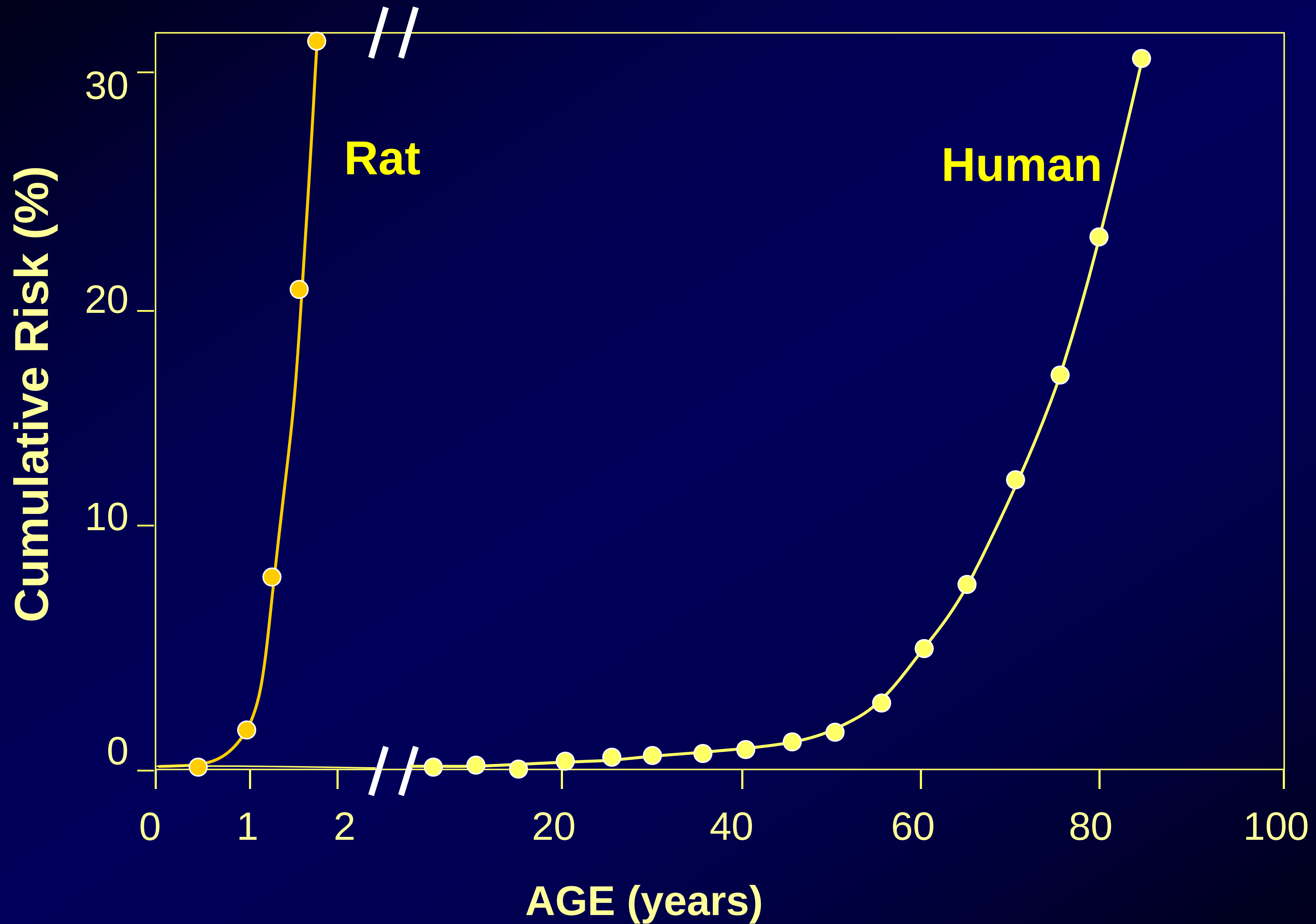
14May 2013
Istanbul

Cumulative Net Risk of Death from Cancer for Rat and Human



The Causes of Cancer

~30% Smoking
~35% Unbalanced Diets
- Too Many Calories: Obesity
- Too Little Fiber & Micronutrients

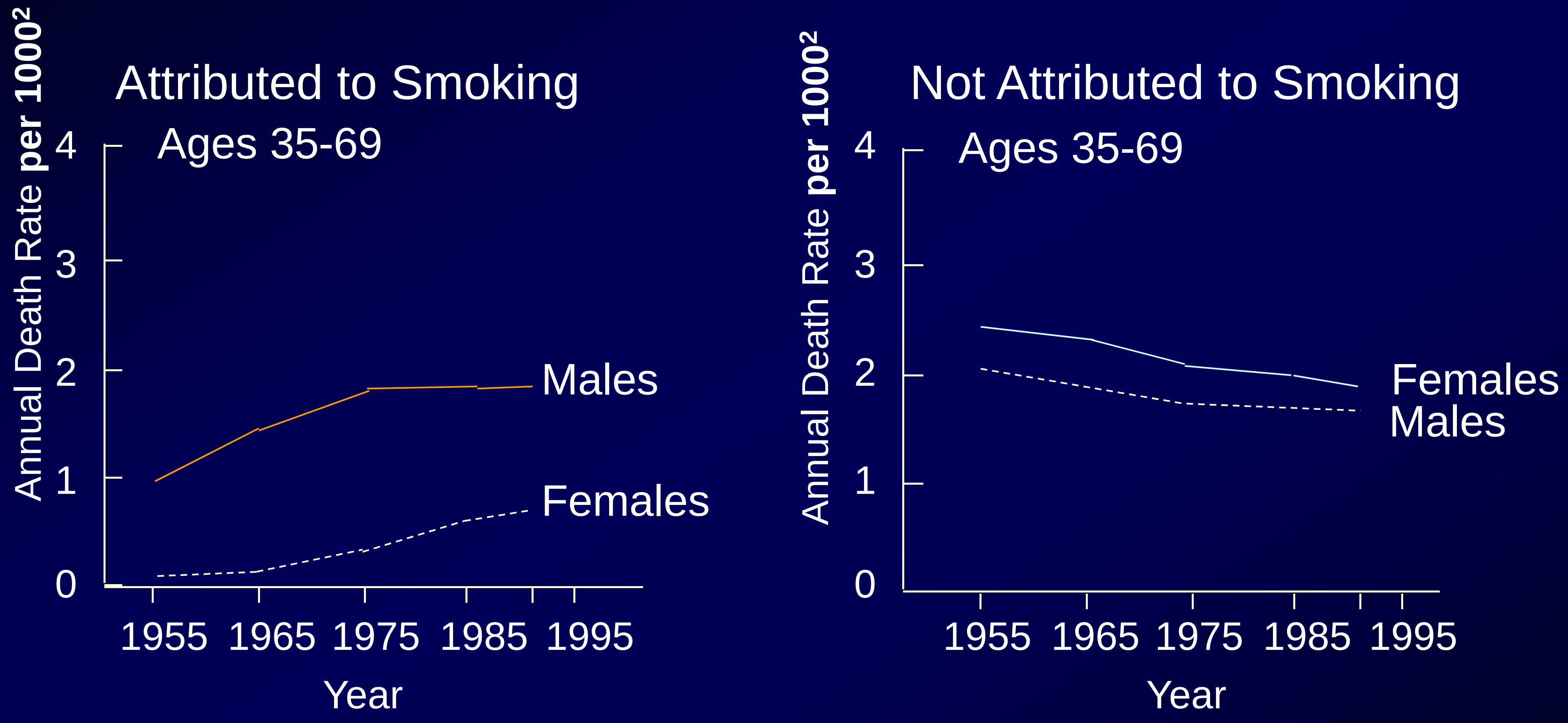
~20% Chronic Infections
- Mostly in Poor Countries

~20% Hormones
- Breast, Endometrial, Etc.

~2% Occupation
<1% Pollution
- Mostly Heavy Air Pollution

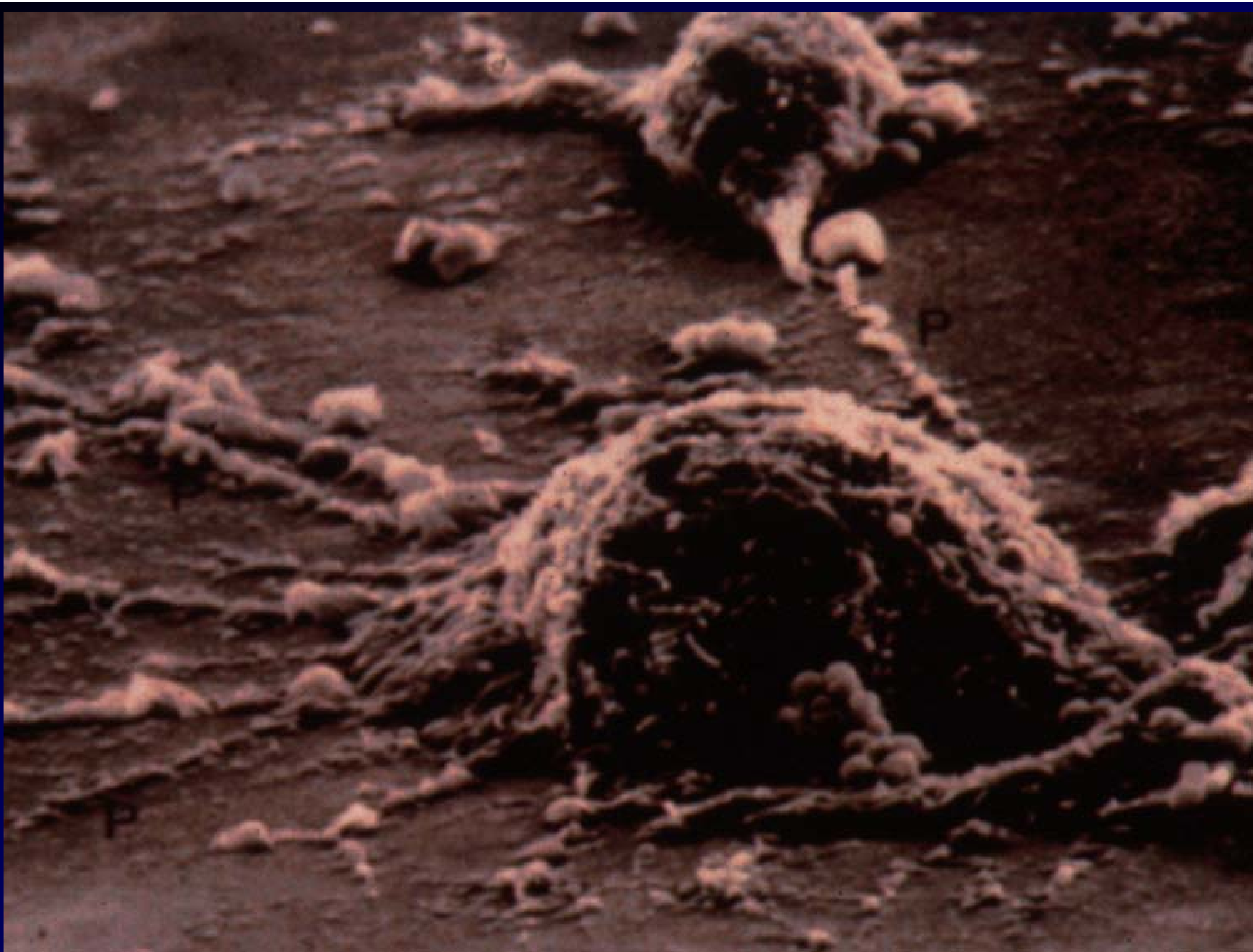
Total = 107% because of multiple causes

Total Cancer Mortality in the United States, 1955-1990



* Mean of seven age-specific rates, ages 35-69; annual death rate/1000.
Source: R. Peto, A.D. Lopez, J. Boreham,. M.Thun, and C. Heath, Jr., *Mortality from Smoking in Developed Countries*. 1950-2000 (Oxford: Oxford University Press, 1994)

Van Gogh, 1885, Skull with Cigarette


P
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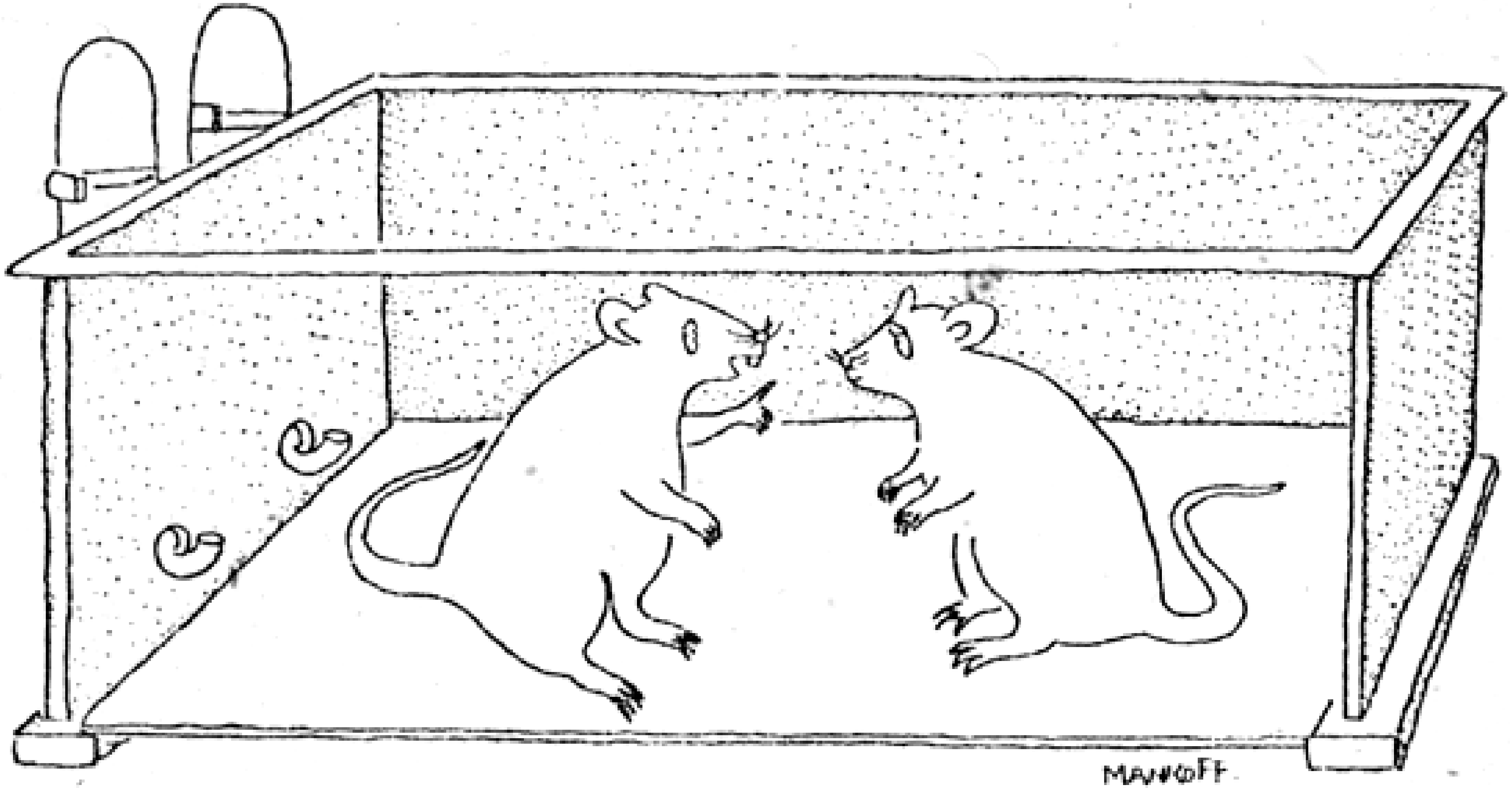
Oxidants from Phagocytic Cells

$$\left.\begin{matrix} NO\bullet \\ \\ O_2^{-}\bullet \end{matrix}\right\} \longrightarrow ONOO^{-}$$

H_2O_2

OCl^{-}



"MY MAIN FEAR USED TO BE CATS – NOW IT'S CARCINOGENS."

Bna_0011_0

Proportion of Chemicals Evaluated as Carcinogenic

Chemicals tested in both rats and mice	
All Chemicals	377/636 (59%)
Naturally-occurring chemicals	86/152 (57%)
Synthetic chemicals	291/484 (60%)
Chemicals tested in rats and/or mice	
All Chemicals	748/1430 (52%)
Natural pesticides	39/73 (53%)
Mold toxins	15/24 (63%)
Natural chemicals in roasted coffee	21/30 (70%)
Commercial pesticides	79/196 (40%)
Mutagens	287/382 (75%)
Non-mutagens	200/428 (47%)
INNES negatives chemicals retested	16/34 (47%)
PDR drugs with reported cancer tests	117/241 (49%)
FDA database of drug submission	125/282 (44%)

49 NATURAL PESTICIDES (AND METABOLITES) IN CABBAGE

GLUCOSINOLATES

2-propenyl glucosinolate (sinigrin)*
3-methyl-thio-propyl glucosinolate
3-methyl-sulfinyl-propyl glucosinolate
3-butenyl glucosinolate
2-hydroxy-3-butenyl glucosinolate
4-methyl-thio-butyl-glucosinolate
4-methyl-sulfinyl-butyl-glucosinolate
4-methylsulfonyl-butyl-glucosinolate
Benzyl glucosinolate
Propyl glucosinolate
Butyl glucosinolate

INDOLE GLUCOSINOLATES AND RELATED INDOLES

2-indolyl-methyl glucosinolate (glucobrassicin)
1-methoxy-3-indolylmethyl (neoglucobrassicin)
3-indole-3-carbinol (IC)*
3-indole-3-acetonitrile*
3,3'-diindolylmethane*

ISOTHIOCYANATES AND GOITRIN

allyl isothiocyanate*
3-methyl-thio-propyl isothiocyanate
3-methyl-sulfinyl-propyl isothiocyanate
3-butenyl isothiocyanate
5-vinyloxazolidine-2-thione (goitrin)
4-methylthiobutyl isothiocyanate
4-methylsulfonylbutyl isothiocyanate
4-pentenyl isothiocyanate
Benzyl isothiocyanate
Pheylethyl isothiocyanate

ALCOHOLS

Menthol
Neomenthol
Isomenthol

KETONES

Carvone*

CYANIDES

1-cyano-2,3-epithiopropane
1-cyane-3,4-epithiobutane
1-cyano-3,4-epithiopentane
Threo-1-cyano-2-hydroxy-3,4 epithiobutane
Erythro-1-cyano-2-hydroxy-3,4 epithiobutane
2-phenylpropionitrile
Allyl cyanide*
1-cyano-2-hydroxy-3-butene
1-cyano-3-methylsulfinylpropane
1-cyano4-methylsulfinylbutane

PHENOLS AND TANNINS

2-methoxyphenol
3-caffoylquinic acid (chlorgenic acid
4-caffoylquinic acid*
5-caffoylquinic acid (neochlorogenic acid)*
4-p-coumaroylquinic acid
5-p-coumaroylquinic acid
5-feruloylquinic acid

Plant Food	Rodent Carcinogen	Concentration (ppm)
Parsley	5- and 8-methoxypsoralen	14
Parsnip, cooked	"	32
Celery	"	.8
Celery, new cultivar	"	6.2
Celery, stressed	"	25
Mushroom, commercial	*p*-hydrazinobenzoate	11
Mushroom, commercial	glutamyl-*p*-hydrazinobenzoate	42
Cabbage	sinigrin (allylisothiocyanate)	35-590
Radish	"	11
Cauliflower	"	12-66
Brussels sprouts	"	110-1,560
Mustard (brown)	"	16,000-72,000
Horseradish	"	4,500
Orange juice	limonene	31
Mango	"	40
Pepper, black	"	8,000
Basil	estragole	3,800
Fennel	"	3,000
Nutmeg	safrole	3,000
Mace	"	10,000
Pepper, black	"	100
Sesame seeds (heated oil)	sesamol	75
Basil	benzyl acetate	82
Jasmine tea	"	230
Honey	"	15

PESTICIDE RESIDUES	**NATURAL PESTICIDE RESIDUES**
1) US Consumption FDA Estimate = 0.09 mg/day • 0.04 mg known **non-carcinogens** • 0.05 mg potential **carcinogens** **~105 chemicals in ppb range**	1) US Consumption Ames Estimate = ~1500 mg/day ∴99.99% of pesticides are natural **~5000 chemicals at 1000 ppb or more** 2) 73 assayed in animal cancer tests: 39 are **carcinogenic** 3) 72 tested for **clastogenicity**: 35 (48%) positive in all tests Of synthetic chemicals tested (951) 53% were **clastogenic**

Comparison of average exposures to natural and synthetic pesticides.

HERP (%)	Average daily human exposure	Human dose of rodent carcinogen
0.1	Coffee (from 13.3 g) (3 cups)	Caffeic acid, 23.9 mg
0.04	Lettuce (14.9 g) (1/67th head)	Caffeic acid, 7.90 mg
0.03	Safrole in spices	Safrole, 1.2 mg
0.03	Orange juice (138 ml) (4/5th glass)	d-Limonene, 4.28 mg
0.03	pepper, black (446 mg)	d-Limonene, 3.57 mg
0.02	Mushroom (2.55 g)(1/6th)	Mix of hydrazines, etc.
0.02	Apple (32.0g) (1/7th)	Caffeic acid, 3.40 mg
0.01	Celery, (21.6g) (2/5th stalk)	Caffeic acid, 2.33 mg
0.006	Coffee (from 13.3 g) (3 cups)	catechol, 1.33 mg
0.004	potato (54.9 g; peeled) (1/4th)	caffeic acid, 867 µg
0.003	nutmeg (27.4 mg)	d-Limonene, 466 µg
0.003	carrot (12.1 g) [1/10th]	Caffeic acid, 624 µg
0.002	**DDT: daily dietary average**	**[DDT, 13.8 µg (before 1972 ban)]**
0.002	**apple juice (6 oz.;177 ml)**	**[UDMH, 5.89 µg (from Alar, 1988)]**
0.001	Plum (1.86 g)(1.25th)	Caffeic acid, 257 µg
0.001	Pear (3.29 g) (9/100th)	Caffeic acid, 240 µg
0.0009	Brown mustard (68.4 mg)	Allyl isothiocyanate, 62.9 µg
0.0008	**(DDE: daily dietary average)**	**[DDE, 6.91 µg (before 1972 ban)]**
0.0006	Celery (21.6 g) [2/5th stalk]	8-Methoxypsoralen, 13.2 µg
0.0006	Mushroom (2.55g) [1/6th]	Glutamyl-p-hydrazinobenzoate, 107 µg
0.0004	**EDB: Daily dietary average**	**[EDB, 420 ng (before 1984 ban)]**

Comparison of average exposures to natural and synthetic pesticides (continued).

HERP (%)	Average daily human exposure	Human dose of rodent carcinogen
0.0003	Carbaryl: daily dietary avg.	Carbaryl, 2.6µg (1990)
0.0002	Toxaphene: daily dietary avg.	Toxaphene, 595 ng (1990)
0.0002	Apple, 1 whole (230 g)	[UDMH, 598 ng (from Alar, 1988)]
0.0001	Mango (522 mg) (1/500th)	d-Limonene, 20.9 µg
0.00009	Mushroom (2.55 mg) (1/6th)	p-Hydrazinobenzoate, 28 µg
0.00008	DDE/DDT: daily dietary avg.	DDE, 659 ng (1990)
0.00007	Parsnip (54 mg) (1/3300th)	8-Methoxypsoralen, 1.57 µg
0.00005	parsley, fresh (324 mg)	8-Methoxypsoralen, 1.17 µg
0.00002	Dicofol: daily dietary avg.	Dicofol, 544 ng (1990)
0.00001	Cocoa (3.34g) (4/5th serving)	α-Methylbenzyl alcohol, 4.3 µg
0.000001	Lindane: daily dietary avg.	Lindane, 32 ng (1990)
0.0000004	PCNB: daily dietary avg.	PCNB (Quintozene), 19.2 ng (1990)
0.0000001	Chlorobenzilate: daily dietary avg.	Chlorobenzilate, 6.4 ng (1989)
<0.00000001	Chlorothalonil: daily dietary avg.	Chlorothalonil, <6.4 ng (1990)
0.000000008	Folpet: daily dietary avg.	Folpet, 12.8 ng (1990)
0.000000006	Captan: daily dietary avg.	Captan 11.5 ng (1990)

Carcinogenicity Status of Natural Pesticides Tested in Rode

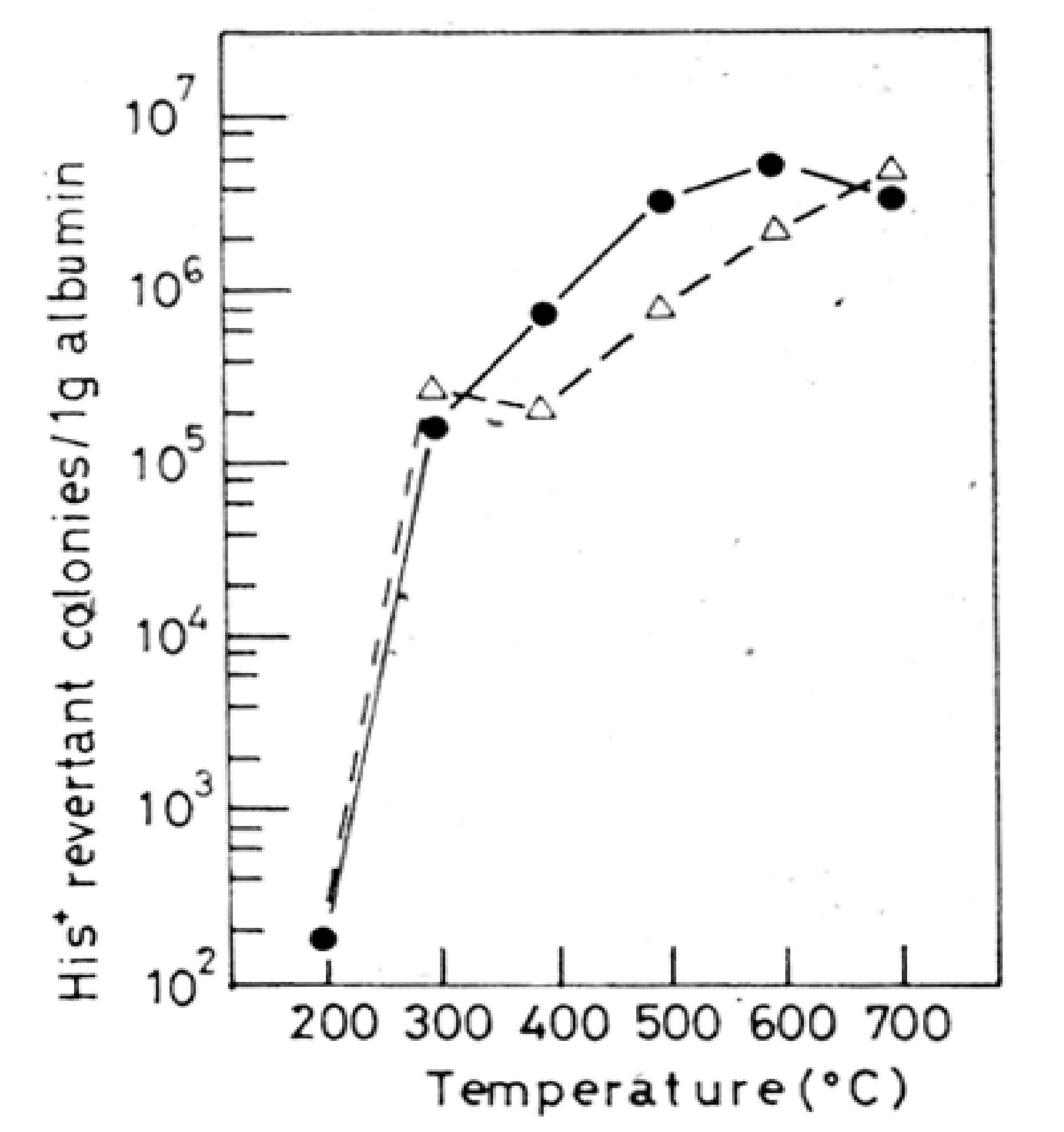
Carcinogens: N=37	Acetaldehyde methylformylhydrazone, allyl isothiocyanate, arecoline.HCL, benzaldehyde, benzyl acetate, caffeic acid, capsaicin, catechol, clivorine, coumarin, crotonaldehyde, 3,4-dihydrocoumarin, estragole, ethyl acrylate, N2- γ -glutamyl-p-hydrazinobenzoic acid.HCL, hydroquinone, 1-hydroxyanthraquinone, lasiocarpine, d-limonene, 3-methoxycatechol, *8*-methoxypsoralen, N-methyl-N-formylhydrazone, 4-methylcatechol, methylhydrazine, monocrotaline, pentanal methylformylhydrazone, petasitenine, quercetin, reserpine, safrole, safrole, senkirkine, sesamol, symphytine
Noncarcinogens: N=34	Atropine, benzyl alcohol, benzylixothiocyanate, benzyl thiocyanate, biphenyl, d-carvone, codeine, deserpidne, disodium glycirrhysinate, ephedrine sulphate, epigallocatechin, eucalyptol, eugenol, gallic acid, geranyl acetate, β-N-[γ-/(+)-glutamyl]-4-hydroxymethylphenylhydrazine, glycyrrhetirric acid, p-hydrazino-benzoic acid, isosafrole, kaempferol, *dl*-menthol, nicotine, norharman, phenethyl, isothiocyanate, pilocarpine, piperidine, protocatechaic acid, rotenone, rutin sulfate, sodium benzoate, tannic acid, 1-trans-δ^9-tetrahydrocannabinol, turmeric oleoresin, xinblastine

These rodent carcinogens occur in: absinthe, allspice, anise, apple, apricot, banana, basil, beer, Broccoli, Brussels sprouts, cabbage, cantaloupe, caraway, cardamom, carrot, cauliflower, celery, cherries. Chili pepper, chocolate, cinnamon, cloves, coffee, collard greens, comfrey herb tea, corn, coriander, currants, dill., eggplant, endive, fennel, garlic, grapefruit., grapes, guava, honey, honeydew, melon, horseradish, kale, lemon, lentils, lettuce, licorice, lime, mace, mango, marjoram, mint, mushrooms, mustard, nutmeg,m onion, orange, paprika, parsley, parsnip, peach, pear, peas, black pepper, pineapple, plum, potato,radish, raspberries, rhubarb, rosemary, rutabaga, sage, savory, sesame seeds, soybean, star anise, tarragon, tea thyme, tomato, turmeric, and turnip.

Ranking possible carcinogenic hazards (HERP) from natural and synthetic chemicals: Part 1

HERP (%)	Daily human exposure	Human dose of rodent carcinogen
140	EDB: workers; daily intake (high exposure)	Ethylene dibromide, 150 mg
17	Clofibrate (average daily dose)	Clofibrate, 2g
16	Phenobarbital, 1 sleeping pill	Phenobarbital, 60 mg
[14]	Isoniazid pill (prophylactic dose)	Isoniazid, 300 mg
6.2	Comfrey-pepsin tablets, 9 daily	**Comfrey root, 2.7g**
[5.6]	Metronidazole (therapeutic dose)	Metronidazole, 2g
4.7	**Wine (250 ml)**	**Ethyl alcohol, 30 ml ***
4.0b	Formaldehyde: Workers' average daily intake	Formaldehyde, 6.1 mg
2.8	**Beer (12 ounces; 54 ml)**	**Ethyl alcohol, 18 ml**
1.4b	Mobile home air (14 hour/day)	Formaldehyde, 2.2 mg
1.3	Comfrey-pepsin tablets, 9 daily	**Symphytine, 1.8 mg**
0.4b	Conventional home air (14 h/day)	Formaldehyde, 598 µg
[0.3]	Phenacetin pill (average dose)	Phenacetin, 300 mg
0.3	**Lettuce, 1/8 head (125 g)**	**Caffeic acid, 66.3 mg**

*** Natural chemicals in the diet are in yellow**



Mutagenic Activity (Number of His$^+$ Revertant Colonies) of Albumin Pyrolyzed at Different temperature Under N_2 or Air Atmosphere

Yoshida, Matsumoto, & Nishigata, *Agric. Biol. Chem*. **44**:253 (***1980***)

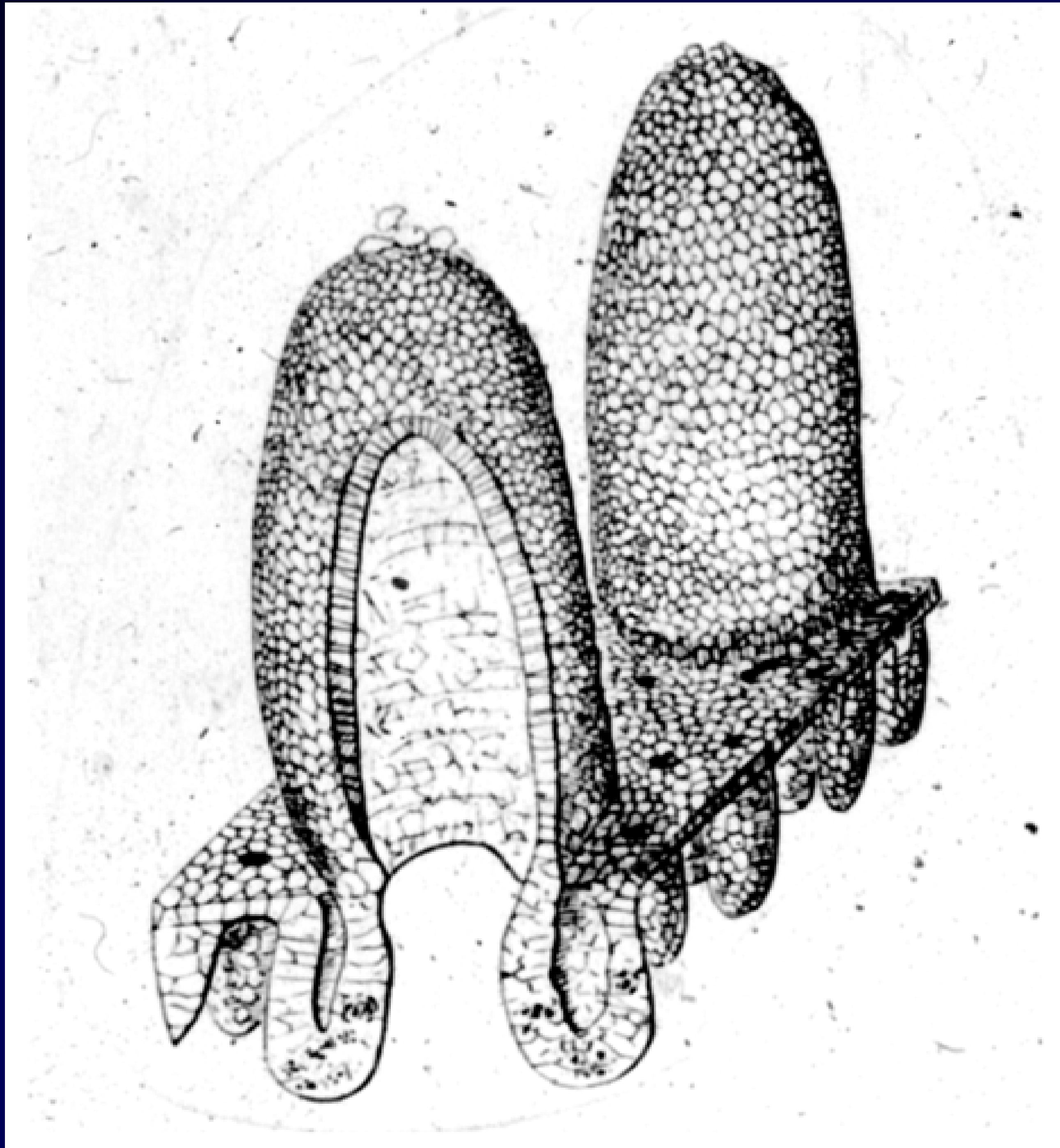
CARCINOGENICITY STATUS OF NATURAL CHEMICALS IN COFFEE

Carcinogens	Acetaldehyde, Benzaldehyde, Benzene, Benzofuran, Benzo(a)Pyrene, Caffeic Acid,Catechol, 1,2,5,6-Dibenzanthracene, Ethanol, Ethylbenzene, Formaldehyde,Furan, Furfural, Hydrogen Peroxide, Hydroquinone, Limonene, Styrene, and Toluene
Noncarcinogens	Biphenyl, Eugenol, Phenol,Piperidine, and Acrolein
Yet to be Tested	~ 1,000 chemicals

Vehicular Pollution

Means of Transport	Pollutant	Emissions (grams per mile)
Horses	Waste, solid	640
	Waste, liquid	300
Automobiles	Hydrocarbons	0.25
	CO	4.7
	NO_x	0.4

J.H. Ausubel in: "*Technology and Environment*", National Academy of Engineering, **1989**.



Relax, I’ve come for your toaster.

Moderate Deficiency of an Essential Vitamin or Mineral Accelerates Diseases of Aging

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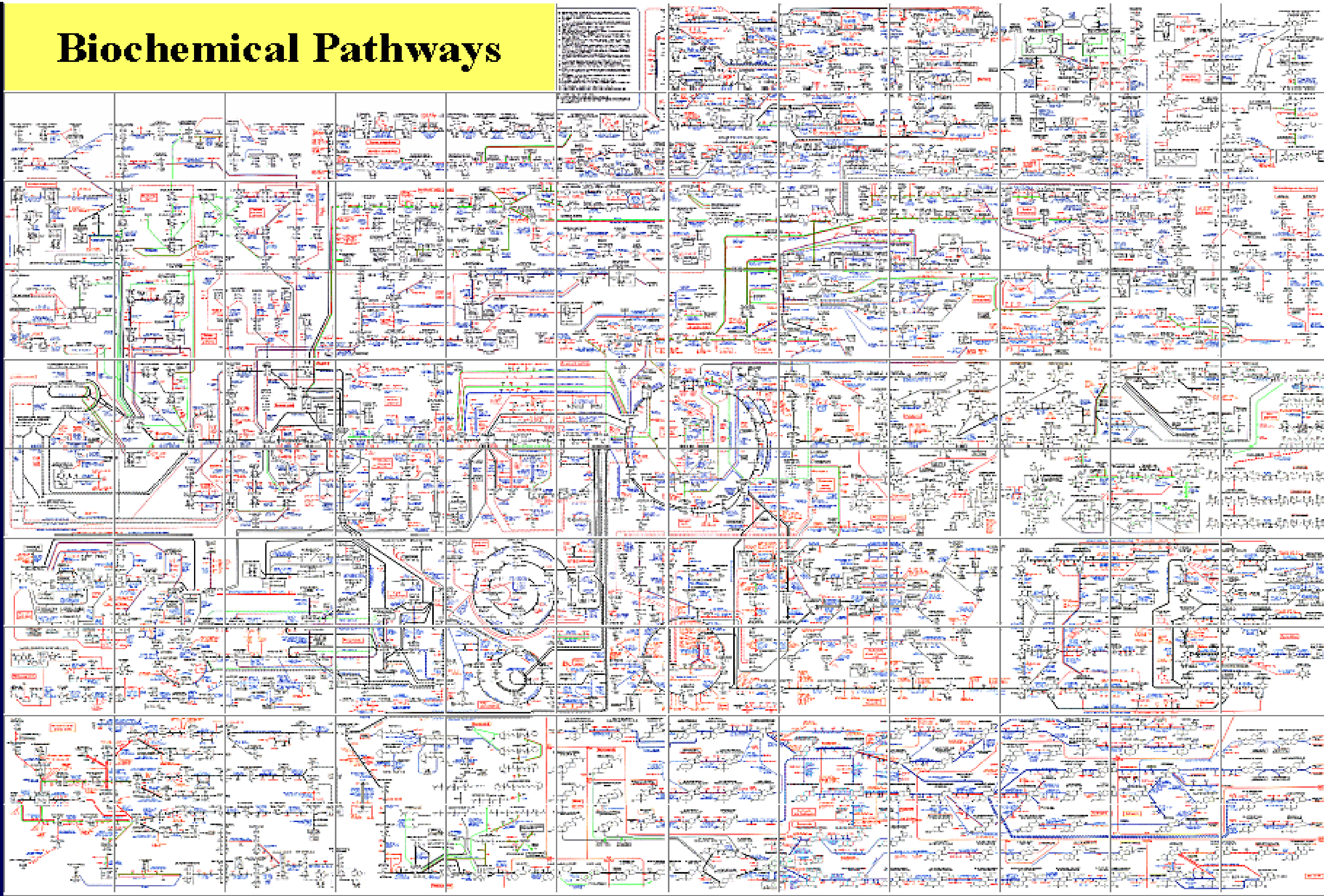
14 May 2013
Istanbul

Biochemical Pathways



~40 Essential Micronutrients

- Biotin
- Folic acid
- Niacin
- Pantothenate
- Riboflavin
- Thiamine
- VitA
- VitB6
- VitB12
- VitC
- VitD
- VitE
- VitK

- Calcium
- Chloride
- Chromium
- Cobalt
- Copper
- Iodide
- Iron
- Magnesium
- Manganese
- Molybdenum
- Phosphorus
- Potassium
- Selenium
- Sodium
- Zinc

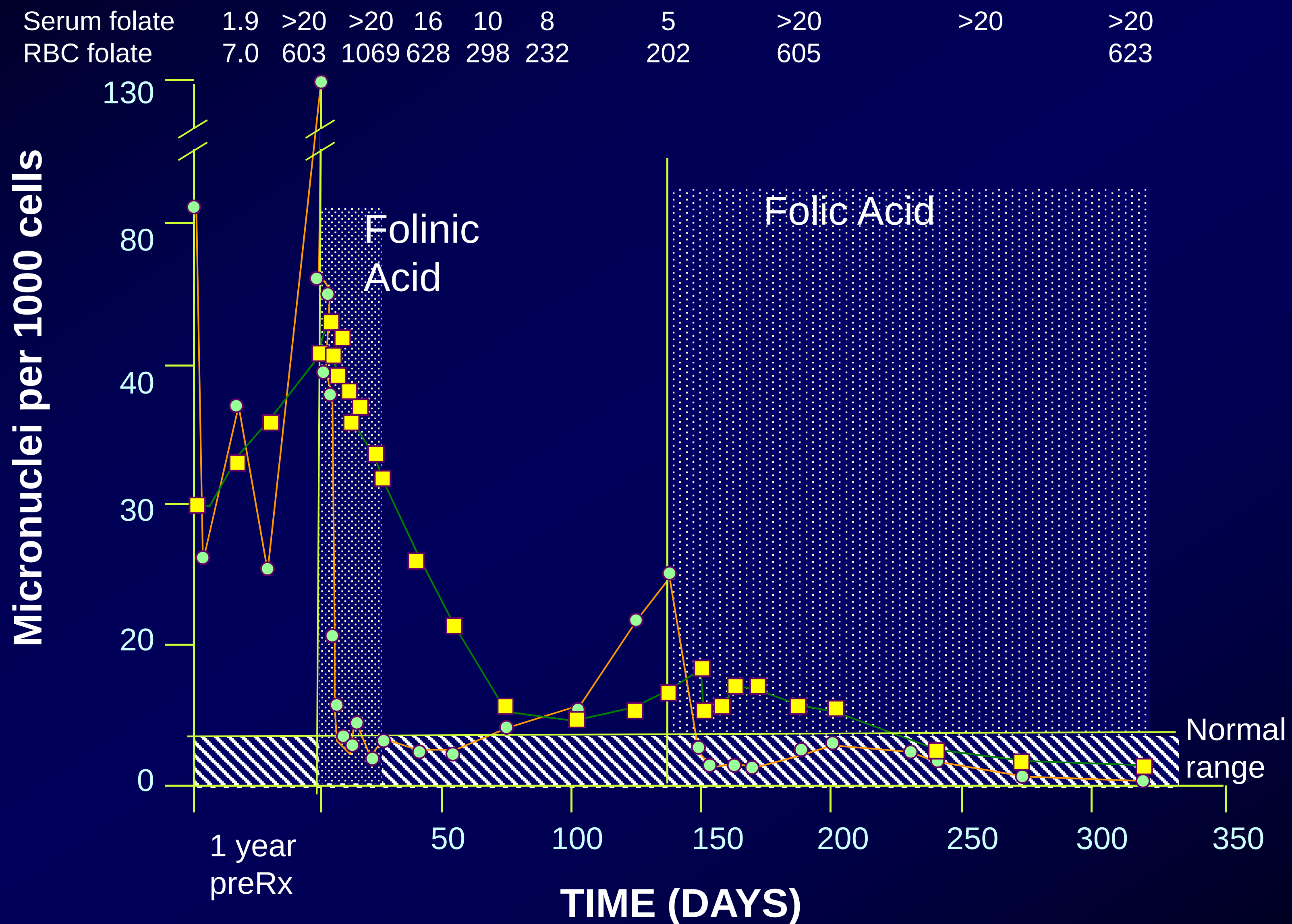
- Linolenic acid/DHA [ω-3]
- Linoleic acid [ω-6]
- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Threonine
- Tryptophan
- Valine
- Histidine
- Choline

Micronutrient Undernutrition in Americans

Nutrient	Population Group	% Ingesting < EAR * From Food
Minerals		
Iron	Menstruating Women	16 %
Magnesium	All	56 %
Zinc	All	12 %
Vitamins		
B6	Women > 70 years	49 %
Folate	Adult Women	16 %
E	All	93 %
C	All	31 %
Very low intake: vitamins K, D; calcium, potassium, omega-3		

•USDA What we Eat in America (NHANES 2001-2002) Sept. 2005

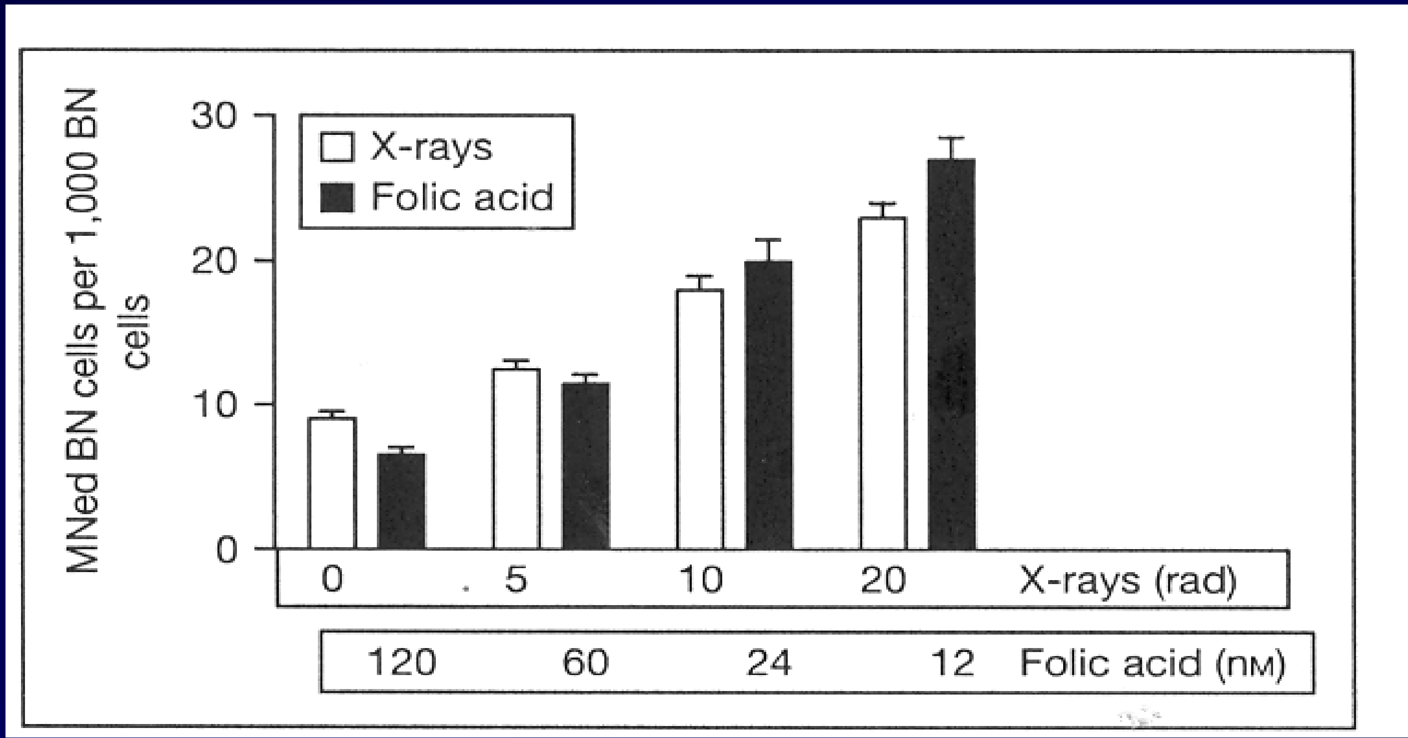
Micronuclei in: RNA positive erythrocytes
RNA negative erythrocytes



Everson RB, Wehr CM, Erexson GL, and MacGregor JT. (1988) *J Natl Cancer Inst* 80:525-9.

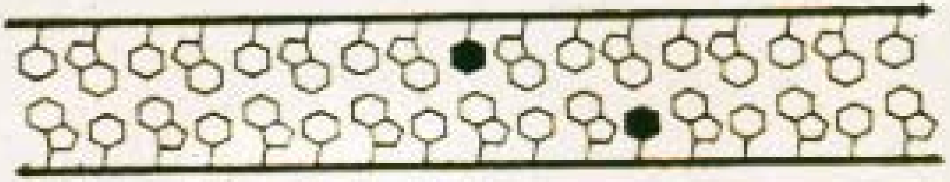
Dose-response on micronuclei induction in cultured lymphocytes

Acute exposure to X-rays vs. Folic Acid deficiency

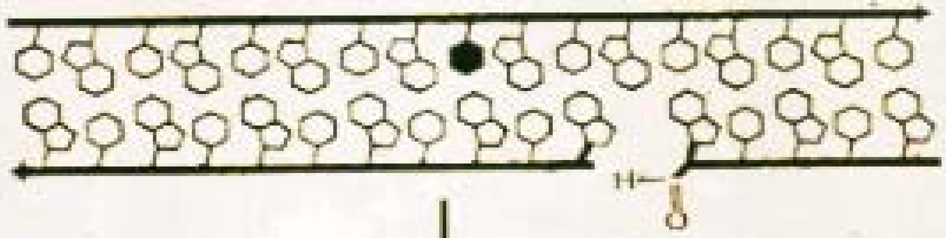


Fenech 2003, Nutrition Research Reviews

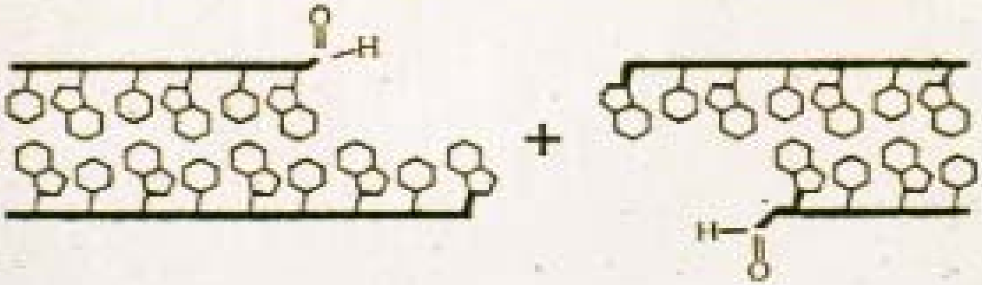
Base excision repair processing of opposed lesions



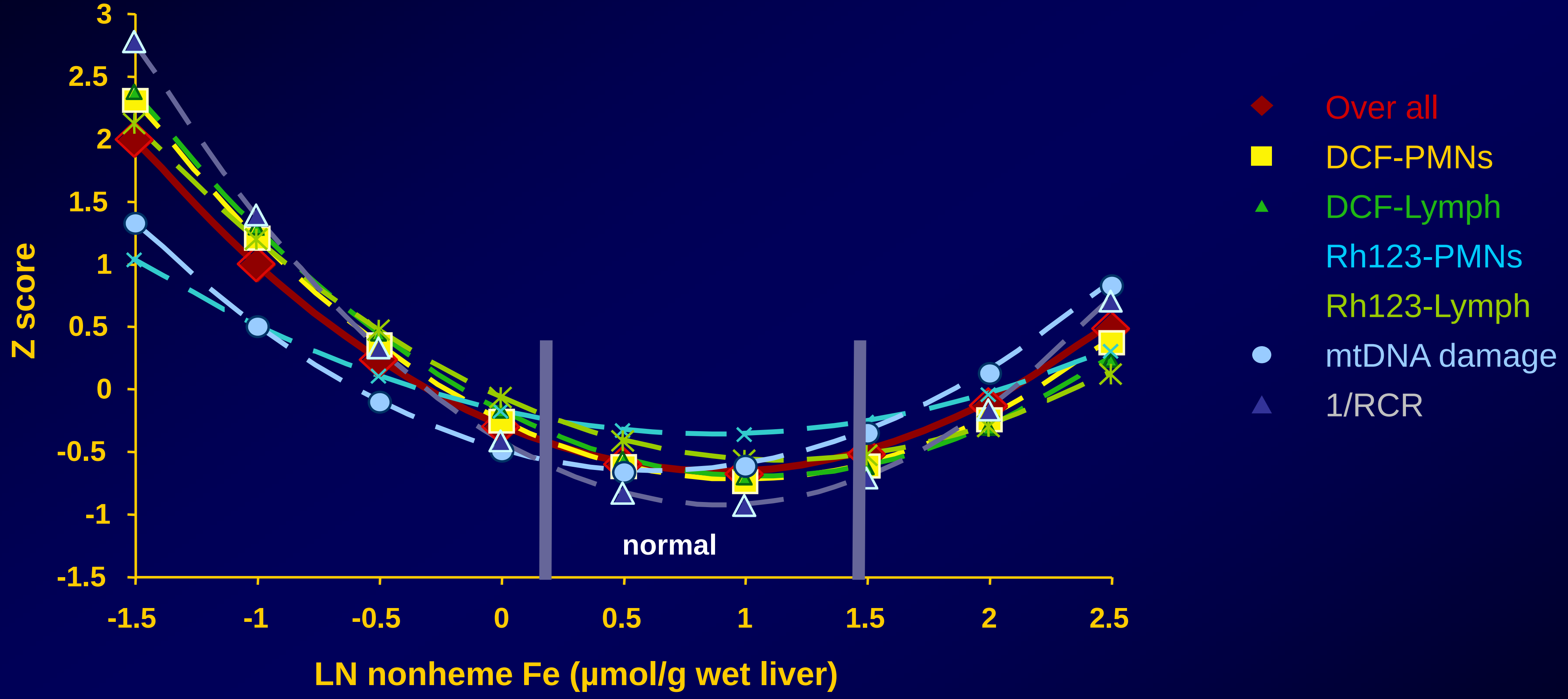
Gap three or more nucleotides away from base lesion



DNA double strand break formed by processing the second lesion

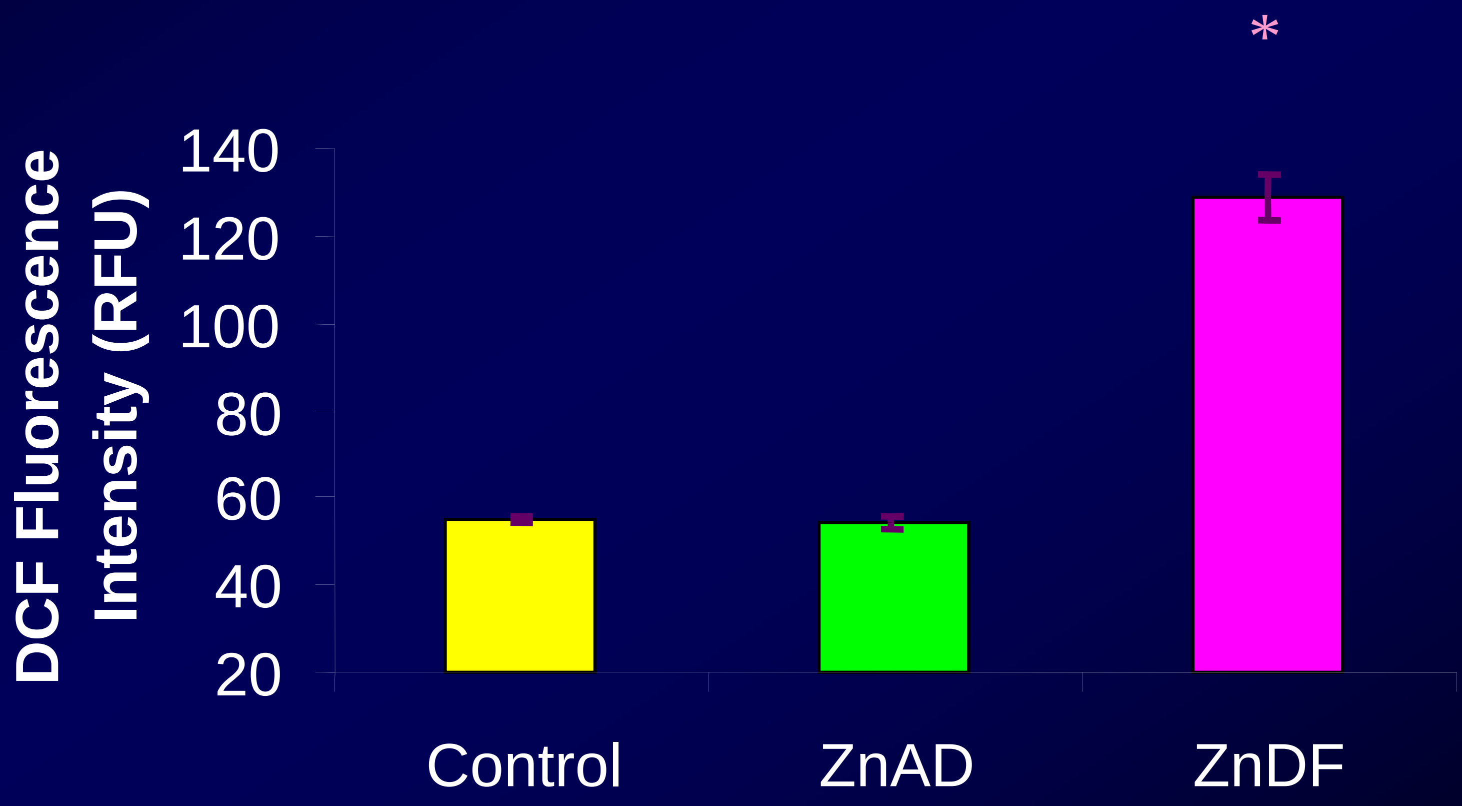


Analysis of nonlinear regression models: comparison of an overall model and individual models of Z-transformed values vs. ln- nonheme liver iron

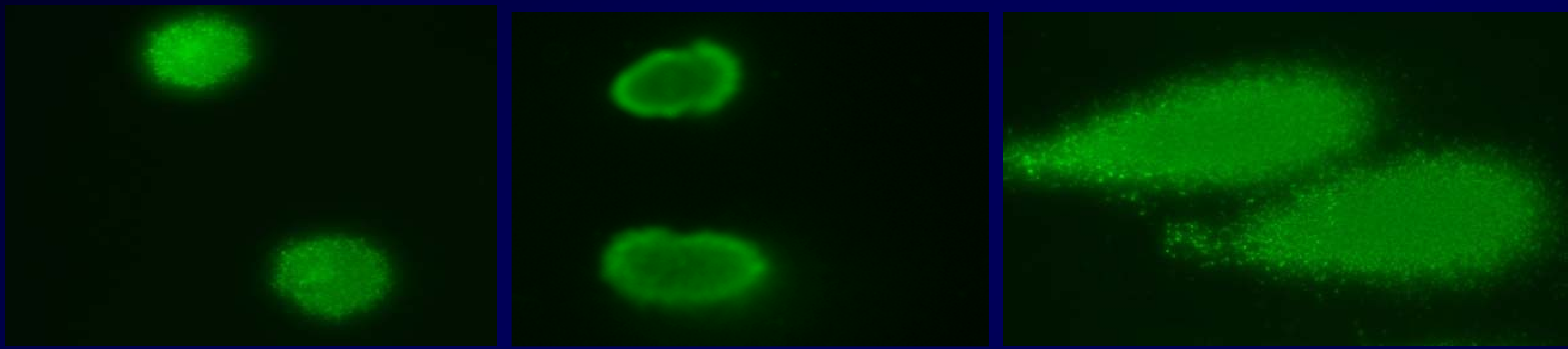


Each of the six dependent variables (that were analyzed by nonlinear regression in former figures) were transformed to Z scores and modeled as a quadratic function of the ln-liver nonheme iron as the independent variable. The equation for the RCR ratio's Z score was obtained from inverted RCR values (1/RCR) so that normal rats had the lower instead of the higher values. For presentation purposes each model line was obtained from 9 values of liver iron. All statistics were performed as in materials and methods.

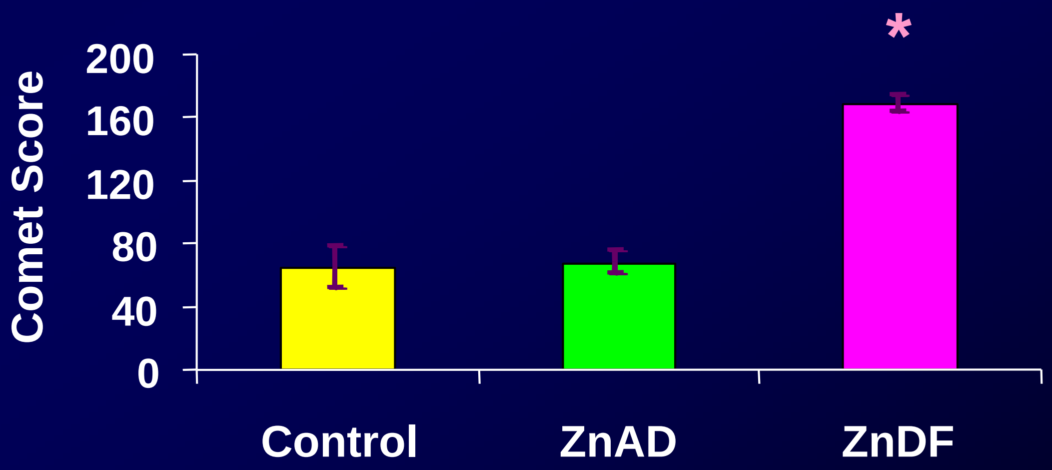
Zinc Deficiency Induces Increased Oxidative Stress in C6 Glioma Cells



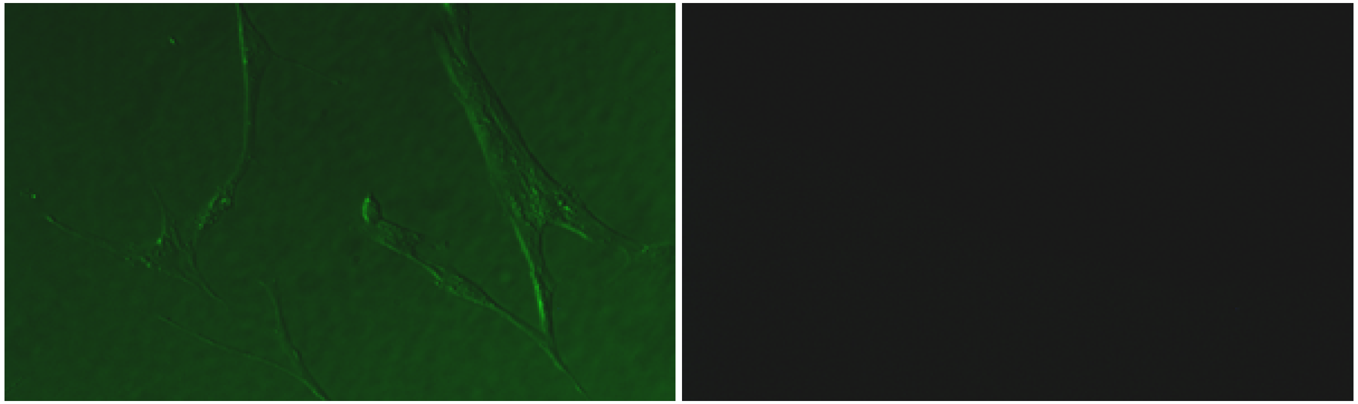
Zinc Deficiency Induces Fapy Glycosylase (Fpg)-sensitive Single Strand Breaks in Human Lung Fibroblasts



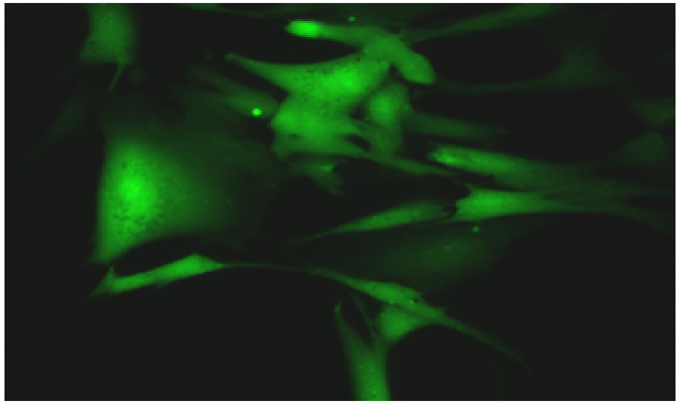
Control (+Fpg) **ZnAD (+Fpg)** **ZnDF (+Fpg)**



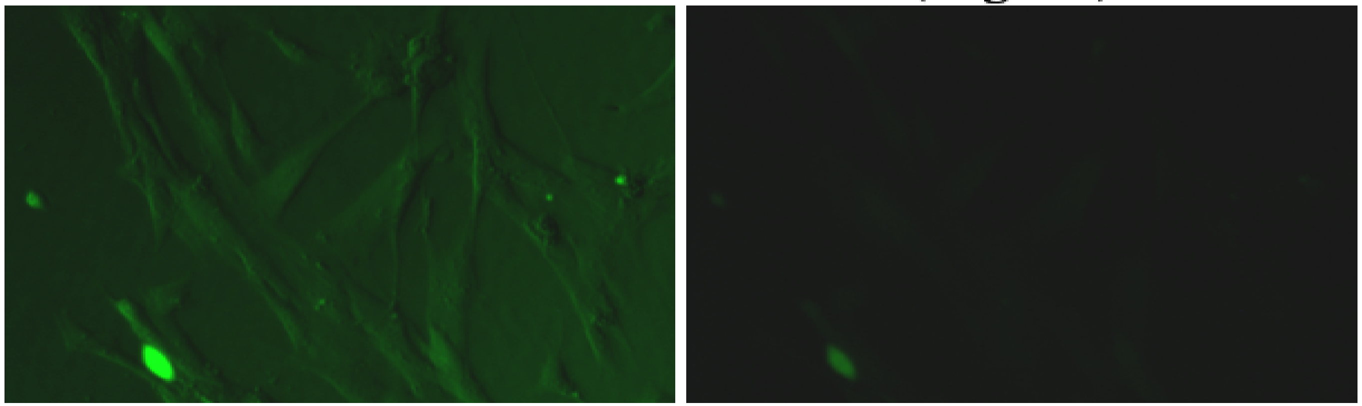
Biotin Sufficient

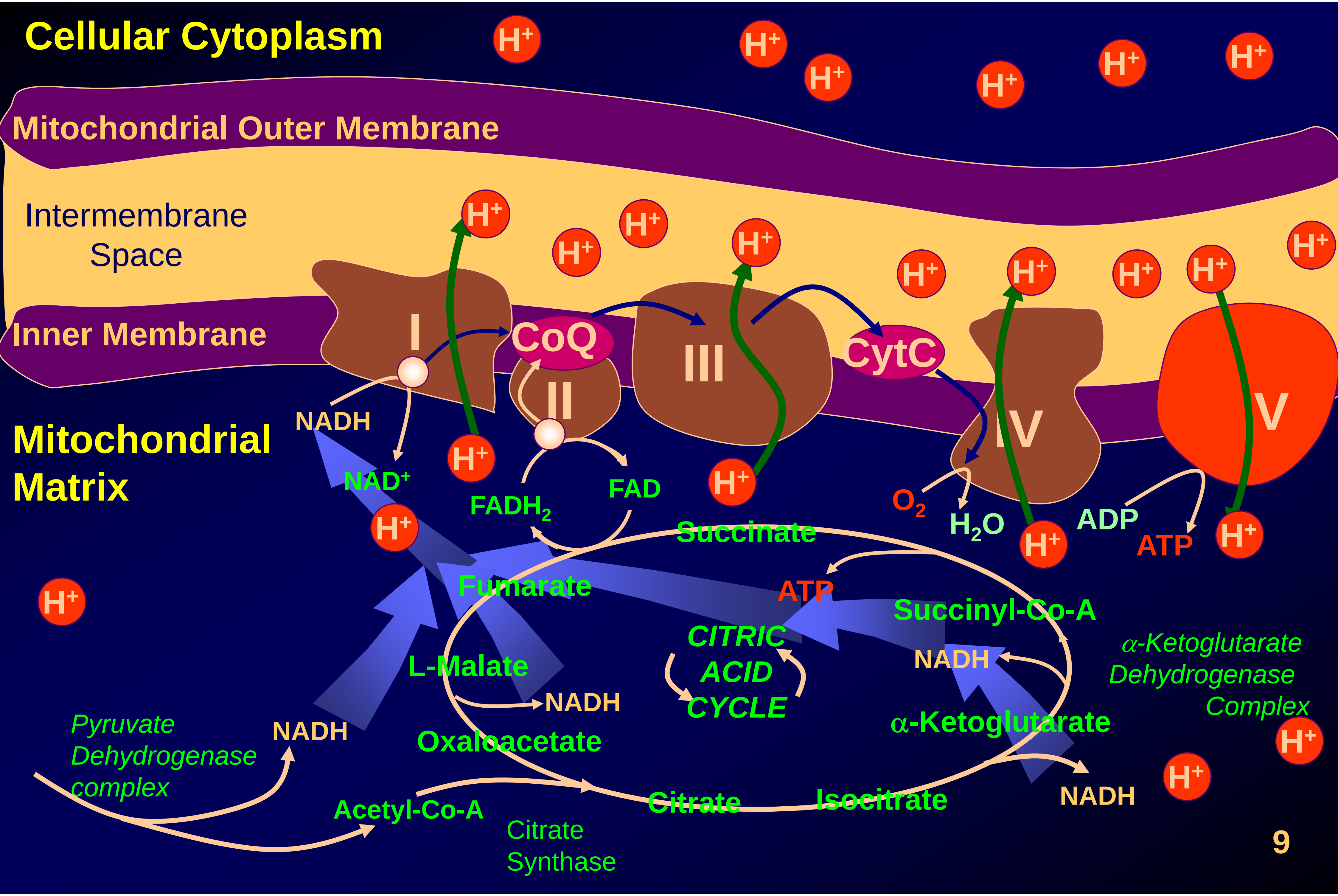


Biotin Deficient



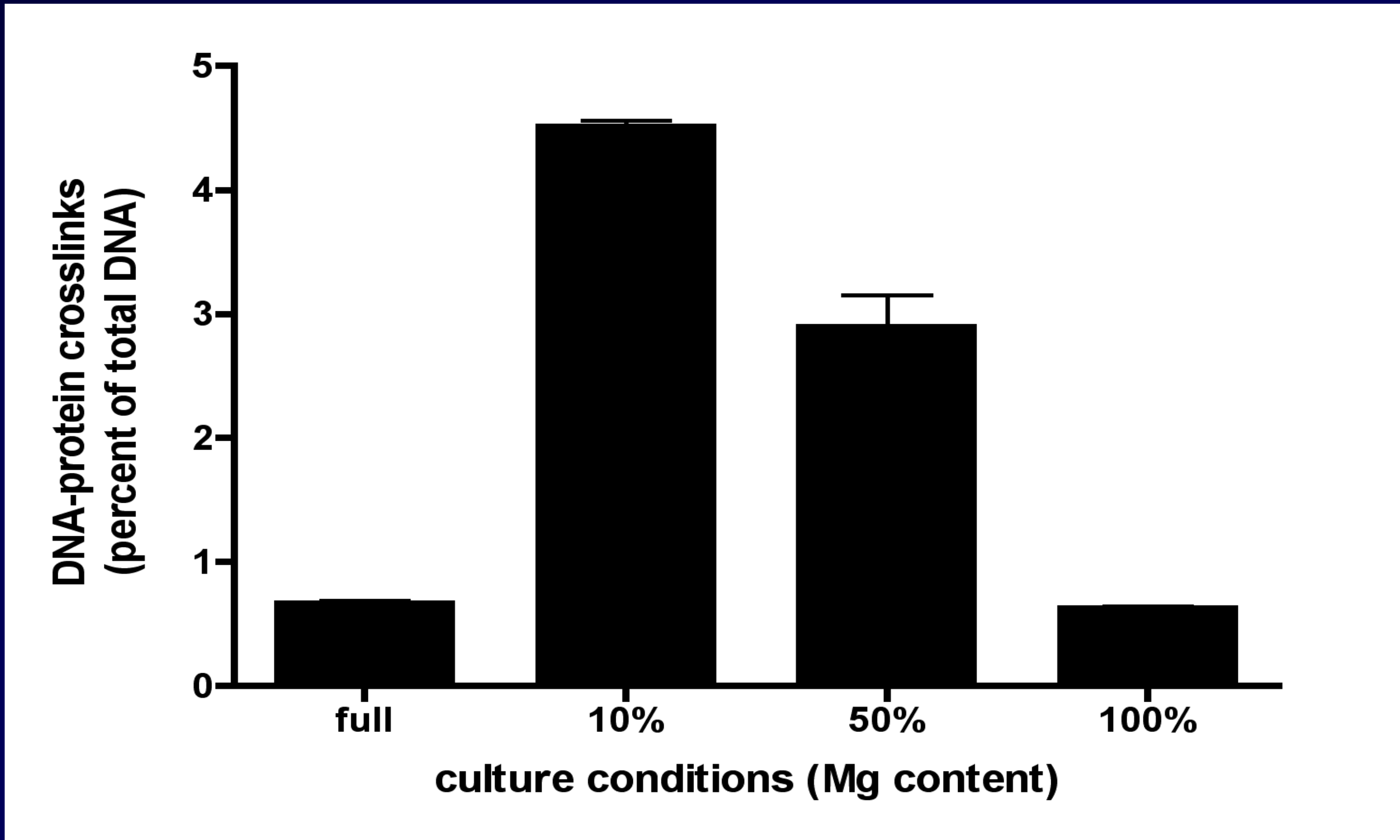
Biotin deficient + Biotin (5ng/ ml)





Cellular Cytoplasm
Mitochondrial Outer Membrane
Intermembrane Space
Inner Membrane
Mitochondrial Matrix
I
II
III
IV
V
CoQ
CytC
NADH
NAD^+
$FADH_2$
FAD
O_2
H_2O
ADP
ATP
Succinate
Fumarate
ATP
Succinyl-Co-A
CITRIC ACID CYCLE
L-Malate
NADH
NADH
α-Ketoglutarate Dehydrogenase Complex
α-Ketoglutarate
Pyruvate Dehydrogenase complex
NADH
Oxaloacetate
Acetyl-Co-A
Citrate
Isocitrate
NADH
Citrate Synthase

Magnesium Deficiency Induces mtDNA-Protein Crosslinks



Calcium Deficiency

Fenech: chromosome breaks

Lipkin: colon cancer mice

Folate Deficiency

MacGregor/Ames/Fenech: chromosome breaks mice/humans

Willett: epi colon cancer humans

Vitamin D Deficiency

Holick: epi many types of cancer

Magnesium Deficiency

Bell: chromosome breaks humans

Larsson: epi colorectal cancer humans

Zinc Deficiency

Fong: esophageal cancer humans/rodents

Potassium Deficiency

[Chang: Cardiovascular Disease]

Vitamin B12 Deficiency

Fenech: Chromosome breaks

Selenium Deficiency

Rao: DNA damage

Combs/Trumbo: Cancer humans

Omega-3 FA Deficiency

Denkins: Cancer

Niacin Deficiency

Kirkland/Depeint: DNA damage

Choline Deficiency

da Costa: DNA damage in humans

Proc. Natl. Acad. Sci. USA
Vol. 103, pp. 17589-17594, November 2006

Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage

Bruce N. Ames
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5700 Martin Luther King Jr. Way, Oakland, CA 94609

- Most of the world's population has inadequate intake of one or more micronutrients.
- Triage theory posits as a results of recurrent shortages of micronutrients during evolution, natural selection developed a metabolic rebalancing response to shortage.
- The rebalancing favors micronutrient-dependent protein needed for short term survival while those only required for long-term health are starved.
- This impairment results in insidious damage (e.g. increased DNA damage) that, over time, leads to the acceleration of age-associated diseases (e.g. increased cancer).

40 Essential Micronutrients

- Biotin
- Folic acid
- Niacin
- Pantothenate
- Riboflavin
- Thiamine
- Vitamin A
- Vitamin B6
- Vitamin B12
- Vitamin C
- Vitamin D
- Vitamin E
- Vitamin K

- Calcium
- Chromium
- Cobalt
- Copper
- Fluoride
- Iodine
- Iron
- Magnesium
- Manganese
- Molybdenum
- Phosphorus
- Potassium
- Selenium
- Sodium
- Zinc

- Linolenic acid/DHA [ω-3]
- Linoleic acid [ω-6]
- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Threonine
- Tryptophan
- Valine
- Histidine
- Choline

16 Vitamin K Dependent Proteins

(γ–glutamyl-carboxylase, vitK quinone reductase and vitK epoxide reductase)

Coagulation Factors	*Other Proteins*
F2 (Prothrombin)	Osteocalcin
F7	Gas 6 protein
F9	Matrix Gla protein
F10	TGFBI
(Anticoagulant protein C)	Periostin
	(Anticoagulation Protein Z)

5 Lethal KO (red) — 6 nonlethal KO (blue)

Four Causes of Functional Deficiency of VKD-Proteins in Humans

Non-lethal VKD-protein	**Function**	**Mouse Knockout Phenotypes**	**Human Mutants**	**Anticoagulant Therapy**	**Modest VitK deficiency**
Osteocalcin	Bone struct. Glucose homeostasis	Fragile bones Insulin resistance	BMD loss (SNPs)	Bone health (men/children/rats)	Bone health Insulin resistance
Matrix Gla Protein (Mgp)	Negative regulator of vascular calcification	Arterial calcification	Abnormal soft tissue calcification (Keutel Syndrome; SNPS)	Arterial calcification (humans/rats)	Arterial calcification

McCann & Ames (2009) Vitamin K, an example of triage theory: is micronutrient inadequacy linked to diseases of aging? Am J Clin Nutr *90,889-907.*


Natto

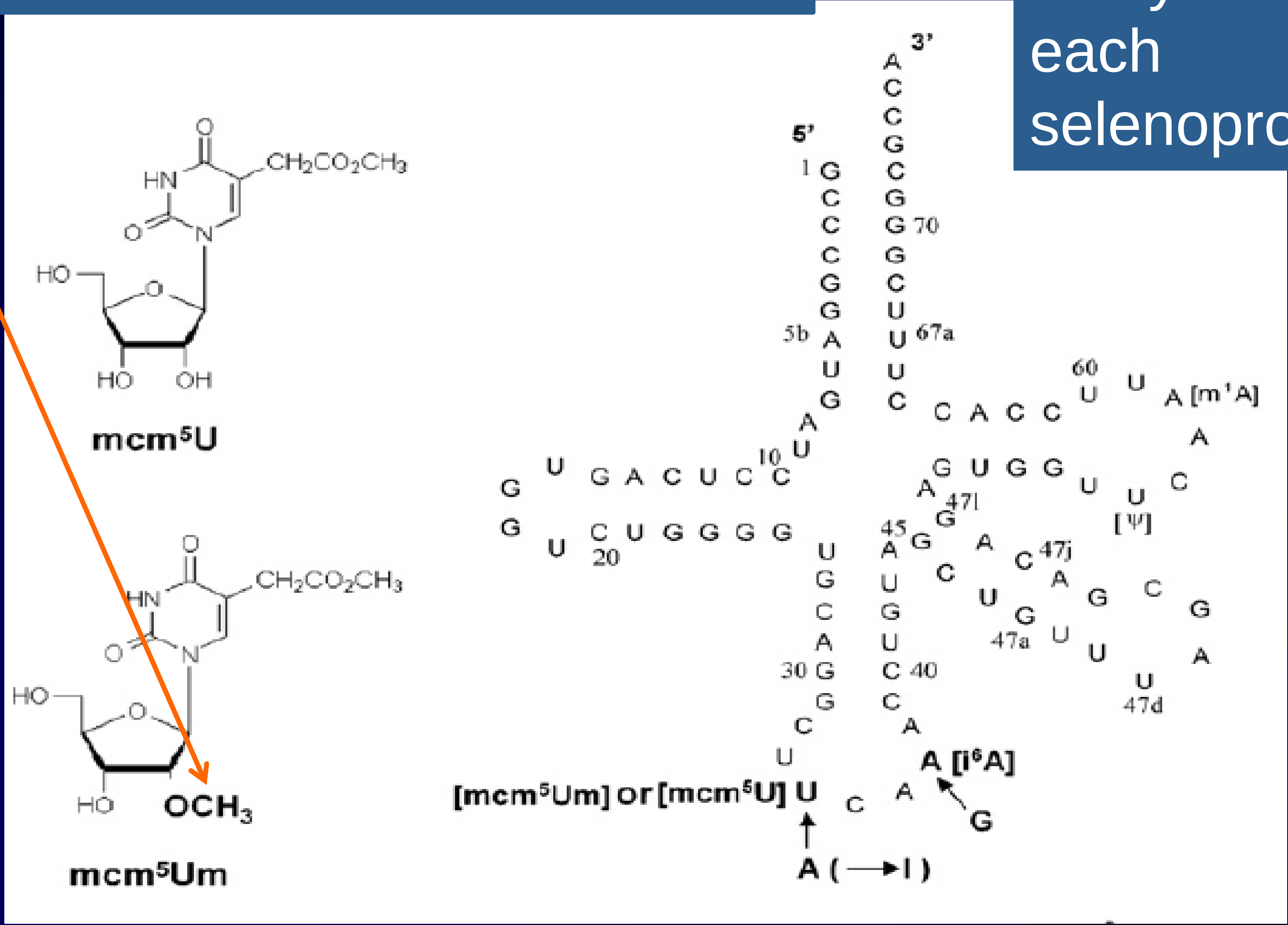
Selenium deficiency, genetic impairment of nonessential selenoproteins, and diseases or conditions associated with aging

Selenoprotein genetic loss		Se dietary loss
Rodent	Human	Human
Gpx1 KO: Senescence		Mortality
Gpx2 KO: UV-induced cancer	Gpx1 SNP, LOH, HYP: Various cancers	Cancer
Gpx1 Knockdown: UV-induced micronuclei		DNA damage
Gpx1 Heterozygote: Heart abnormalities	Gpx3 SNP: Stroke & thrombosis Dio2 SNP: Hypertension (mixed)	Heart disease, hypertension, mortality; *Keshan's disease*
Gpx1 KO: Viral induced myocarditis Gpx2 KO: Airway inflammation		Reduced resistance to infection (primarily viral)
	Dio1 SNP: Muscle weakness SELN Homozygote: Myopathy	*Muscle weakness/muscular dystrophy-like symptoms*
Dio2 KO: Bone fracture	Dio2 SNP: Osteoarthritis	*Kashin-Beck disease (osteoarthropathy)*
Gpx1 KO: Induced neurotoxicity	Dio2 SNP: Retardation (+ iodine def); psychological well-being	Poor cognitive function (1 study) *Mental retardation (+ iodine def)*
Gpx1 KO: <u>Less</u> fat-induced insulin resistance	Dio2 SNP: Insulin resistance (mixed)	Increased type 2 diabetes risk in older men (1 study)

McCann and Ames FASEB J 2011

The methylation reaction is the last step in Sec tRNA synthesis; methylation dramatically changes the structure of Sec tRNA. This reaction is inhibited by Se deficiency.

One of two Sec tRNAs is used for synthesis of each selenoprotein



Immune Risk Phenotype of Aging

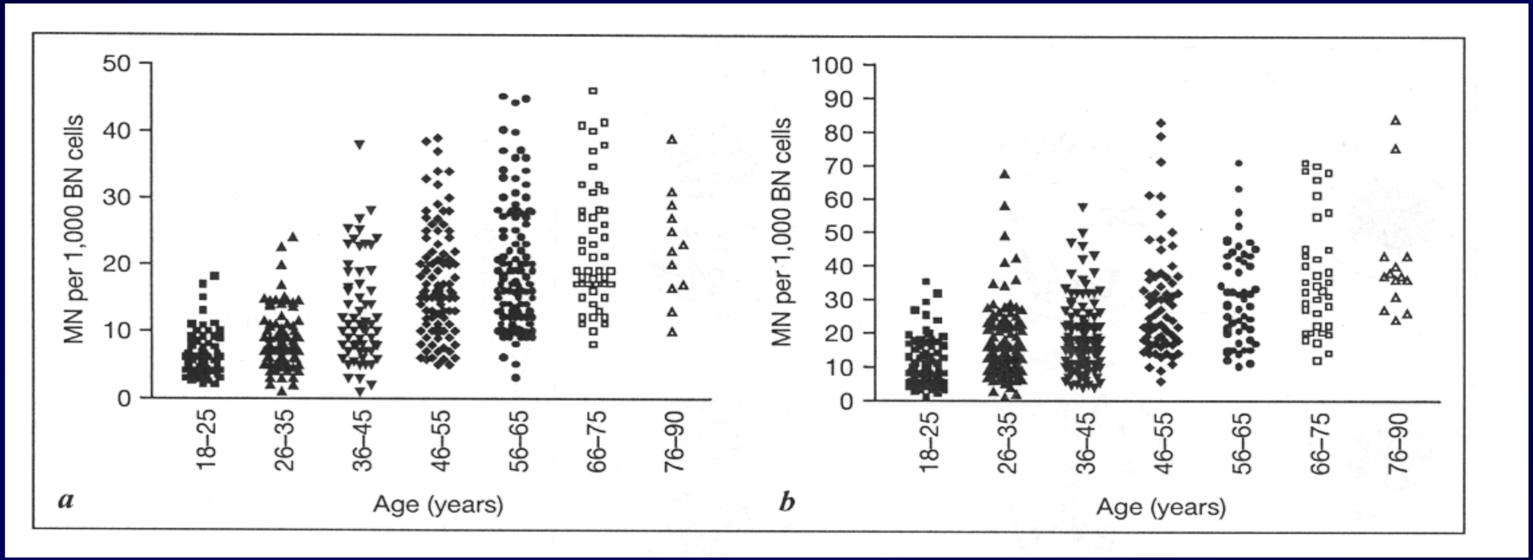
- Lower CD4 and CD8 T-lymphocytes
- Increase in anergic effector ($CD8^{+}CD28^{-}$) T-cells
- Low lymphoproliferative response
- Decline in antigen-presenting cells
- Decreased expression of co-stimulatory molecules
- Decline in IL-12 production and Th1 response

Immune Risk Phenotype of Aging

- Lower CD4 and CD8 T-lymphocytes
  - Def: vit A., zinc, folate
- Increase in anergic effector ($CD8^{+}CD28^{-}$) T-cells
  - Def: tryptophan, zinc,
- Low lymphoproliferative response
  - Def: vit C, vit E, zinc. Vit B6
- Decline in antigen-presenting cells
  - Def: vit E
- Decreased expression of co-stimulatory molecules
  - Def: vit E, tryptophan. zinc
- Decline in IL-12 production and Th1 response
  - Def: vit B6, Vit E, zinc

Variation in chromosomal DNA damage rates within and between age groups measured as MN frequency.

Healthy Non-smoking Males | **Healthy Non-smoking Females**



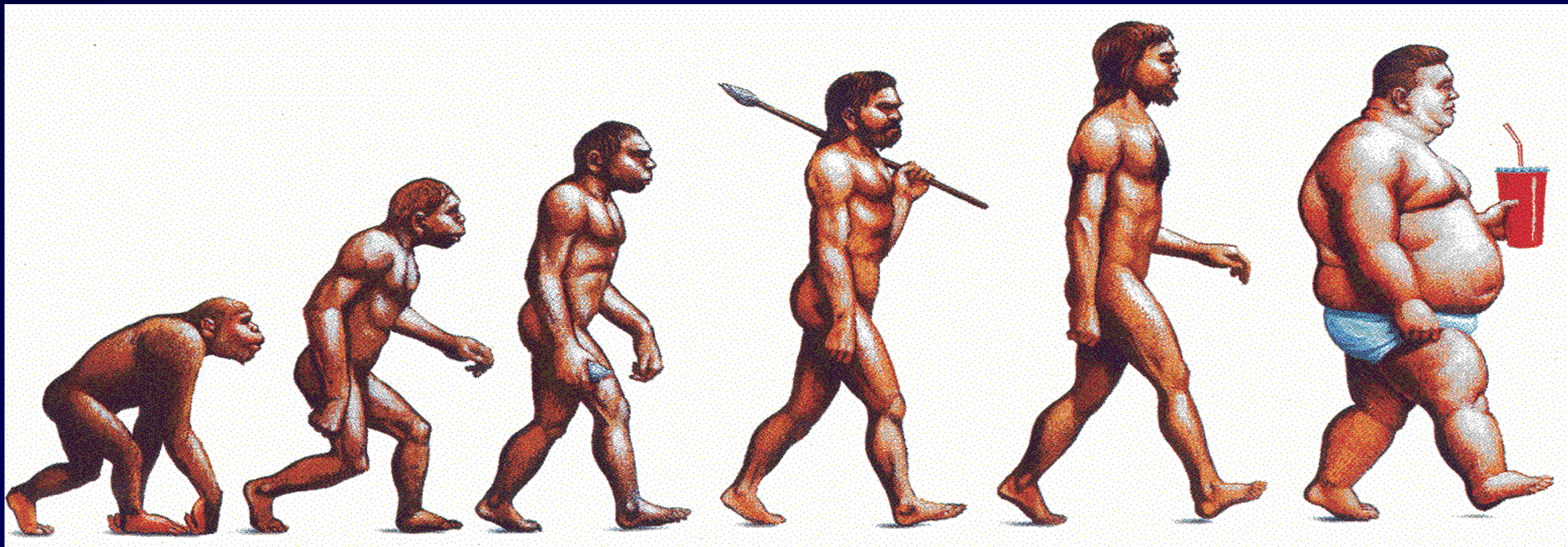
Fenech 2007, Forum Nutr.

Benefits of a Triage Analysis

1. Provides a mechanism for how moderate V/M deficiency increases risk of a disease of aging, and suggests a prevention strategy.
2. Indicates about half of proteins analyzed are “longevity proteins” which suggests:

a) biomarker assays for setting EARs; and

b) a class of undiscovered “longevity V/Ms”.



The Economist, December 13, 2003

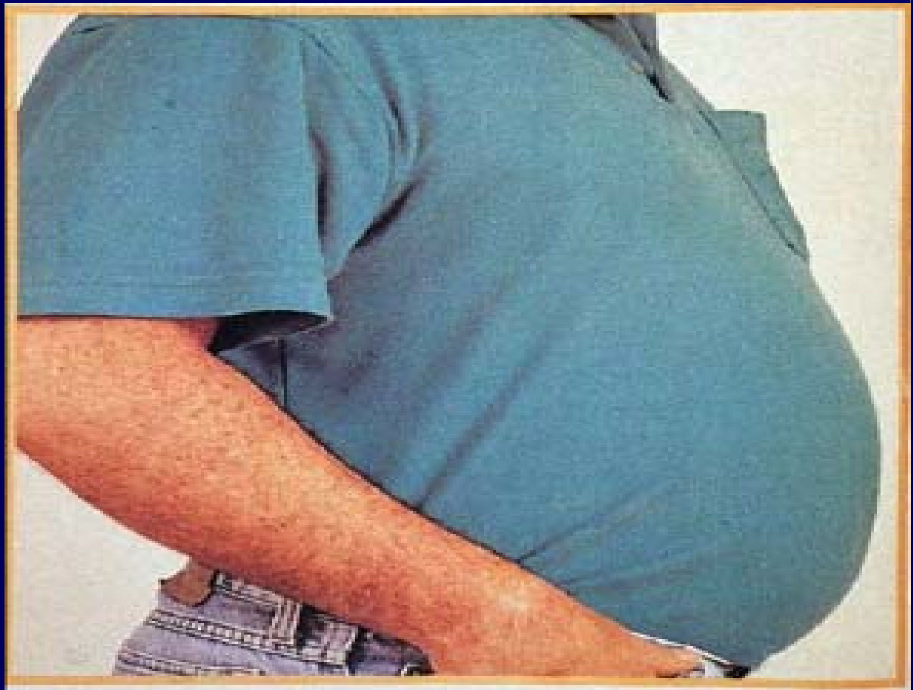
Dr. Allen Spiegel, NIDDK/NIH

Top Sources of "Nutrition" for 20-30 year olds

	% total energy
1. Regular soft drinks	8.8
2. Pizza	5.1
3. Beer	3.9
4. Hamburgers, meat loaf	3.4
5. White bread	3.3
6. Cake, doughnuts, pastries	3.3
7. French fries, fried potatoes	3.0
8. Potato chips, corn chips, popcorn	2.7
9. Rice	2.6
10. Cheese or cheese spread	2.5
	38.6%

NHANES III (1988-1994) Wakimoto P & Block G. J Gerontol A Biol Sci Med Sci, 2001

CAUTION: HAZARDOUS WAIST



Visceral fat increases your risk of cancer, heart disease, cognitive dysfunction, diabetes, etc.

Start a waist disposal program today.

Supplementation Strategies

<u>Conventional</u>
- cumbersome
- compliance
- incomplete

<u>CHORI Bar</u>
- convenient
- complete

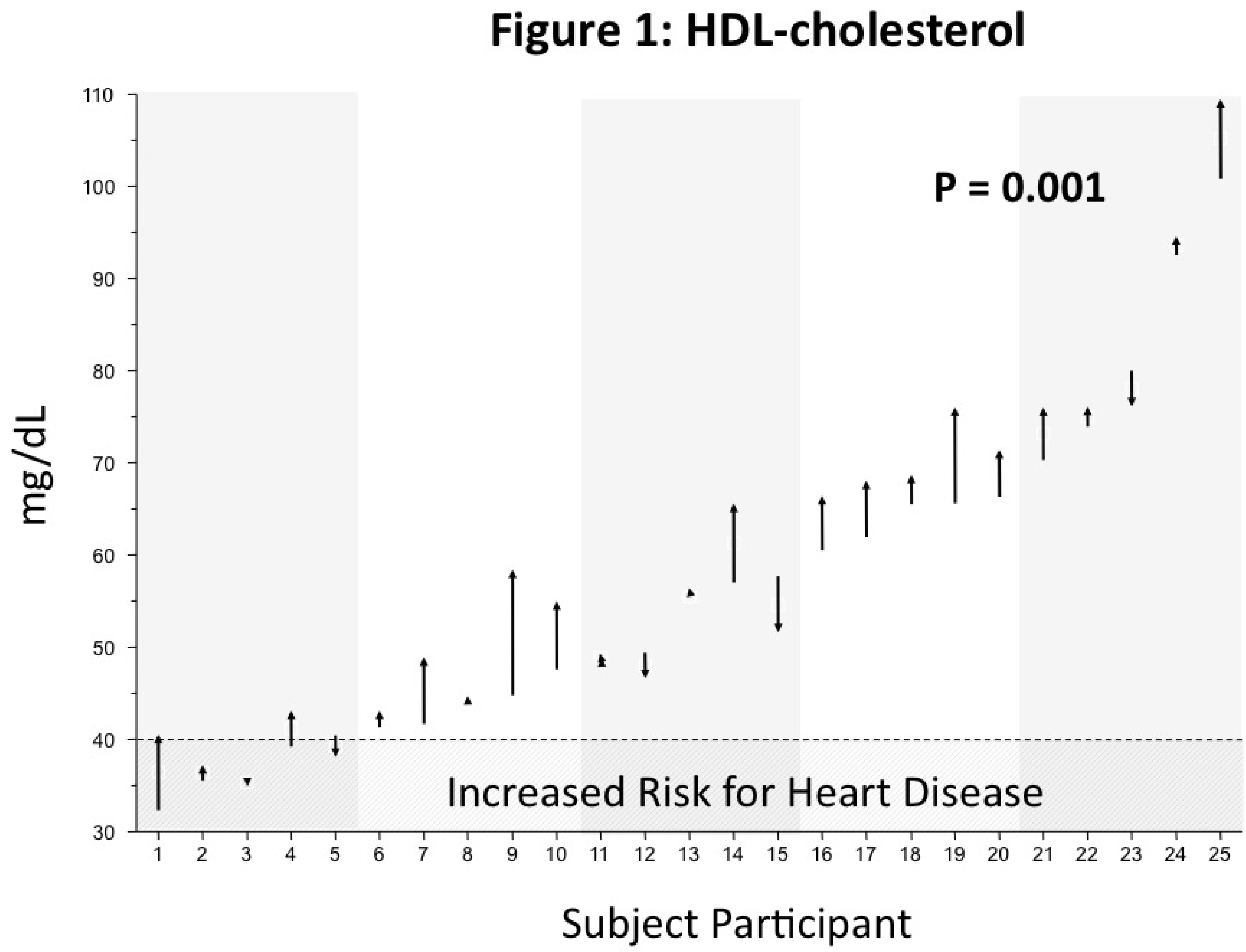
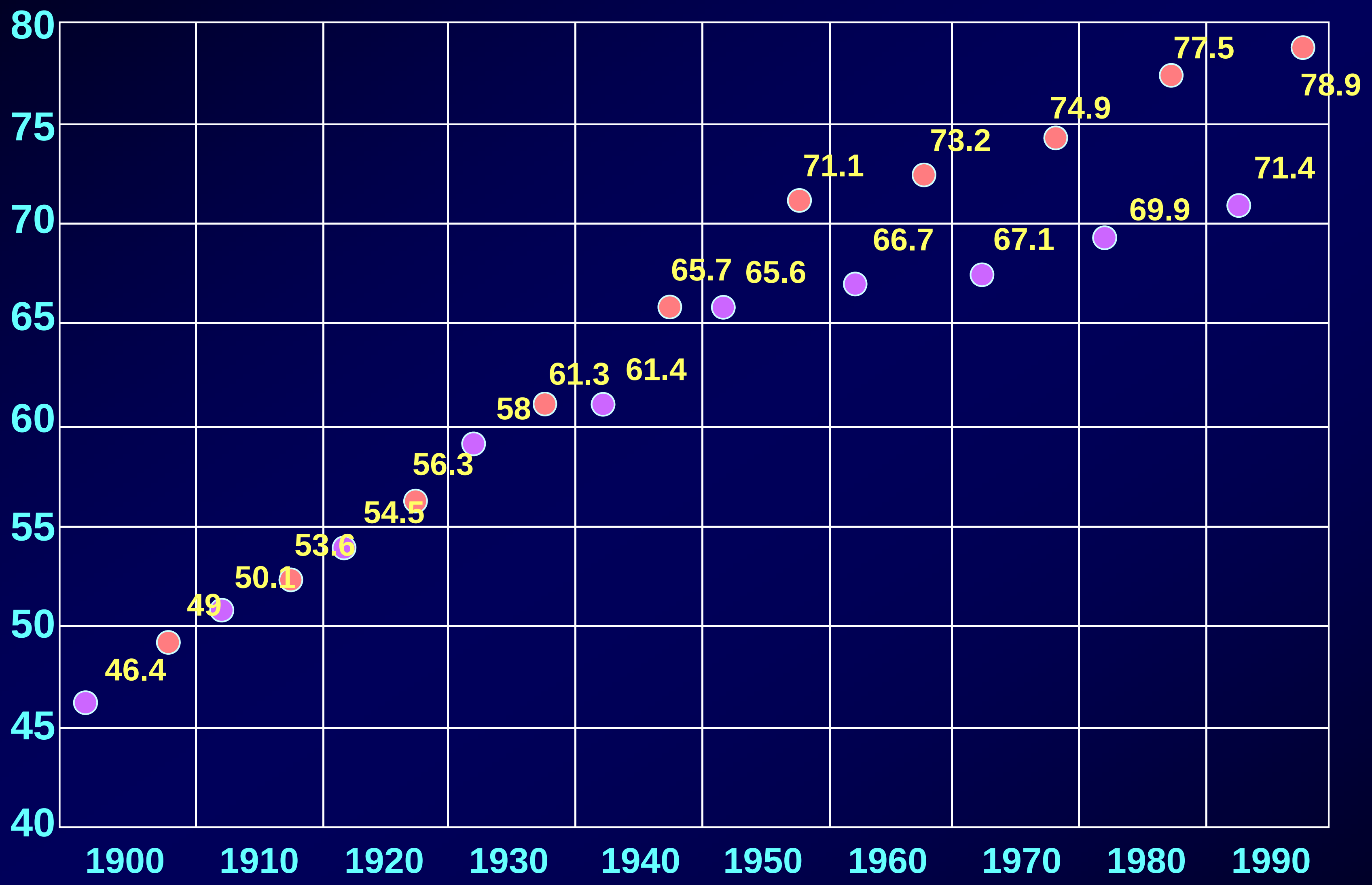


Figure 1: HDL-cholesterol
P = 0.001
mg/dL
110
100
90
80
70
60
50
40
30
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Increased Risk for Heart Disease
Subject Participant

Life Expectancy of Men and Women at Birth

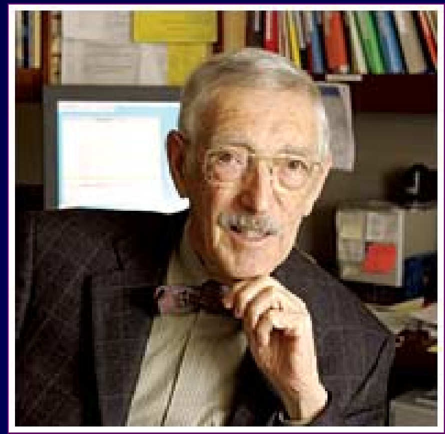


SOURCE: National Institute on Aging

Nutrition & Metabolism Center

Jung Suh

Joyce McCann



Bruce Ames

Swapna Shenvi

David Killilea

Ash Lal

Michele Mietus-Snyder

Mark Shigenaga

Sandy Calloway

Harold Helbock

END