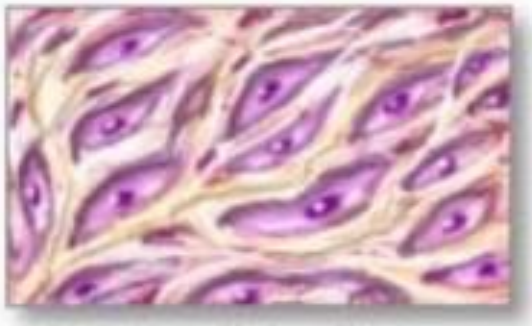
CANCER = Malignant Tumor = Malignant Neoplasm

A tissue growth:

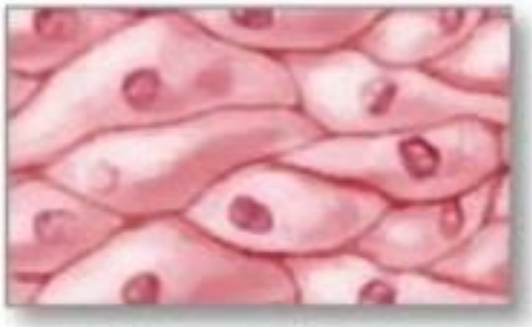
- Not necessary for body's development or repair
- Invading healthy tissues
- Spreading to other sites of the body (metastasizing)
- Lethal because of its invasion, metabolism, and complications

Tissues

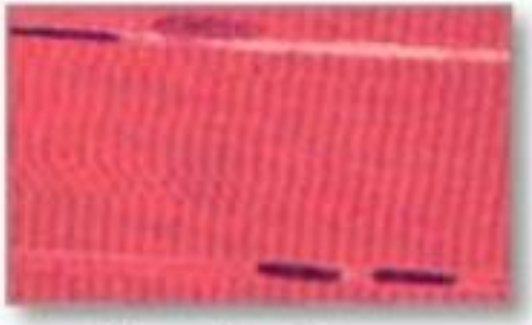
Four types of tissue



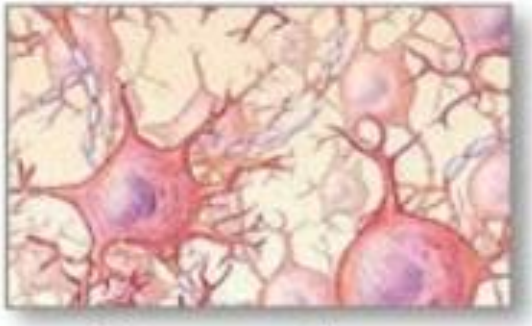
Connective tissue



Epithelial tissue



Muscle tissue



Nervous tissue

Cancer Terms to Know

Origin	Name
• Epithelium (lining tissue)	• Carcinoma
• Glands	• Adenocarcinoma
• Connective tissue	• Sarcoma
• Bones	• Osteosarcoma
• Muscles	• Rhabdomyosarcoma
• Brain tissue (glial cells)	• Glioma
• Lymphatic glands, spleen	• Lymphoma
• Blood cells	• Leukemia

BENIGN TUMORS

Benign tumors do not invade surrounding healthy tissues

Benign tumors do not spread out

Benign tumors may cause complications due to their presence which may obstruct natural conduits [bronchi (airways), intestine]

Terms: Adenoma, lipoma, osteoma

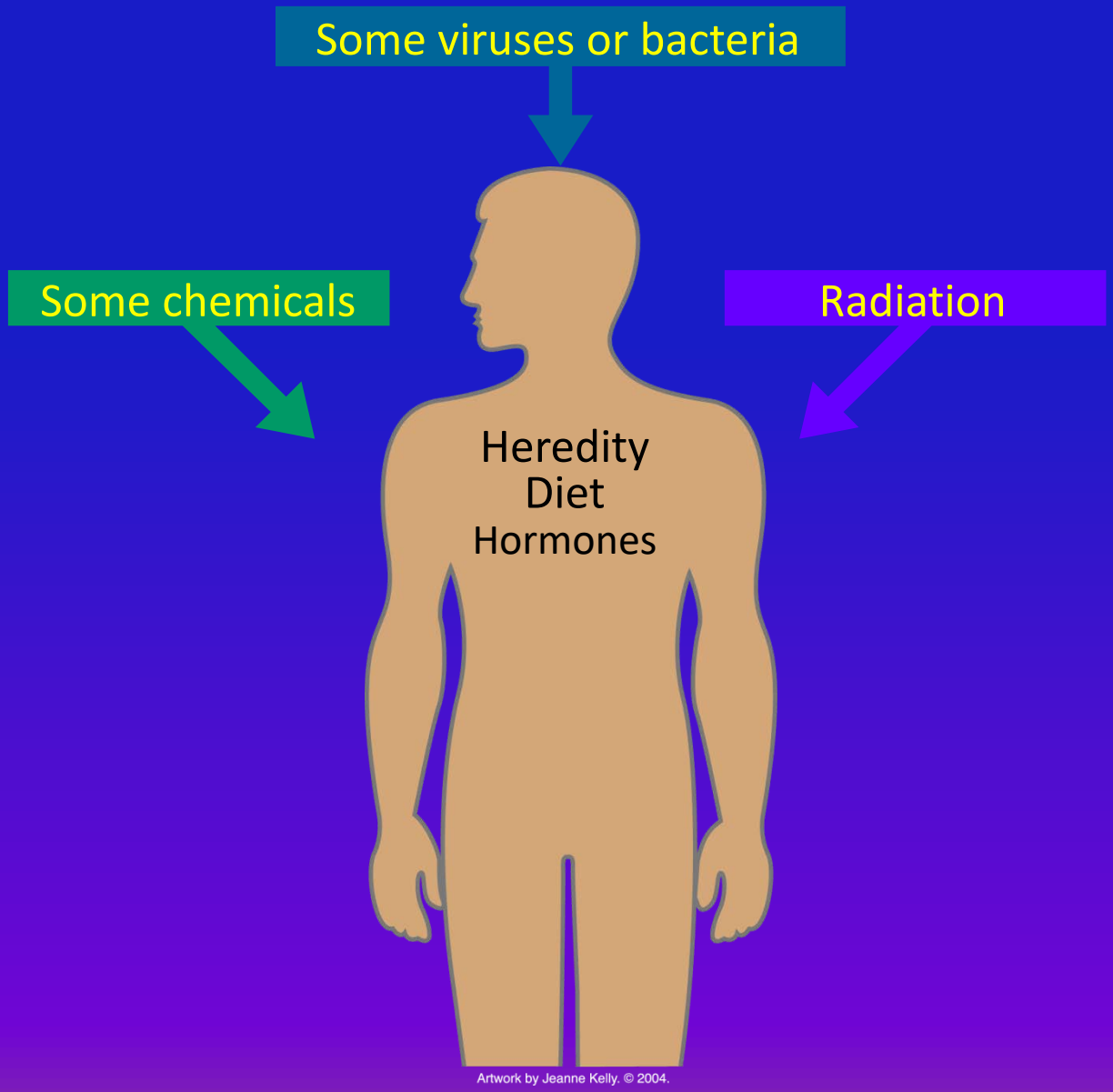
APOPTOSIS = PROGRAMMED CELL DEATH

A highly regulated and controlled cell death. It results in changes that include, cell shrinkage, nuclear breakage, chromatin and chromosomal breakage, and global messenger RNA decay.

Defective apoptotic processes have been implicated in a wide variety of diseases. An insufficient amount results in uncontrolled cell proliferation, such as **cancer.**

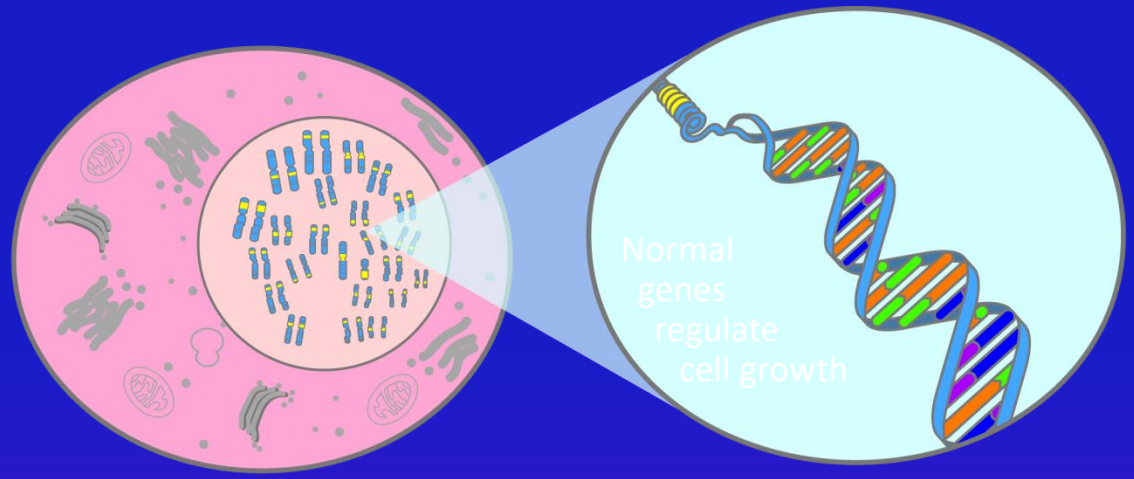
Between 50 and 70 billion cells die each day due to apoptosis in the average human adult.

What Causes Cancer?

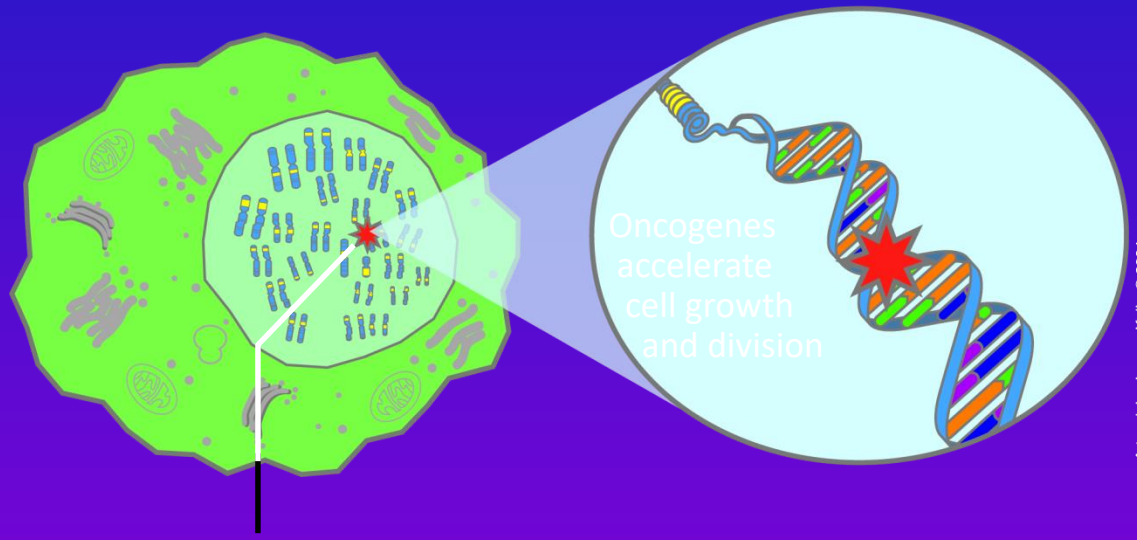


Oncogenes

Normal cell

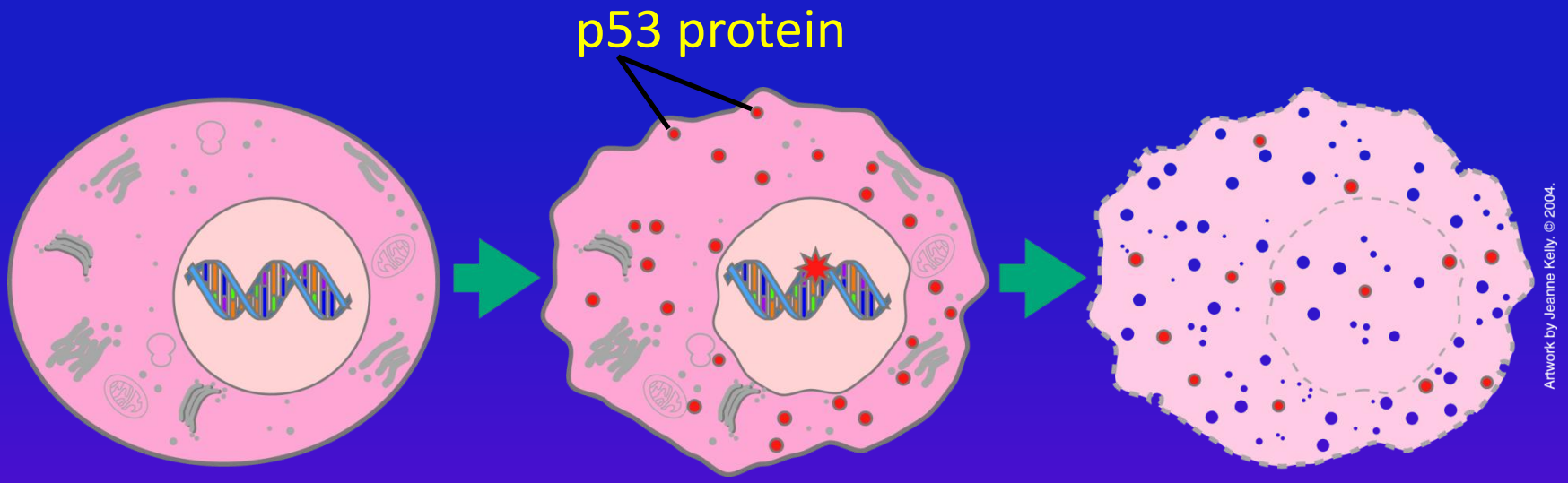


Cancer cell



Mutated/damaged oncogene

p53 Tumor Suppressor Protein Triggers Cell Suicide



Normal cell

Excessive DNA damage

Cell suicide (Apoptosis)

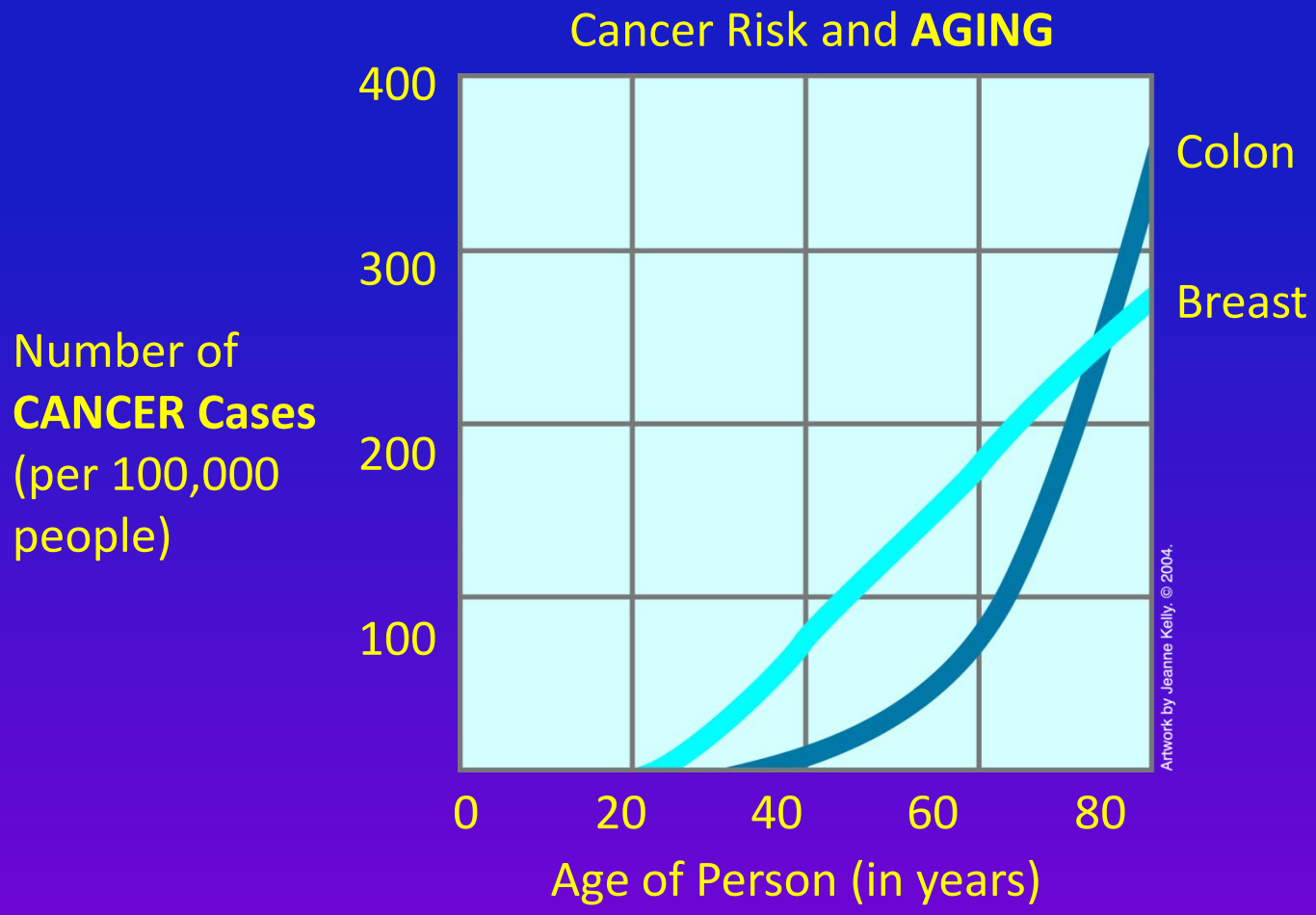
Chances of Genomic Instability

Human Body Cells ~ 10^{14}

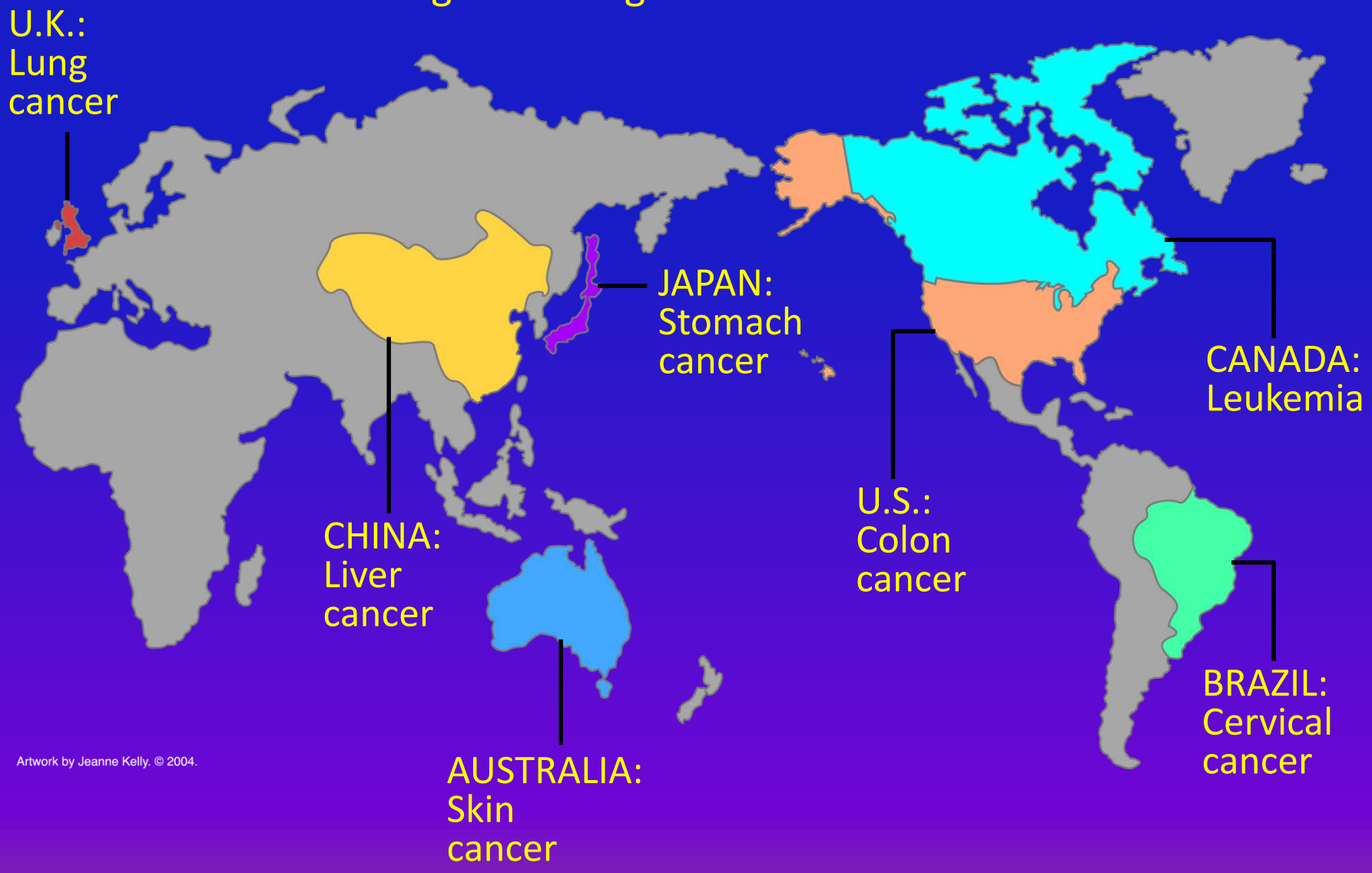
Lifetime Cell Divisions ~ 10^{16}

Chances of Mutation ~ 10^{124}

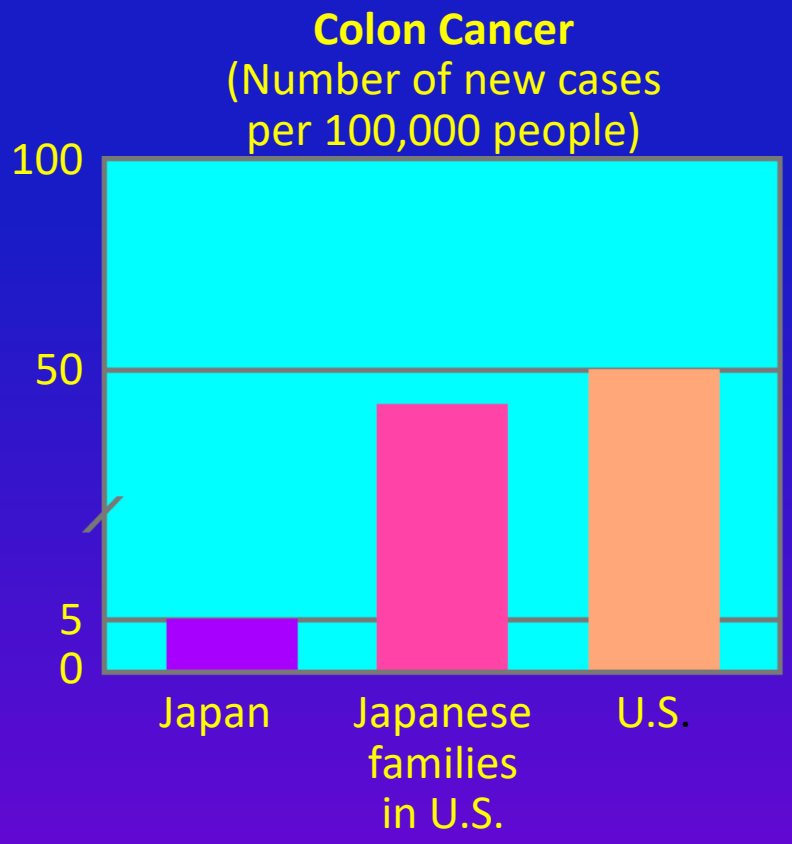
Cancer Risk and Aging

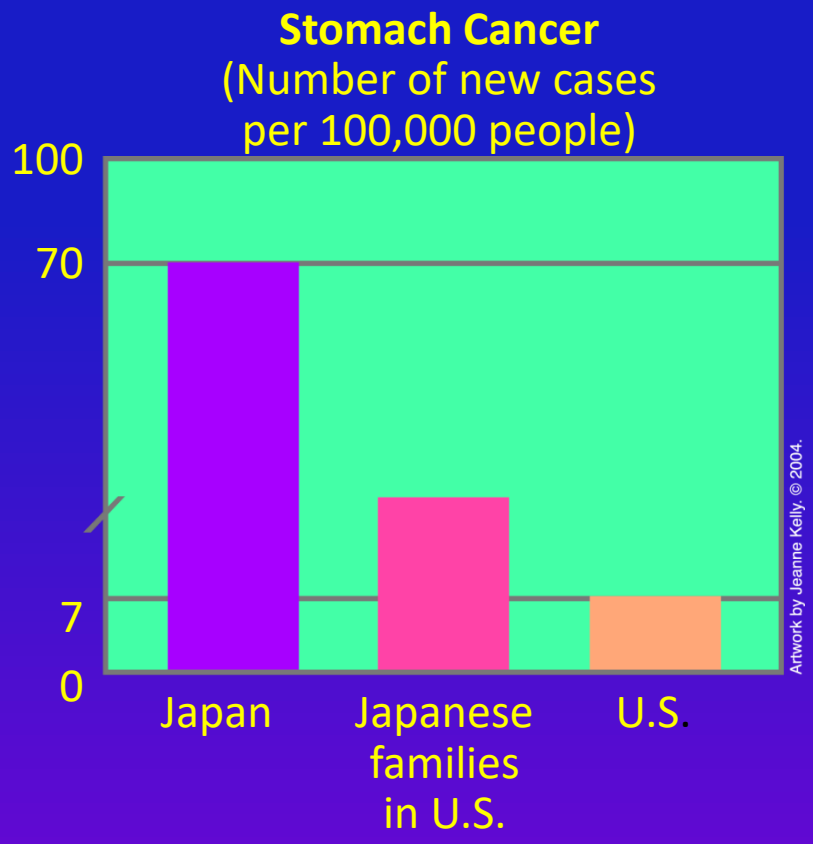


Population - Based Studies



Heredity? Behavior? “Acculturation”?



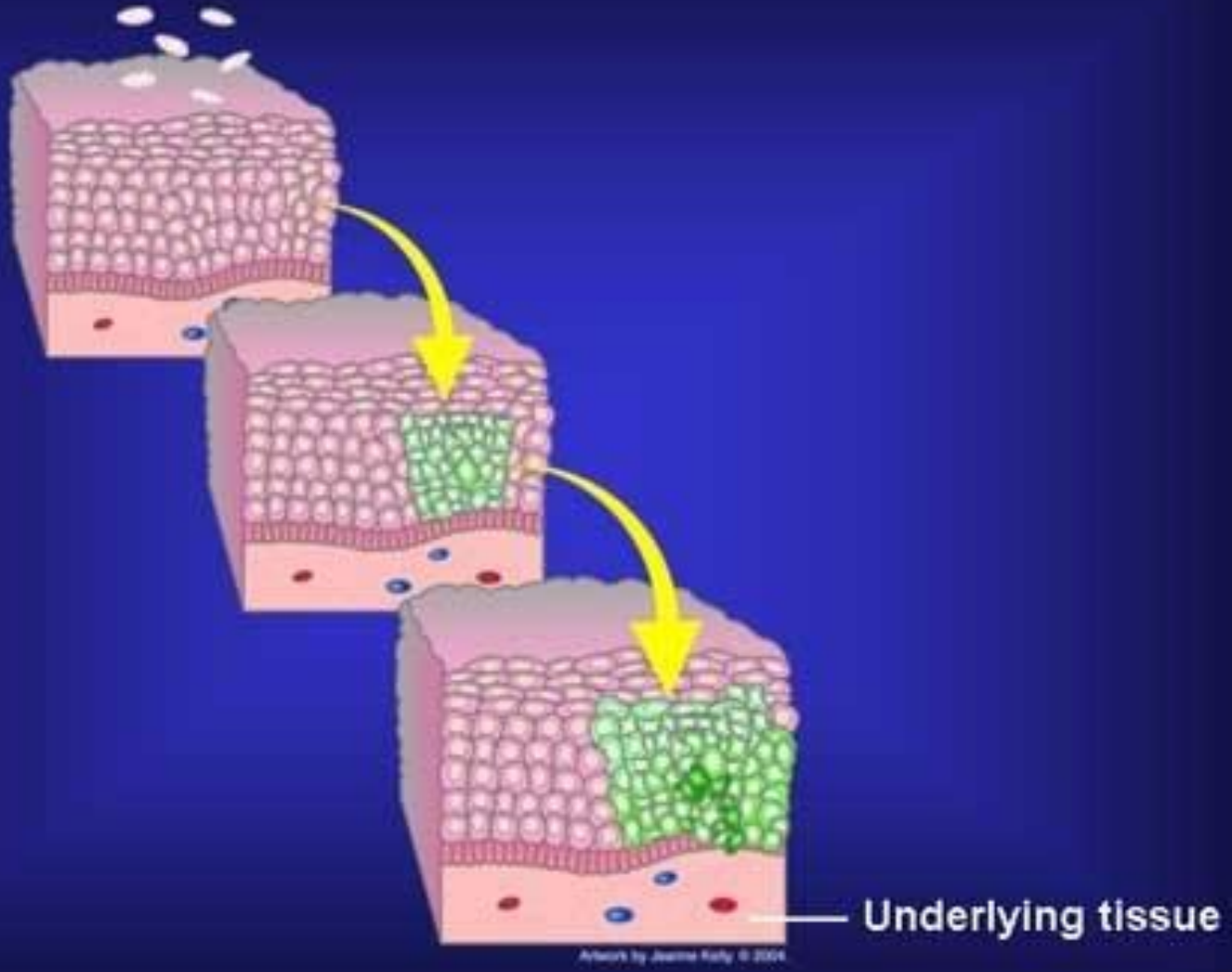


THE DAWN OF MOLECULAR EPIDEMIOLOGY OF HUMAN CANCER

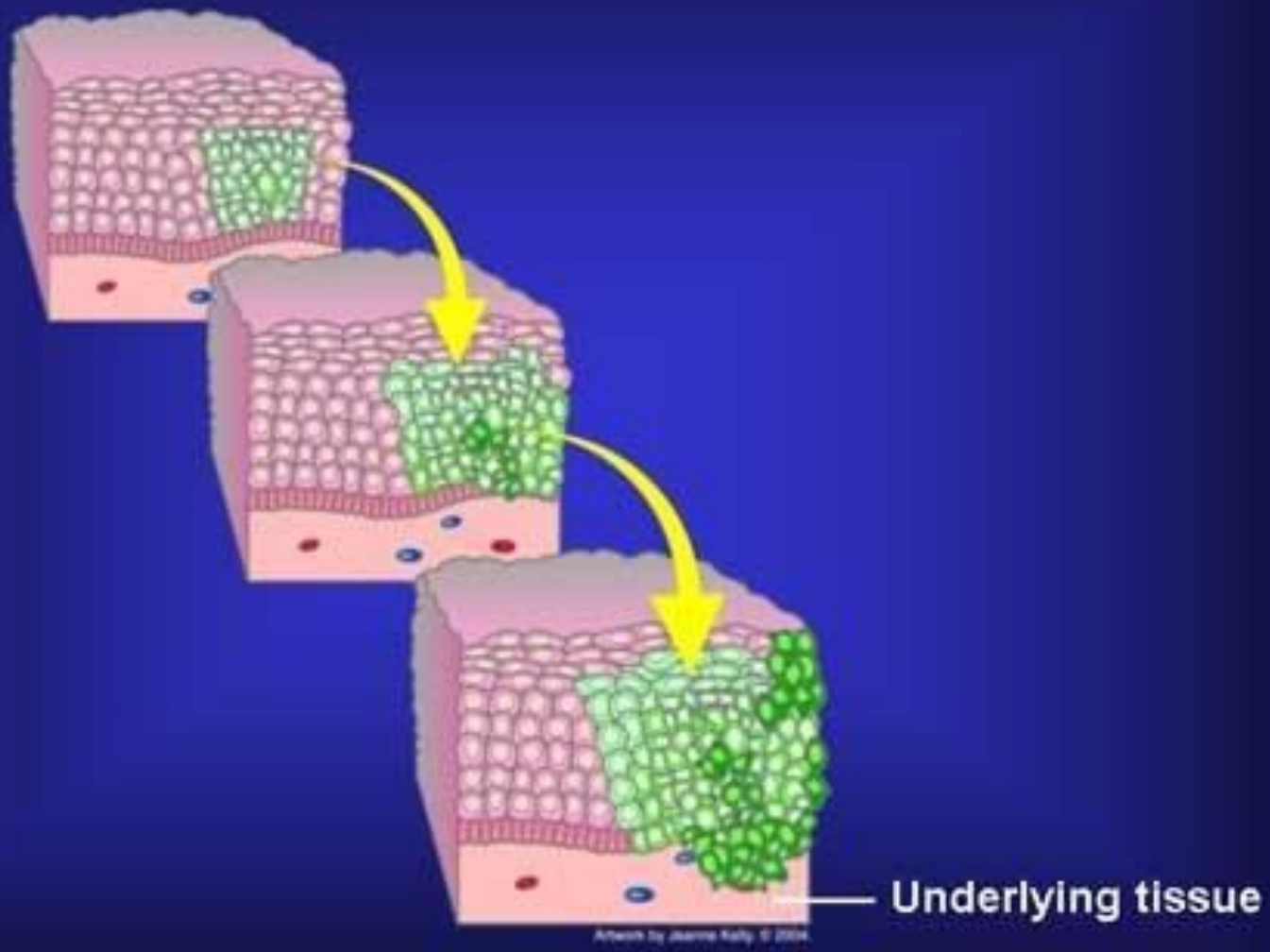
"NO ONE SUPPOSES THAT ALL THE INDIVIDUALS OF THE SAME SPECIES ARE CAST IN THE VERY SAME MOLD"

C. Darwin, 1859

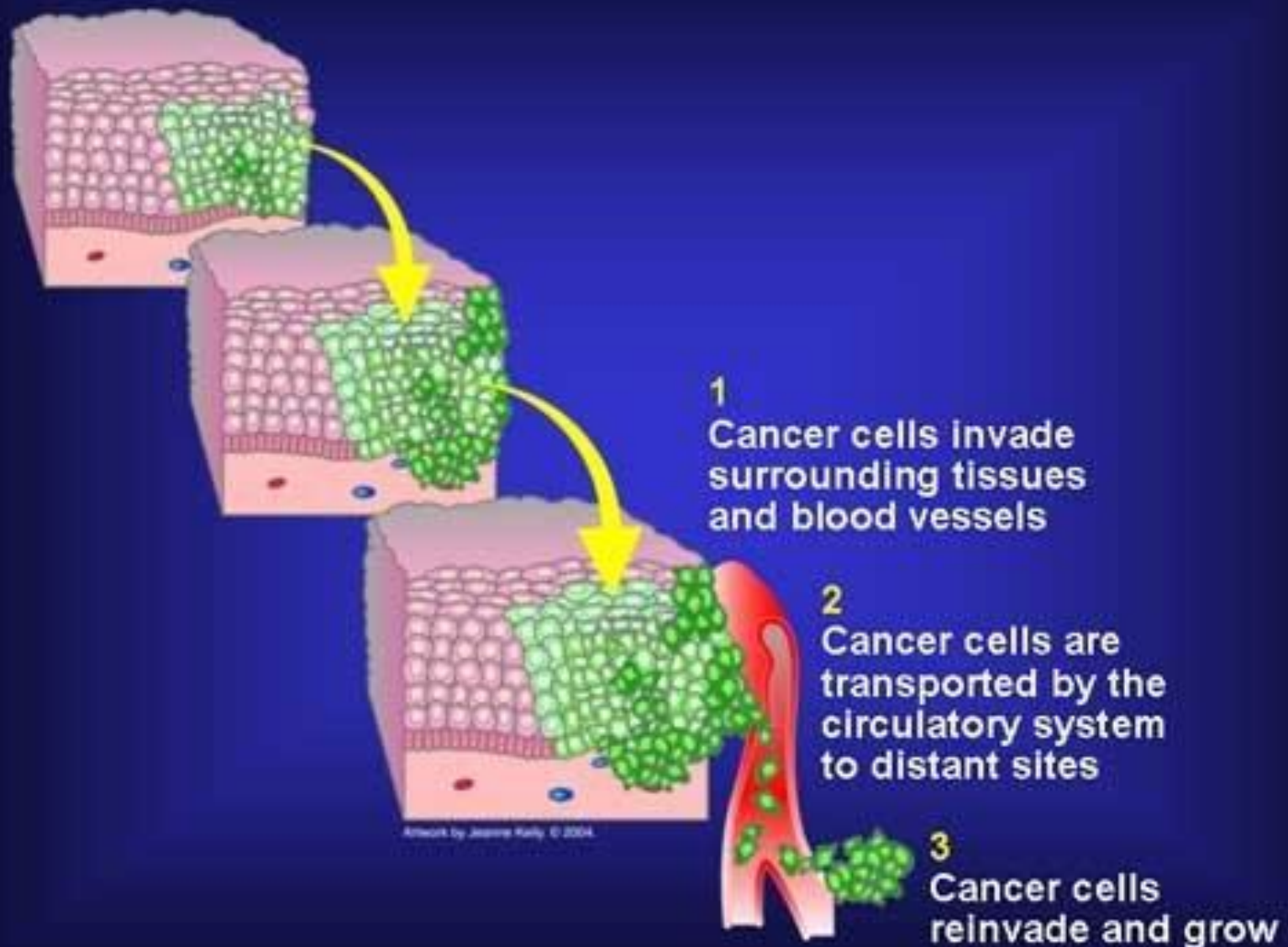
The Beginning of Cancerous Growth



Tumors (Neoplasms)



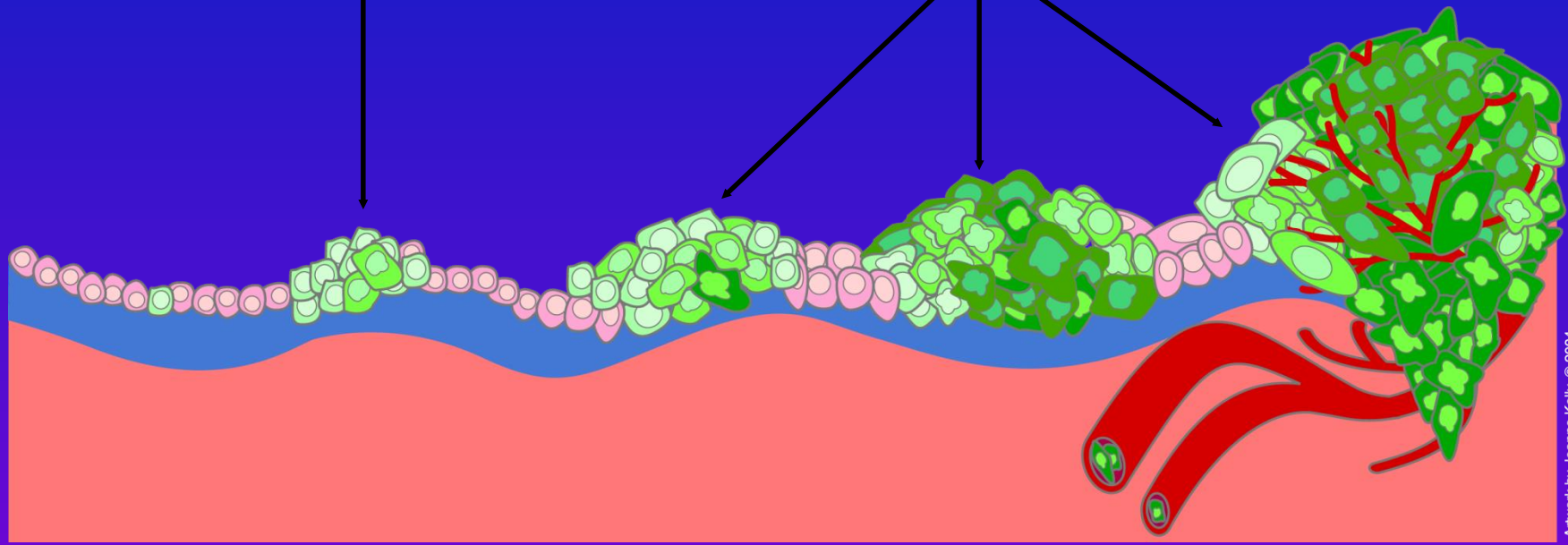
Invasion and Metastasis



Malignant versus Benign Tumors

Benign (not cancer) tumor cells grow only locally and cannot spread by invasion or metastasis

Malignant (cancer) cells invade neighboring tissues, enter blood vessels, and metastasize to different sites



Time

Development of a Malignant Tumor

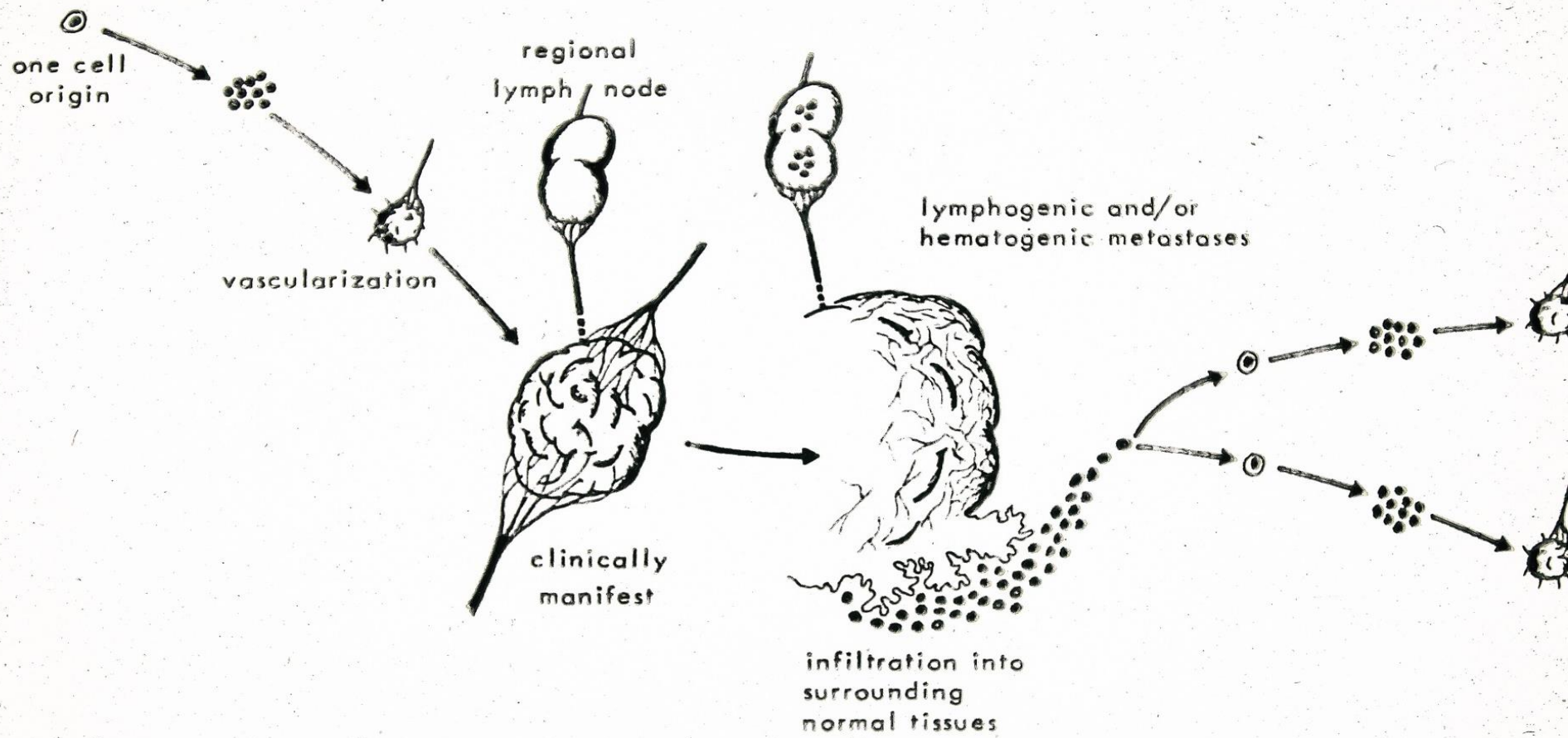
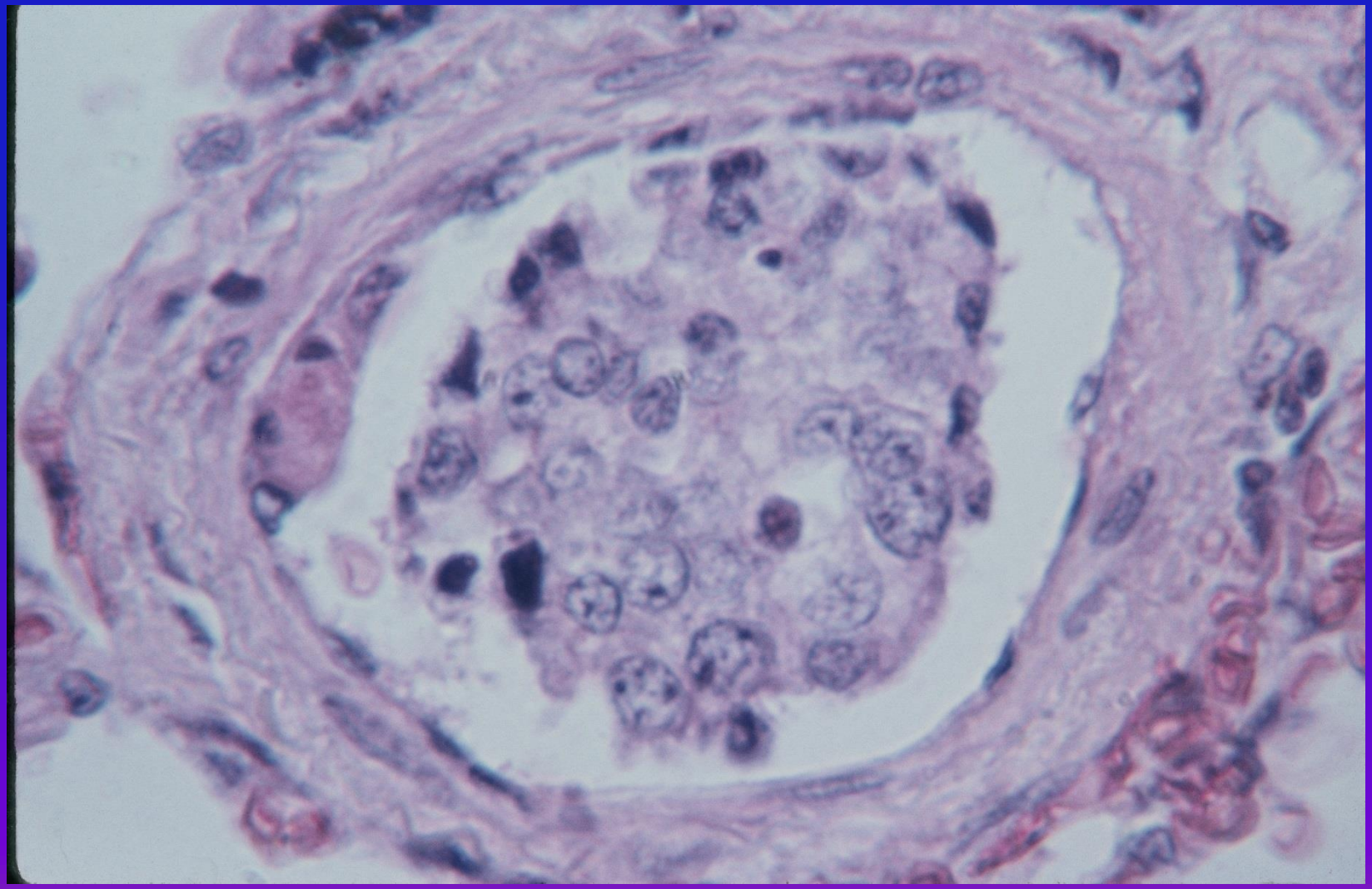


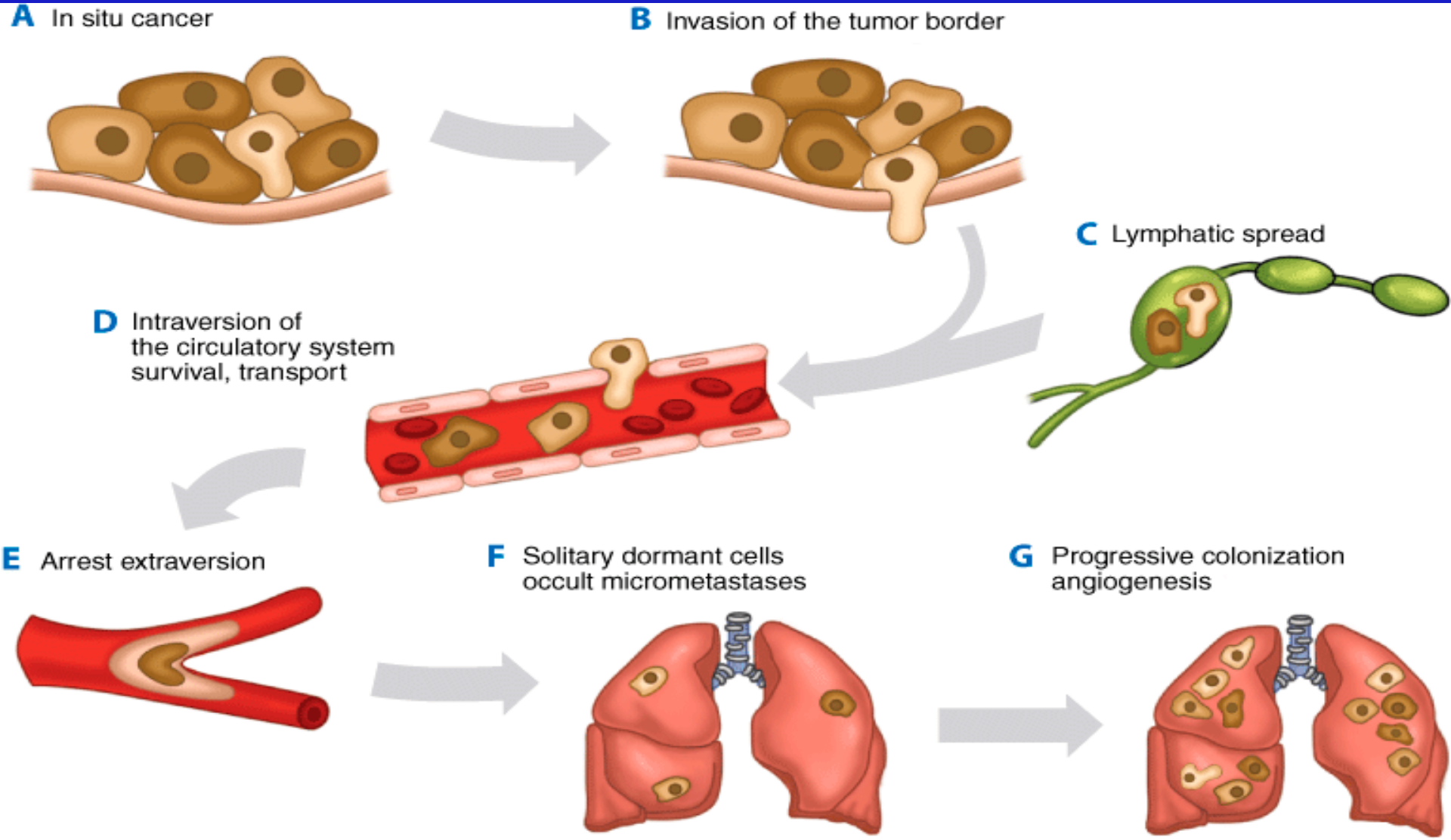
Figure 1. Development of a tumor.

LECTURE #2

TUMOR EMBOLUS

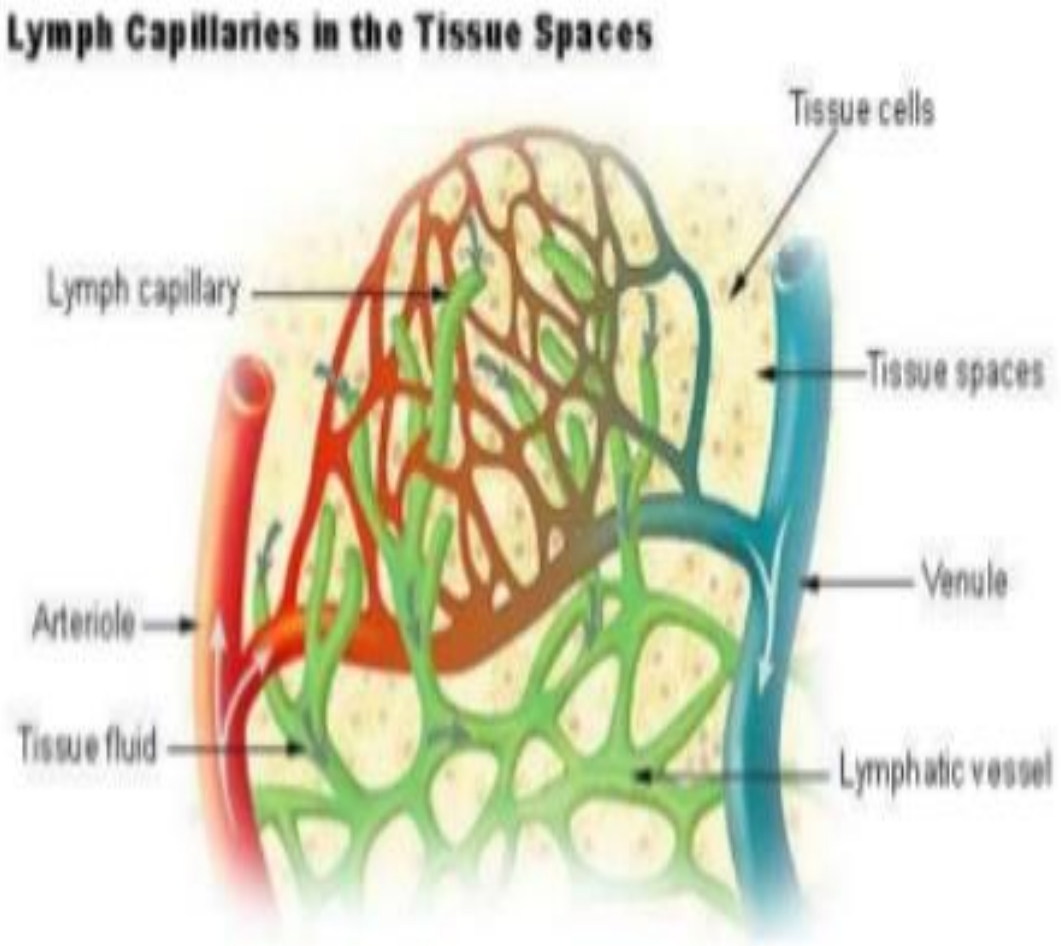


CANCER INVASION

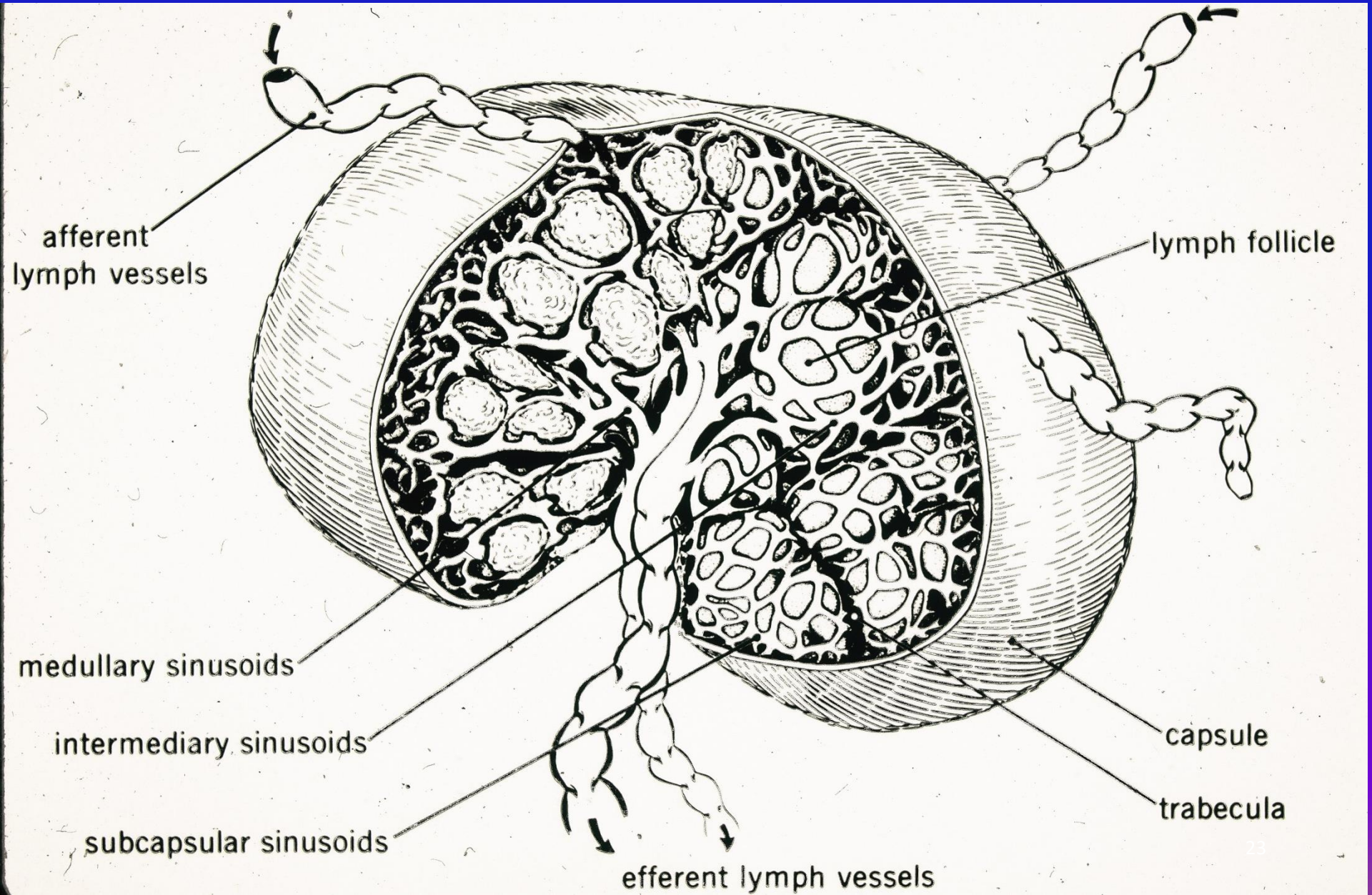


Source: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE: *Schwartz's Principles of Surgery, 9th Edition:* http://www.accessmedicine.com

LYMPHATIC SYSTEM



Lymph Node Structure - Schema



Left cervical lymphadenopathy (Enlarged lymph nodes)

Right Cervical (Neck) Enlarged Lymph Nodes

Swollen glands

Enlarged Glands (Lymphadenopathy)

Subjective: Tender or painless (?)

Objective: Acute or chronic

Local or general

Isolated or matted glands

Differential diagnosis: Chronic infections

Cancer

Diagnosis: Biopsy and pathologic examination

No needle biopsy

Preferential Sites of Cancer Spread

LUNGS ⇨ Lymph nodes, adrenal glands, bones, Liver, Brain

BREAST ⇨ Lymph nodes, lungs, liver, bones, brain

PROSTATE ⇨ Lymph nodes, spine, bones, lungs

COLON ⇨ Lymph nodes, liver, lungs

BRAIN - Rarely to lymph nodes of the neck

ENVIRONMENT and CANCER

ENVIRONMENTAL FACTORS
AIR POLLUTION

COMBUSTION	- Polycyclic hydrocarbons
SMOKING	- Passive smoking - Indoor air pollution
RADON GAS	- Miners
ASBESTOS	- Zeolite fibers - Chrysotile vs. Amphibole
ARSENIC	- Smelters
OIL VAPORS	- Wok cooking

COMBUSTION OF FOSSIL FUELS

Industry, motor vehicle traffic

50% increase in lung cancer

Si and C particles

↓

Inflammatory response

↓

cytokines + free radicals

↓

mutagenic effects

AIR POLLUTION BY COMBUSTION

Epidemiologic Studies

Silesia (Poland) → PAH → genotoxic effects

Yunan (China) - lung cancer in women

Shanghai - lung cancer in non-smoking women

CAUTIONS

Againſt the immoderate Use of

SNUFF.

Founded on the known Qualities of the

TOBACCO PLANT;

And the Effects it muſt produce when this Way taken into the Body:

AND

Enforced by Inſtances of Perſons who have periſhed miſerably of Diſeaſes, occaſioned, or rendered incurable by its Uſe.

By Dr. J. HILL.

* *

THE SECOND EDITION.

* *

LONDON:

Printed for R. Baldwin in Pater-noſter Row, and J. Jackson in St. James's-ſtreet.

MDCCLXI.

[Price One Shilling.]

TOBACCO SMOKING

Dr. John Hill's warning (1761)

Exponential increase with number of cigarettes smoked/day

Genetic Predisposition:

- Mutation of p53 tumor suppressor gene
- Activation of *ras* oncogene
- Deletion of chromosome 3p14-23
- Deregulated expression of *myc* family genes
- Autocrine stimulation by growth factors

TOBACCO AND LUNG CANCER
Genetic Predisposition

Hydroxylation of PAH

Aryl hydrocarbon hydroxylase inducibility

Debrisoquine 4-hydroxylation

PASSIVE TOBACCO SMOKING

- 20-90% increase in lung cancer in non-smoking spouses of smokers
- Increased levels of carcinogens in plasma of non-smoking spouses
- Banning of tobacco smoking from public places

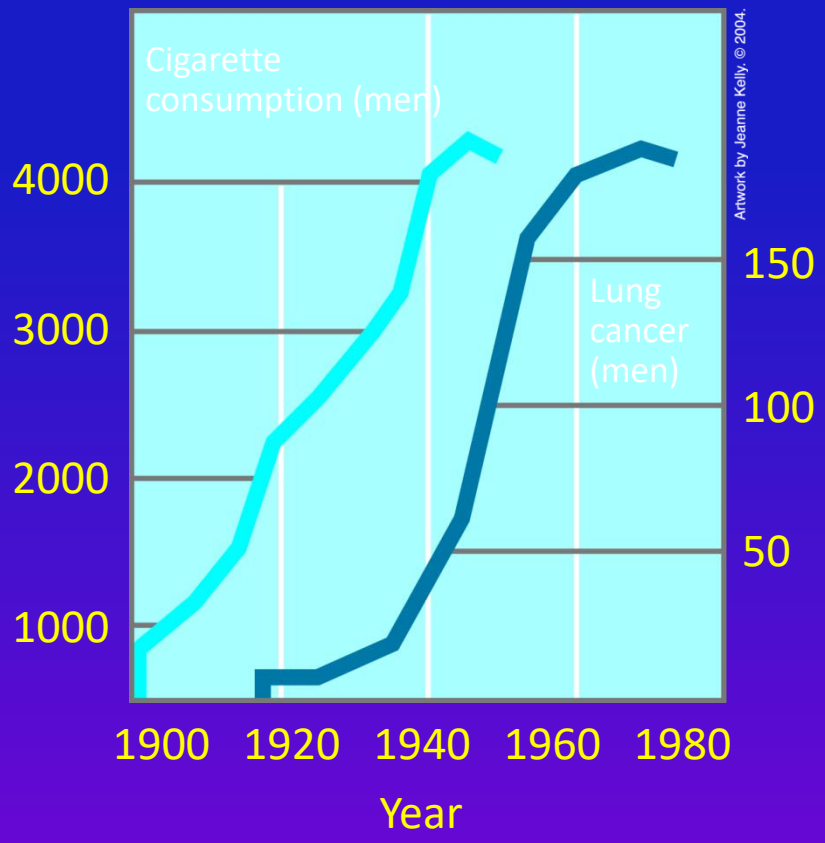
LUNG CANCER

RISK FACTORS

- Active tobacco smoking (87%)
- Passive smoking
- Environmental factors (asbestos, metals)

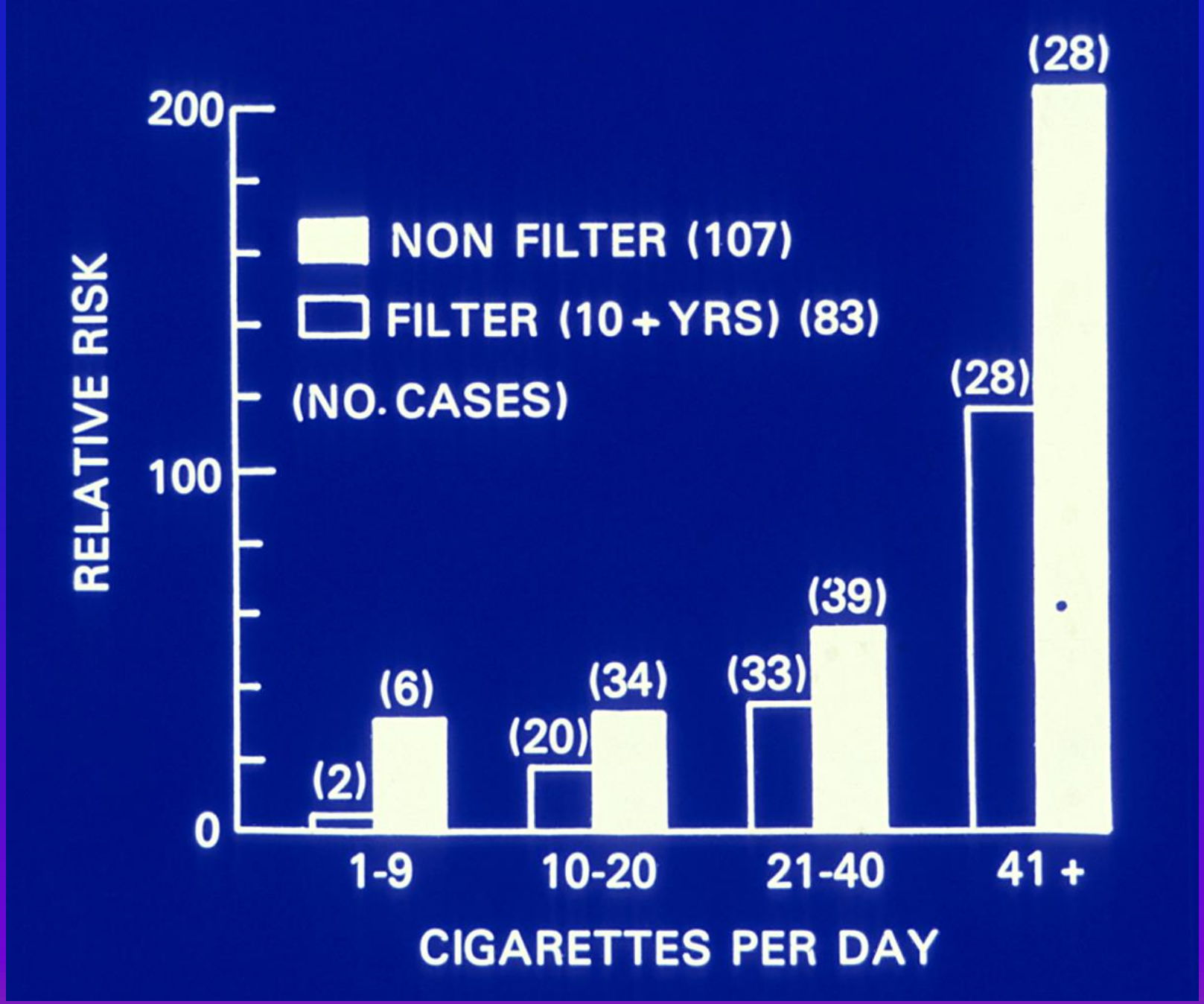
Lag Time

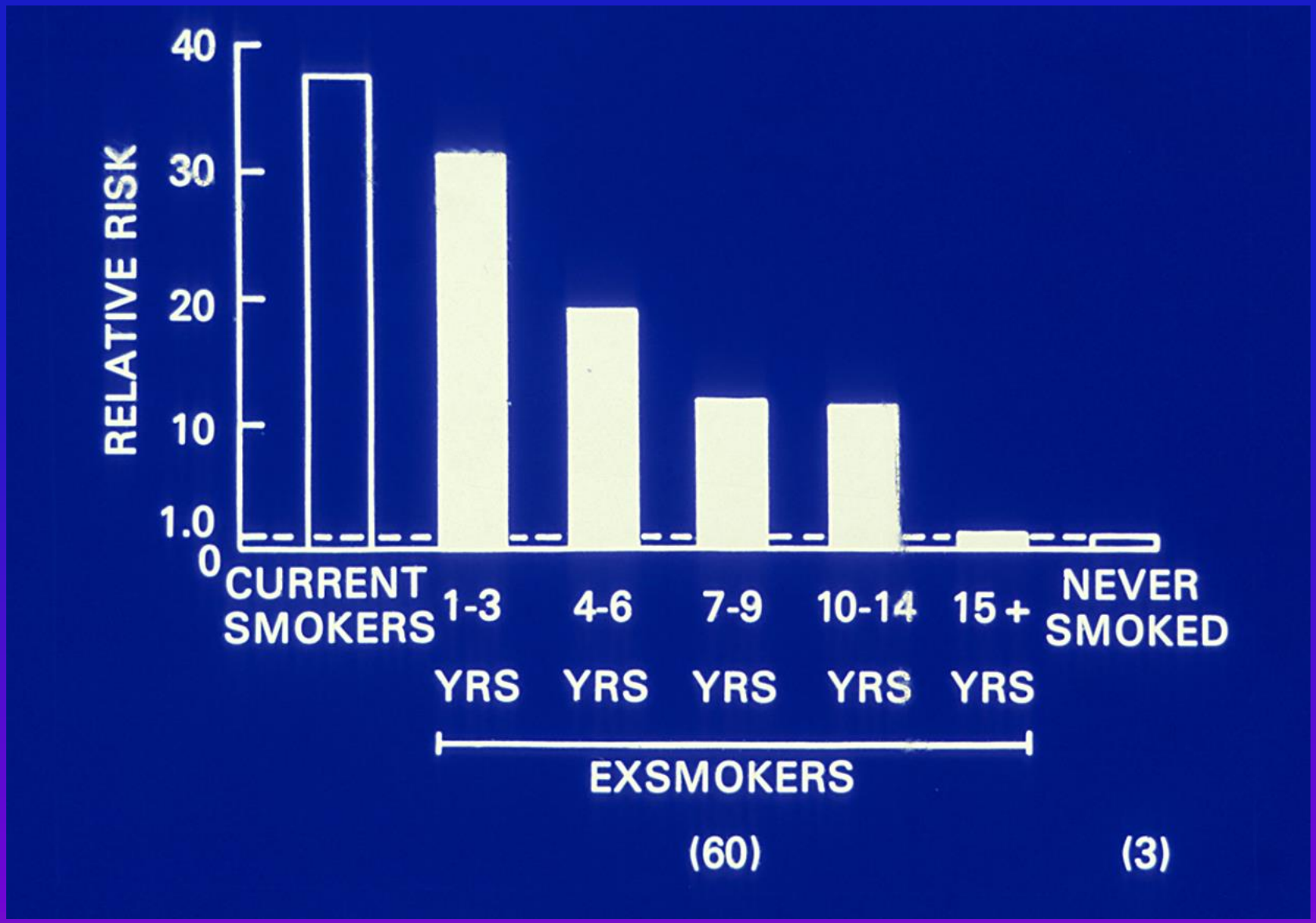
20-Year Lag Time Between **Smoking** and **Lung Cancer**



Cigarettes Smoked Person per Year

Lung Cancer Deaths (per 100,000 people)


RELATIVE RISK
200
100
0
NON FILTER (107)
FILTER (10+YRS) (83)
(NO. CASES)
(2)
(6)
(20)
(34)
(33)
(39)
(28)
(28)
1-9
10-20
21-40
41 +
CIGARETTES PER DAY


RELATIVE RISK
40
30
20
10
1.0
0
CURRENT SMOKERS
1-3 YRS
4-6 YRS
7-9 YRS
10-14 YRS
15 + YRS
NEVER SMOKED
EXSMOKERS
(60)
(3)

INTERMISSION

ASBESTOS

Natural soil deposits

Contamination from mining

↓

Underground water table

↑ Gastric, esophageal, and pancreatic cancer (California)

↑ Gastric, pancreas, and lung (Quebec)

ASBESTOS

Serpentine (chrysotile) - Quebec, S. Africa, N. Italy, Russia

Amphiboles (crocidolite, amosite, tremolite, actinolite)

Domestic - Cappadocia dwellings - zeolite

Industry - Occupational exposure - high friction devices
- insulation

ASBESTOS (cont'd)

Non-Occupational Exposure:

Malignant mesothelioma & lung cancer = 22% of asbestosis cases

Tobacco smoking = co-carcinogen

Genetic susceptibility = defect in gap junctional intercellular communication capacity

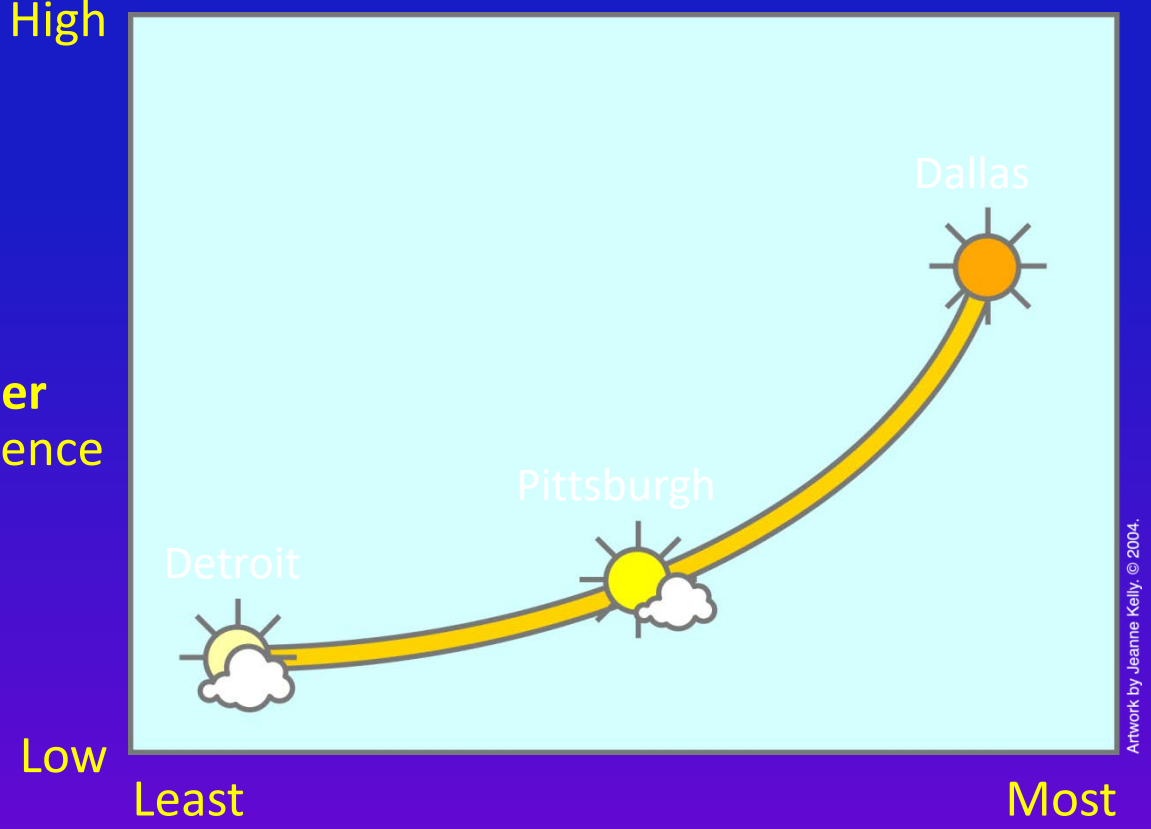
Department of Veterans Affairs

SOLAR RADIATION

SOLAR RADIATION (290-320 nm)

- Skin Cancer
- Melanoma

Low-Strength Radiation



NUCLEAR POWER

THREE MILE ISLAND (1979):

SOLID DECAY PRODUCTS CONTAINED

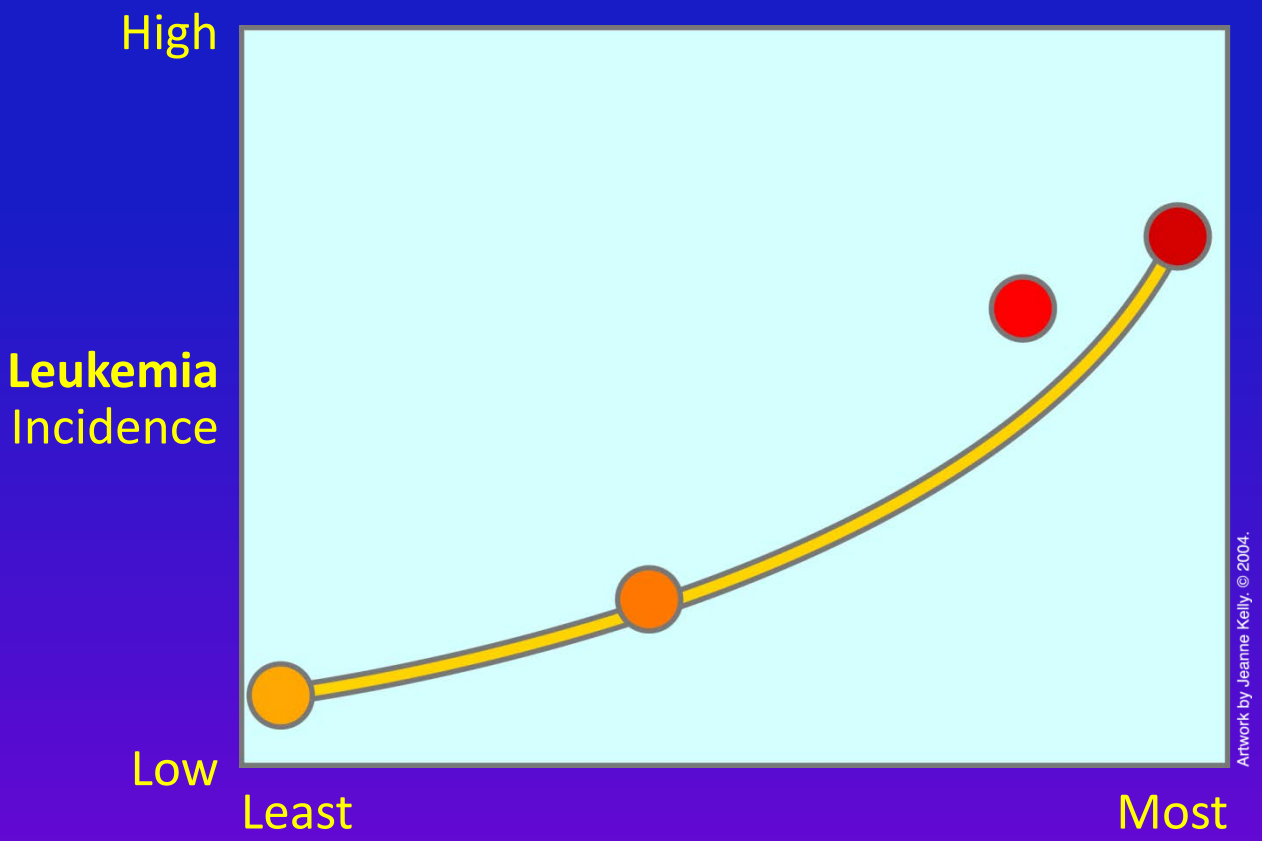
1 cancer death / 2 Mil. people

CHERNOBYL (1986):

SOLID DECAY PRODUCTS RELEASED

2% - 3% increase in cancer deaths

High-Strength Radiation



WATER POLLUTION AND CANCER

Organic compounds

Inorganic solutes

Radionuclides

Particulate matter

Microorganisms

INDUSTRIAL POLLUTION

Contamination of ground water

Dieldrin in rivers - lymphoma

Chlorophenols (sawmills - Finland) - sarcoma & lymphoma

Toxic waste disposal - lung, bladder, stomach, colorectal, esophagus, breast

Chromosomal aberrations

Sister chromatid exchanges

AGRICULTURAL POLLUTION

Chemical Fertilizers (> 150 tons/yr.)

- ➔ ↓ soil microorganisms and small mammals
- ➔ ↓ insects and organic matter
- Phosphates ➔ algal growth in water
- Nitrates ➔ toxic, carcinogenic

Pesticides:
- Arsenic compounds
- Plant parts
- Petroleum products ("dirty dozen")
- ↑ Breast cancer (Hawaii)

CHLORINATION BY-PRODUCTS

Chlorine + natural organic substances present in untreated water → Trihalomethanes (THM's)

THM are organohalogen compounds derivatives of methane

Ecological studies: Bladder, colon, rectal, lung, brain cancer

RADIONUCLIDES

Naturally occurring in water

From industry

From nuclear power generation

Radium-226, Radium-228, Radon-222

^{222}Rn = 1pCi/L → cancer probability = 1×10^{-6}

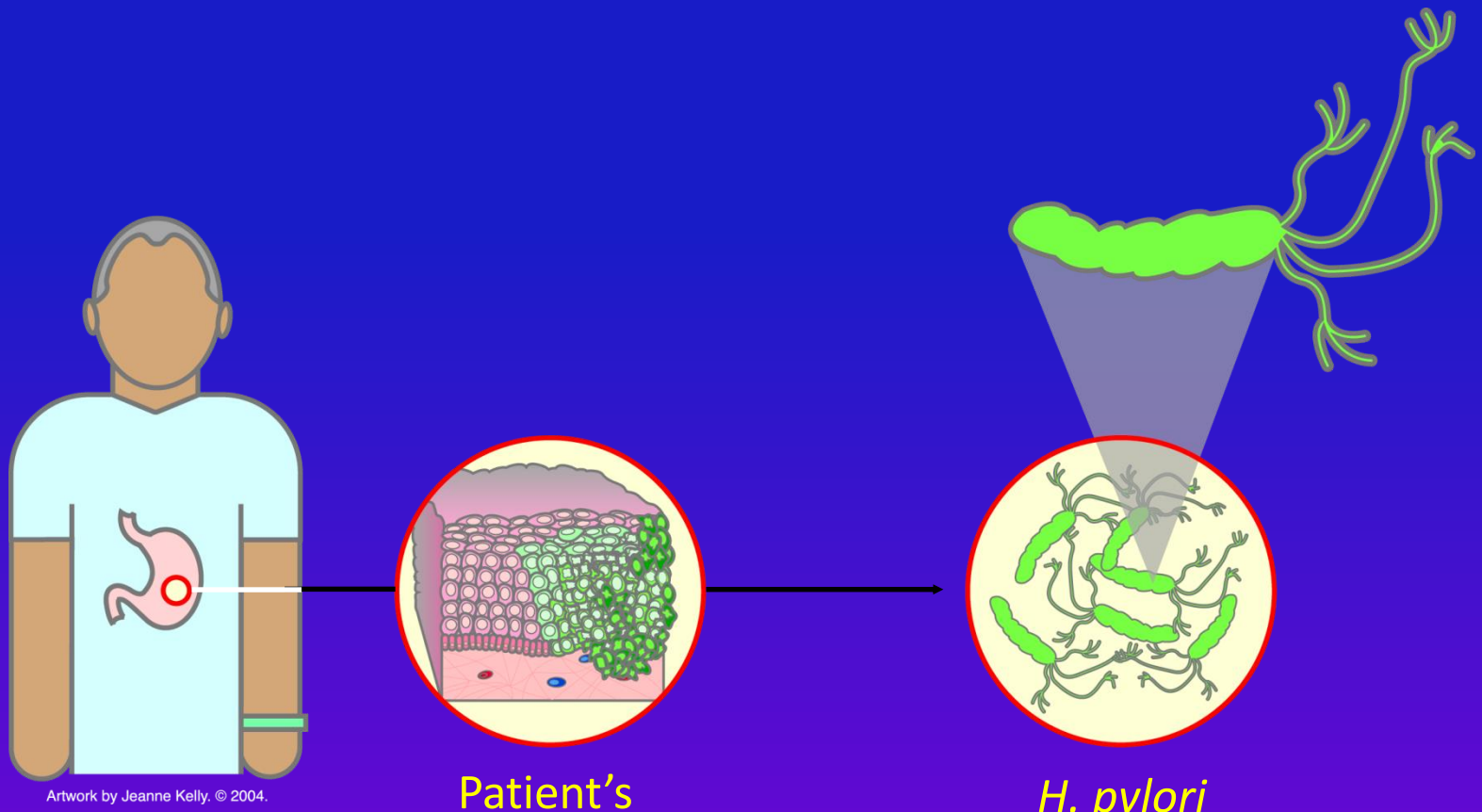
Increased incidence of childhood leukemia, bone sarcoma, lung and bladder cancer

Bacteria and Cancer

- ***Helicobacter pylori*** $\rightarrow$ Stomach cancer

- ***Chlamydia trachomatis*** $\rightarrow$ greater risk of cervical cancer

Bacteria and Stomach Cancer



STOMACH CANCER

H. pylori - 2/3 of world's population harbors the bacterium

- Second cause of cancer deaths worldwide

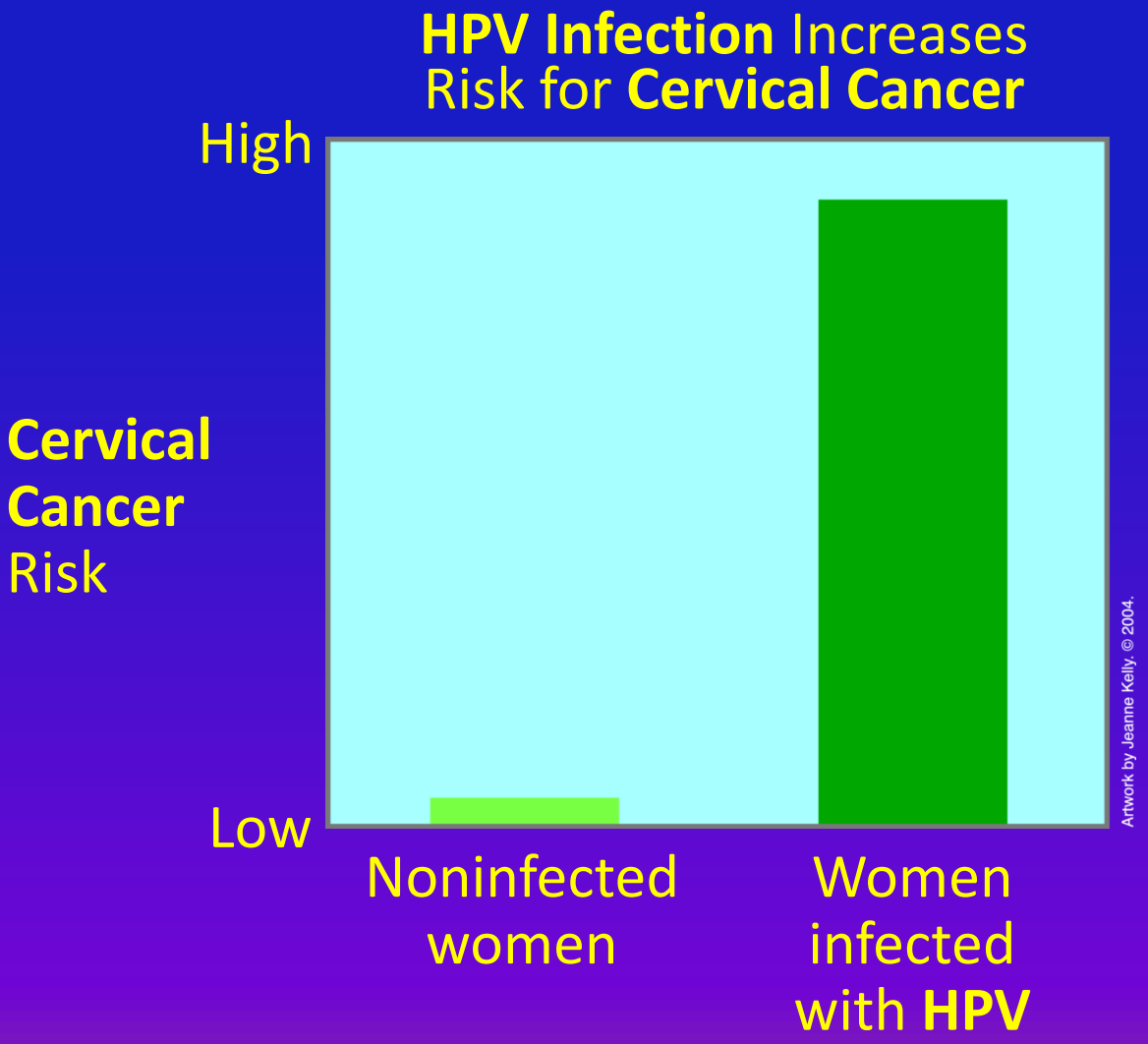
H. pylori → inflammation → reactive $O^{\bullet}$ species → cytokines → mutations → cancer - 6-8 fold increase compared to non-infected individuals

H. pylori → reduced risk of gastroesophageal (cardia) cancer → less acidity.

Human Viruses and Cancer

Virus	Human Cancer
Hepatitis B and C	Liver, pancreas, breast cancer
Herpes virus	Nasopharyngeal carcinoma, Lymphomas
Human Papilloma Virus	Cervical cancer, skin cancer

Avoid Cancer Viruses



CANCER PREVENTION

Disease Prevention

- Primary: Prevent onset of the disease
  - e.g. immunizations, chemoprevention
- Secondary: Prevent preclinical disease
  - cancer screening
- Tertiary: Prevent complications
  - cholesterol reduction in CAD

(US Preventive Service Task Force)

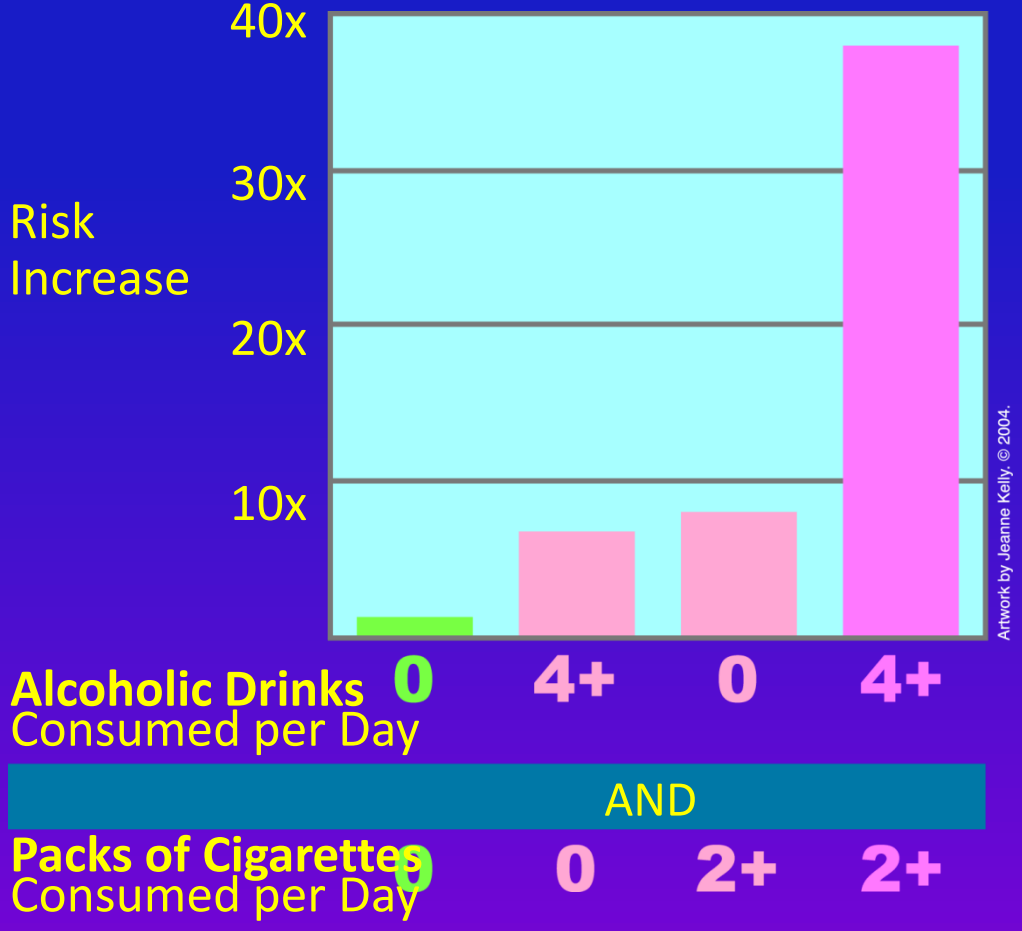

aim to be a healthy weight throughout life
WEIGHT
be physically active every day in any way for 30 minutes or more
CANCER PREVENTION
DIET
PHYSICAL ACTIVITY
choose mostly plant foods, limit red and avoid processed meat

NUTRITION and CANCER

- **Overnutrition**
  - **Colon, breast, and prostate cancer**
- **Undernutrition**
  - **Esophagus, stomach, and liver cancer**

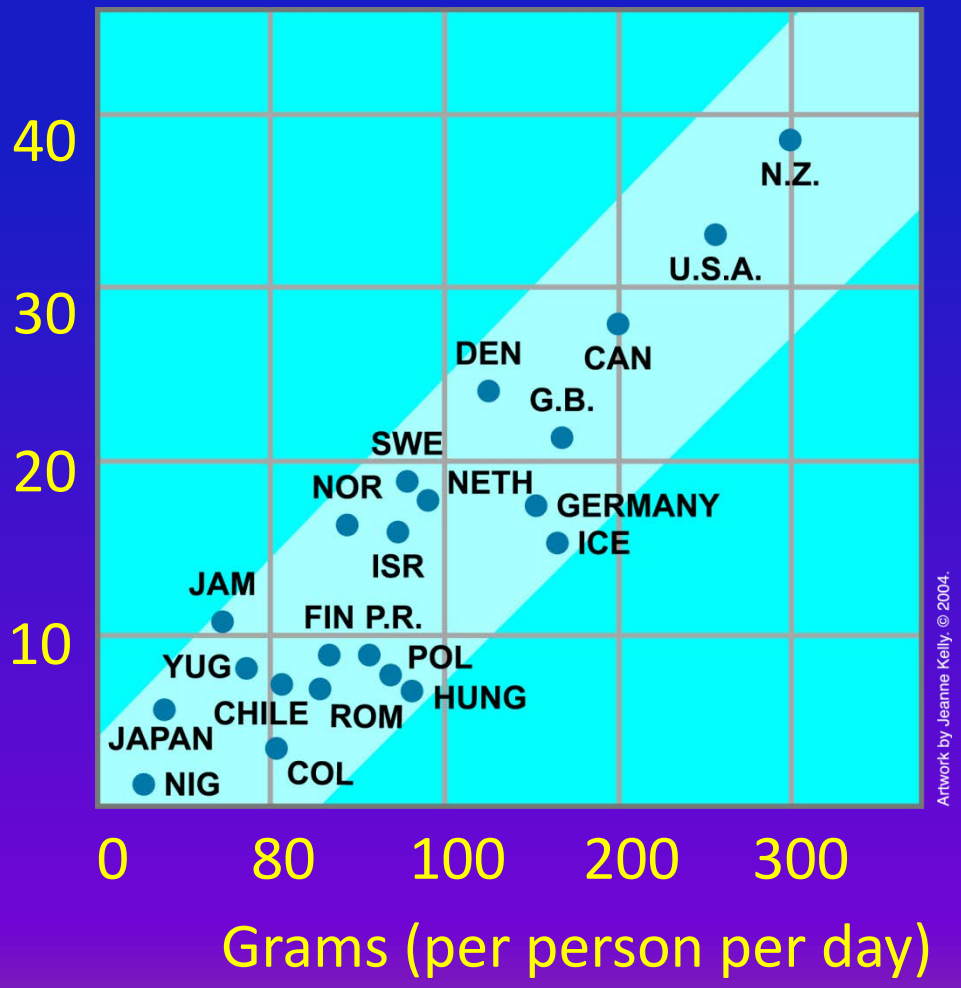
Limit Alcohol and Tobacco

Combination of Alcohol and Cigarettes
Increases Risk for **Cancer of the Esophagus**

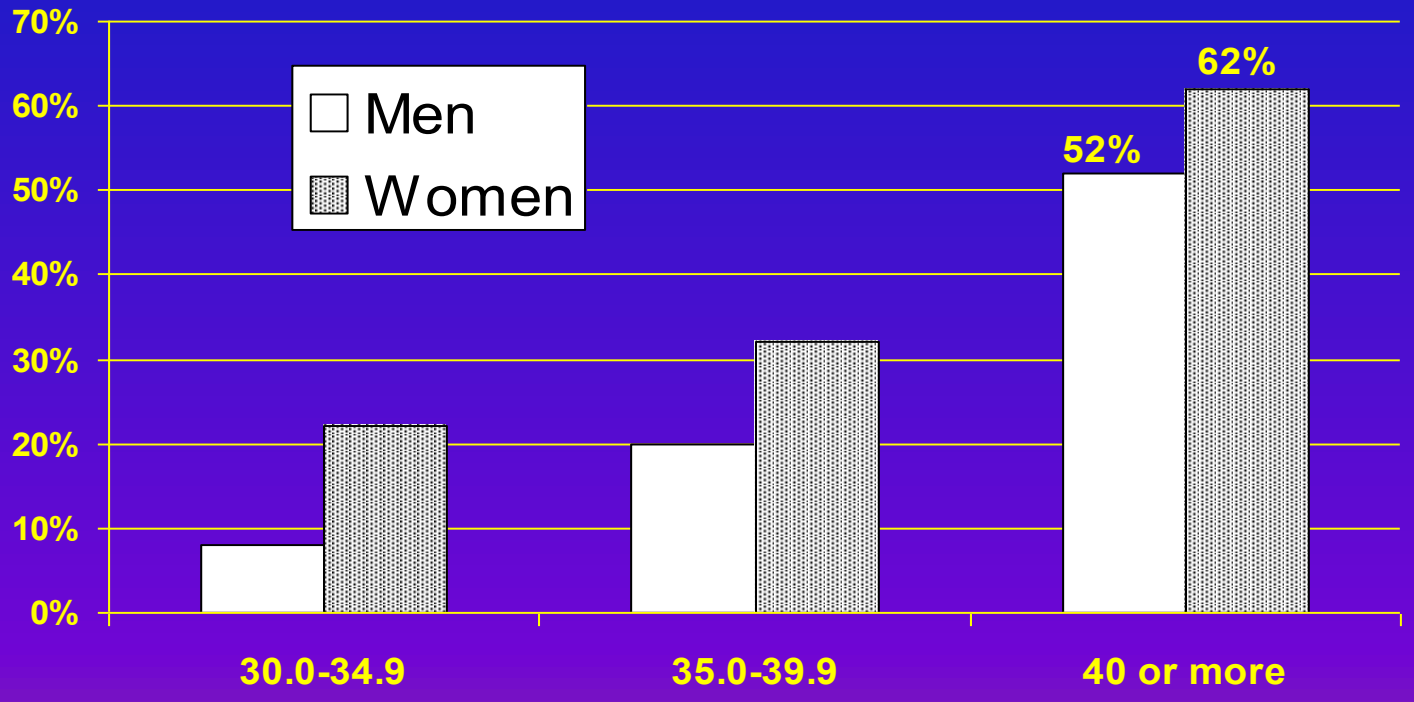


Diet: Limit Fats and Calories

Correlation Between Meat Consumption and Colon Cancer Rates in Different Countries



Cancer Death Rates 0f OBESE Compared to that of INDIVIDUALS with Normal Body Weight (BMI < 25)



OBESITY and CANCER
New Findings

- ~30% of US adults are obese **(BMI > 30)**
- ~35% of USadults are overweight (**BMI 25 - 30**)

- Women: Uterine cancer 6-fold

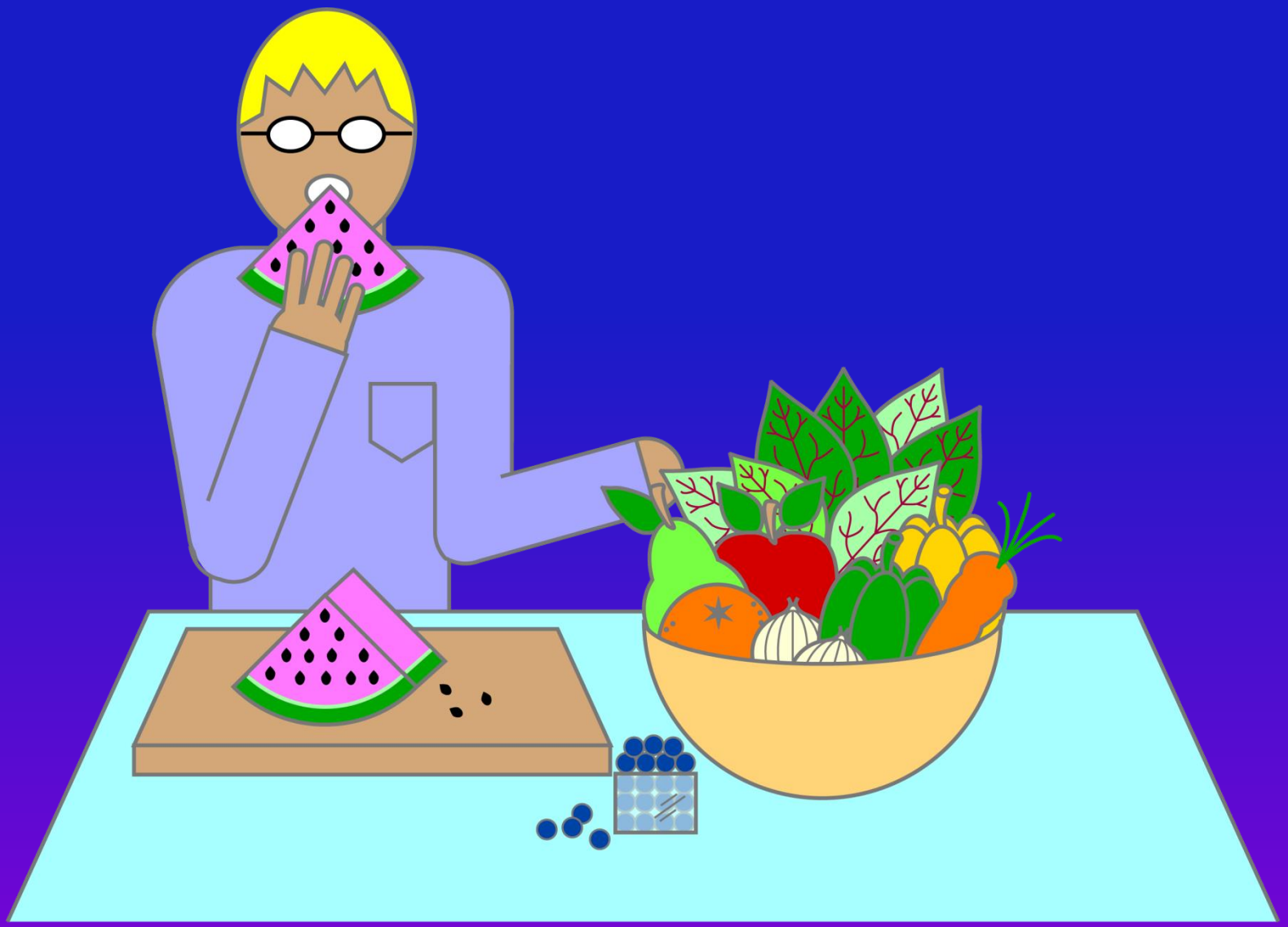
  Kidney cancer x 5-fold
- Men: Liver cancer 6-fold

  Colorectal cancer ~1.75-fold

Recommendations for Cancer Prevention

1. Be as lean as possible within the **normal range of body weight**.
2. Be **physically active** as part of everyday life.
3. **Do not smoke**.
4. Limit consumption of energy-dense foods; **avoid sugary drinks**.
5. **Eat mostly foods of plant origin**.
6. **Limit intake of red meat**; avoid processed meat.
7. **Limit alcoholic drinks**.
8. **Limit consumption of salt**; avoid moldy cereals (grains) or pulses (legumes).
3. Aim to meet nutritional needs through **diet alone**.

Diet: Consume Fruits and Vegetables



Artwork by Jeanne Kelly. © 2004.

Nutrition – Cancer Relationship

The Evidence

Cancer Causing Agents Found in Food

- Chemicals produced during:
  - Cooking meat: at high temperature, over direct flame
  - Preserving meat: smoked, salt-, nitrate- or nitrite- cured
  - Digesting red meat
- Alcohol
- Aflatoxins

Nutrition – Cancer Relationship

The Evidence

Cancer Protective Agents

- Fruits
- Vegetables
- Foods with:
  - Lycopene
  - Selenium
  - Folate
  - Fiber

Cancer Prevention

WCRF & AICR Recommendations

1. Be as lean as possible (normal weight range).

2. Be physically active every day.

3. Limit foods that promote weight gain:
   - Limit intake of processed, energy dense foods.
   - Avoid sugary drinks.
   - Consume fast foods sparingly, if at all.

Cancer Prevention

WCRF & AICR Recommendations

4. Eat mostly plant foods.
   - At least 5 servings of a variety of non-starchy vegetables and of fruits every day.
   - Eat unprocessed grains and/or legumes with every meal.
   - Limit refined starchy foods.

Cancer Prevention

WCRF & AICR Recommendations

5. Limit intake of red meat, and ***avoid*** processed meat.

Red Meat:

Consume less than 18 oz/week.

Processed meat:

Smoked, cured, salted, chemically preserved

Cancer Prevention

WCRF & AICR Recommendations

6. Limit alcohol intake to

   Not more than:

   - 2 drinks per day for men.
   - 1 drink per day for women.

1 drink = 1 ½ oz liquor, 5 oz wine, or
12 oz beer

Cancer Prevention

WCRF & AICR Recommendations

Preserved/Processed Food

7. Limit salt intake.
   - Avoid salt-preserved, salted or salty foods.
   - Limit intake of processed foods with added salt.

Avoid moldy grains or legumes.

- Stored a long time in warm temperatures.

Cancer Prevention

WCRF & AICR Recommendations

8. Aim to meet nutritional needs through diet.

   - Dietary supplements are not recommended for cancer prevention.

Food is!

CANCER CHEMOPREVENTION

CHEMOPREVENTIVE SUBSTANCES IN FOOD (I)

Flavonoids	-	Green plants, fruits, vegetables, tea, coffee, wine
Indoles	-	Cruciferous vegetables
Organic Isothiocyanates	-	Cruciferous vegetables
Monoterpenes	-	Citrus fruits
Phenolic Acids	-	Fruits, vegetables, nuts, coffee, tea
Phytic Acid	-	Legumes, cereals
Protease Inhibitors	-	Seeds, grains, legumes

CHEMOPREVENTIVE SUBSTANCES IN FOOD (II)

Carotenoids	-	Fruits, cereals, vegetables
Chlorophyllin	-	Leafy vegetables
Coumarins	-	Vegetables, citrus fruits, nuts, beans, grains
Diallyl Sulphides	-	Garlic, onions
Dietary Fiber	-	Grains, seeds, berries, fruit skin, legumes,

NUTRITIVE CHEMOPREVENTIVE AGENTS (III)

Agents	Major Food Source	Mode of Action
Vitamin A	Vegetables, fruits	Antioxidant
Vitamin C	Fruits (citrus), vegetables	Antioxidant
Vitamin E	Vegetable oils	Antioxidant
Selenium	Meat, eggs, dairy products	Antioxidant
Calcium	Dairy products	Binds bile and fatty acids

“The doctor of the future will give no drugs, but will interest his patients in the care of the human frame, in diet, and in the cause and prevention of human disease.”

- Thomas A. Edison