National Cancer Institute

Radiation Epidemiology Course

Radiation Epidemiology Branch
Division of Cancer Epidemiology & Genetics
National Cancer Institute
National Institutes of Health
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Introduction and Overview

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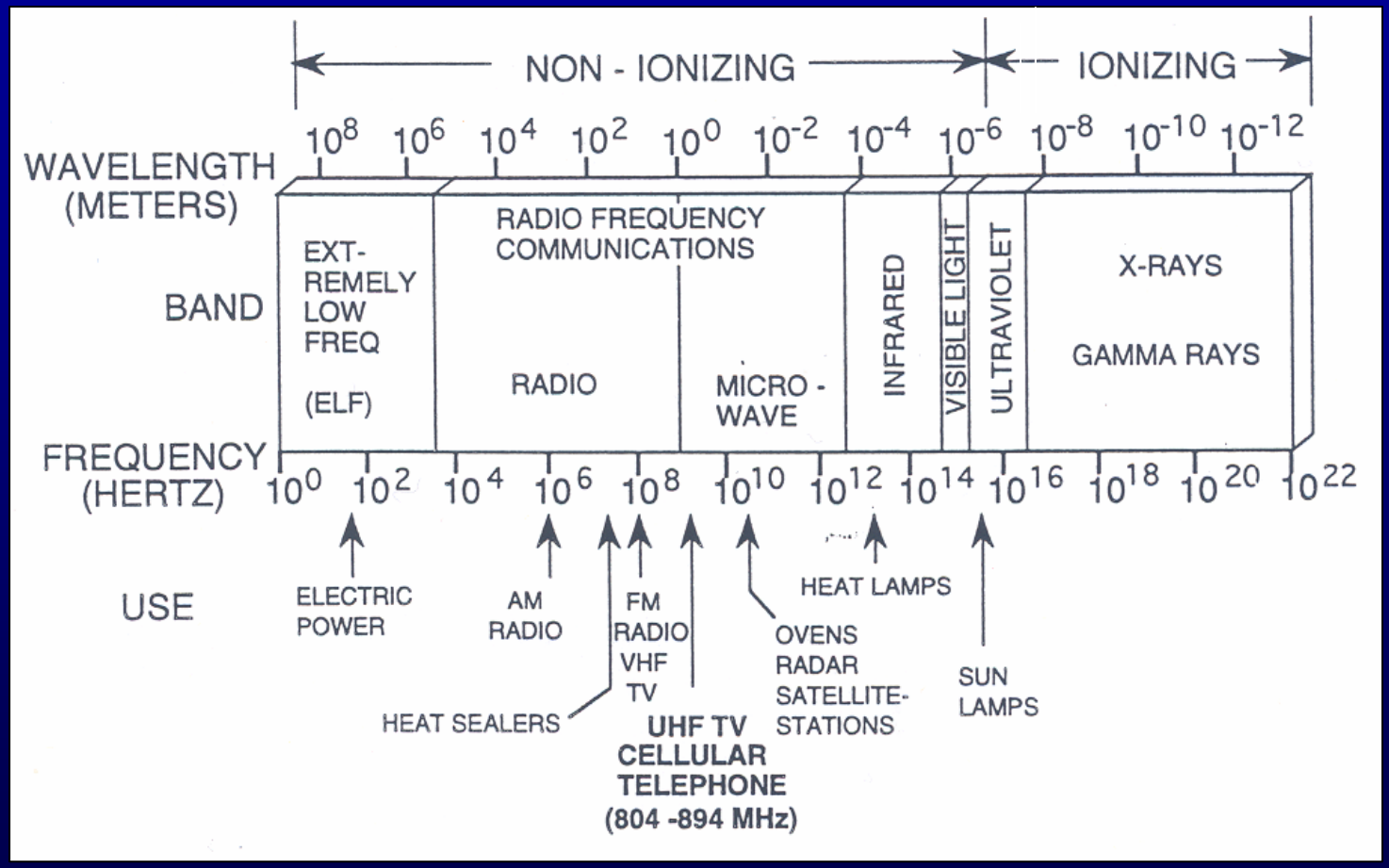
National Institutes of Health

Electromagnetic Spectrum



From: Rothman *et al.*; *Epidemiology* 1996;7:291

Types of Ionizing Radiation

- Electromagnetic
  - X-rays and gamma-rays
  - Identical as to type but differ as to source
- Particulate
  - Alpha-particles
  - Beta-particles
  - Neutrons
  - Protons

Linear Energy Transfer (LET)

- Density of ionizations along path of radiation
- Only physical difference among radiation types that influences biological damage produced

Penetration, By Radiation Type

Radiation Type	Penetration	Extent of Exposure
Alpha (α)	0.05 mm	confined to specific cells in organ
Beta (β)	1-2 cm	confined to particular tissue
Gamma (γ)	10-20 cm	less localized, potentially whole-body

Interaction of Ionizing Radiation with Tissue

charged particles

↓

electrical interactions

↓

ionization

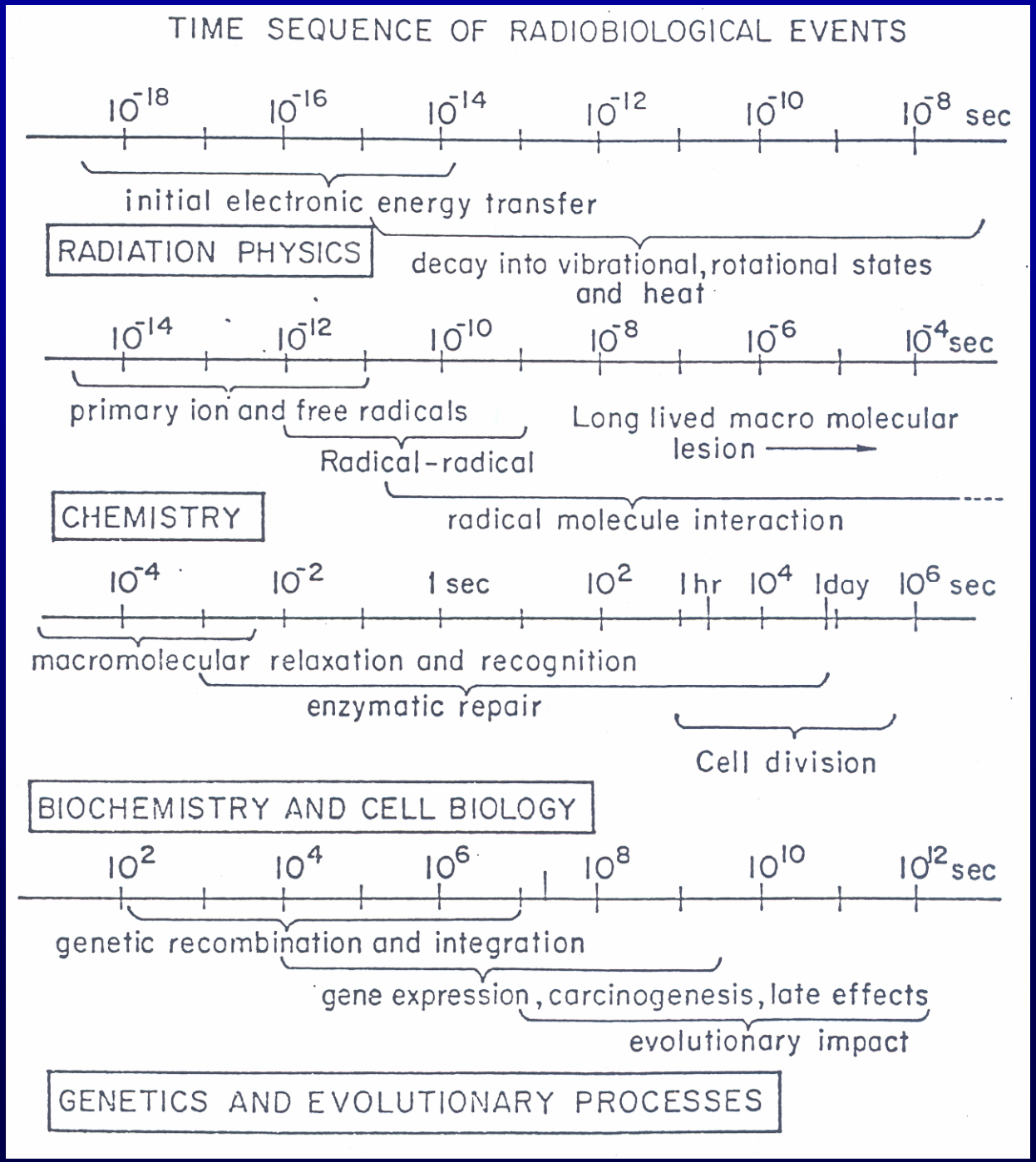
↓

chemical changes

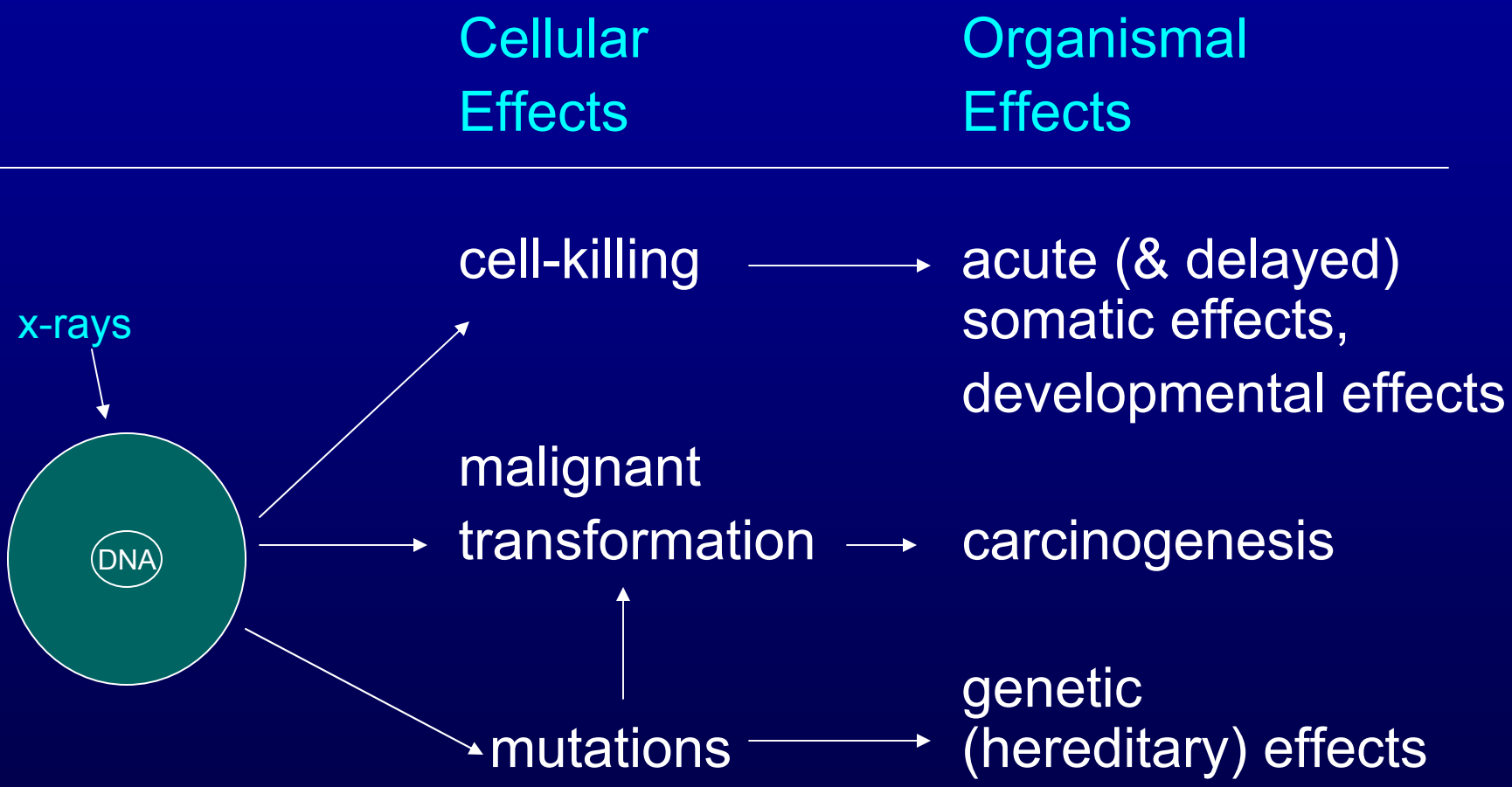
↓

biological effects

From: National Radiological Protection Board. 1998. *Living with radiation*


TIME SEQUENCE OF RADIOBIOLOGICAL EVENTS
10^{-18} 10^{-16} 10^{-14} 10^{-12} 10^{-10} 10^{-8} sec
initial electronic energy transfer
RADIATION PHYSICS
decay into vibrational, rotational states and heat
10^{-14} 10^{-12} 10^{-10} 10^{-8} 10^{-6} 10^{-4} sec
primary ion and free radicals
Radical-radical
Long lived macro molecular lesion
CHEMISTRY
radical molecule interaction
10^{-4} 10^{-2} 1 sec 10^{2} 1 hr 10^{4} 1 day 10^{6} sec
macromolecular relaxation and recognition
enzymatic repair
Cell division
BIOCHEMISTRY AND CELL BIOLOGY
10^{2} 10^{4} 10^{6} 10^{8} 10^{10} 10^{12} sec
genetic recombination and integration
gene expression, carcinogenesis, late effects
evolutionary impact
GENETICS AND EVOLUTIONARY PROCESSES

Biological Effects of Ionizing Radiation



"Stochastic" and "Non-Stochastic" Effects

Stochastic: *random* events leading to effects; probability of effect, but not its severity, depends on dose

e.g., cancer, genetic effects

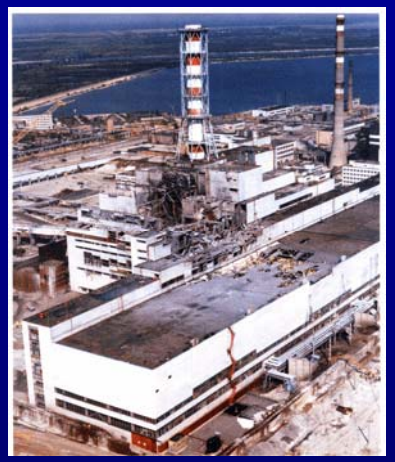
Non-stochastic: severity of effect varies with dose, and threshold may exist

e.g., cataract, loss of hair or skin reddening, bone marrow depletion, impaired fertility

Erythema
(example of non-stochastic effect)

From: National Radiological Protection Board. 1998. *Living with radiation*

Sources of Radiation Exposure



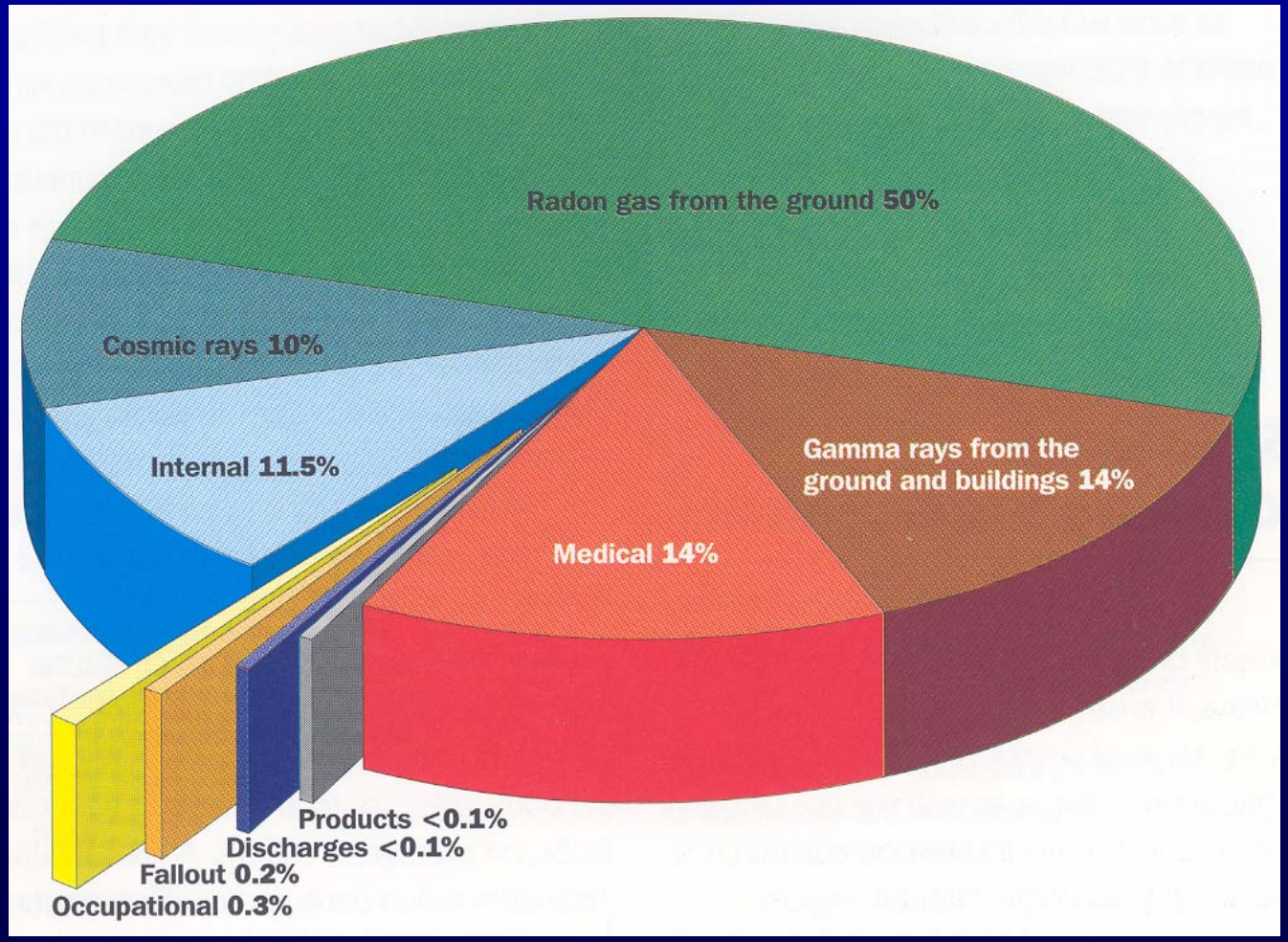
Medical

Environmental

Occupation

Military

Sources of Radiation Exposure



From: National Radiological Protection Board. 1998. *Living with radiation*

General Research Aims

- Dose-response
  - Quantitative estimates of risk
  - Risk at low doses & dose rates
- Influence of radiation type
- Expression of excess risk over time
  - Relation to background incidence
- Transport of risk estimates between populations
- Dependence on host characteristics
- Joint effects of radiation and other exposures
- Insights into mechanisms

Stages in Radiation Interaction With Biologic Systems

- Physical stage (10^{-14} seconds)
- Chemical stage (10^{-7} to 10^{-4} seconds)
- Biological stage (seconds/lifetimes/generations)
  - Biochemical/cellular (seconds to hours)
  - Physiologic (hours to years)
  - Genetic & evolutionary (years to decades+)

Development of Radiation Injury

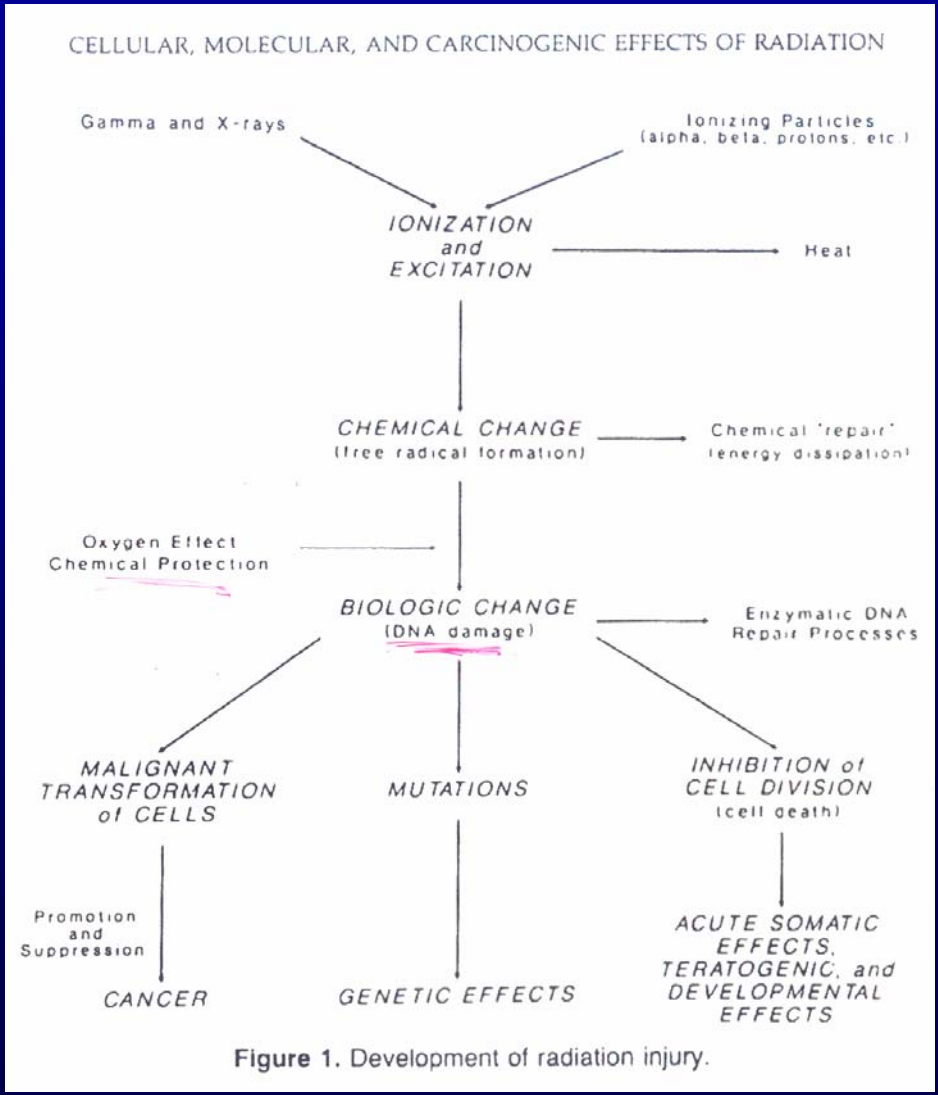


Figure 1. Development of radiation injury.

Little and Williams (1977)

Exposure Parameters Influencing Biological Events

- Dose
- Linear energy transfer (LET)
- Anatomic distribution of dose
  - Whole-body (e.g., atomic bomb explosions)
  - Partial-body (e.g., radiotherapy)
- Dose-rate
  - Instantaneous vs. protracted or fractionated exposures

Energy Deposition Relative to Lethal Radiation Dose

- Proportion of ionized molecules in cell at lethal radiation doses is very small

  → affected macromolecules must be very important

- DNA as a likely essential target

Applications of Radiation Epidemiology

- Inform radiation protection policy
- Risk assessment
- Legal proceedings
- Insights into radiobiology & cancer biology

Future Issues in Radiation Epidemiology

- New medical exposures
- Possible application to radiological terrorism
- Interactions with host factors and environmental exposures
  - e.g. radiation & smoking
  - genetic susceptibility
- Insights to cancer mechanisms

Sources of Human Exposure to Ionizing Radiation

- Natural background radiation
- Man-made sources
  - Medical
  - Occupational
  - Military
  - Environmental

Natural Background Radiation

- Cosmic radiation
  - Primarily neutrons and γ-radiation
  - Exposure varies with altitude
- External γ-radiation
  - Naturally-occurring isotopes of uranium series
  - Depends on local geology & type of building material
- Internal emitters
  - Radon gas

Medical Radiation Exposures

- Diagnostic x-rays
  - High frequency of population exposure, but cancer risks likely small
- Radiation therapy
  - Opportunities for good radiation dosimetry
  - Interactions
- Nuclear medicine

Computed Tomography (CT) Scan

From: National Radiological Protection Board. 1998. *Living with radiation*

Occupational Radiation Exposures

- Nuclear industry
- Medical radiation workers
  - radiologists, x-ray technologists
- Increased exposure to background radiation for some occupations
  - e.g., miners, airline pilots & attendants
- Radium dial painters (historical)

Military & Environmental Exposures

- Atomic bomb explosions in Japan
  - Single most important source of information on radiation effects
- Fallout from weapons tests
  - Estimate your thyroid dose & thyroid cancer risk (http://ntsi131.nci.nih.gov) from U.S. tests
- Nuclear reactor accidents
  - e.g., Chernobyl

Internal Radiation Exposures

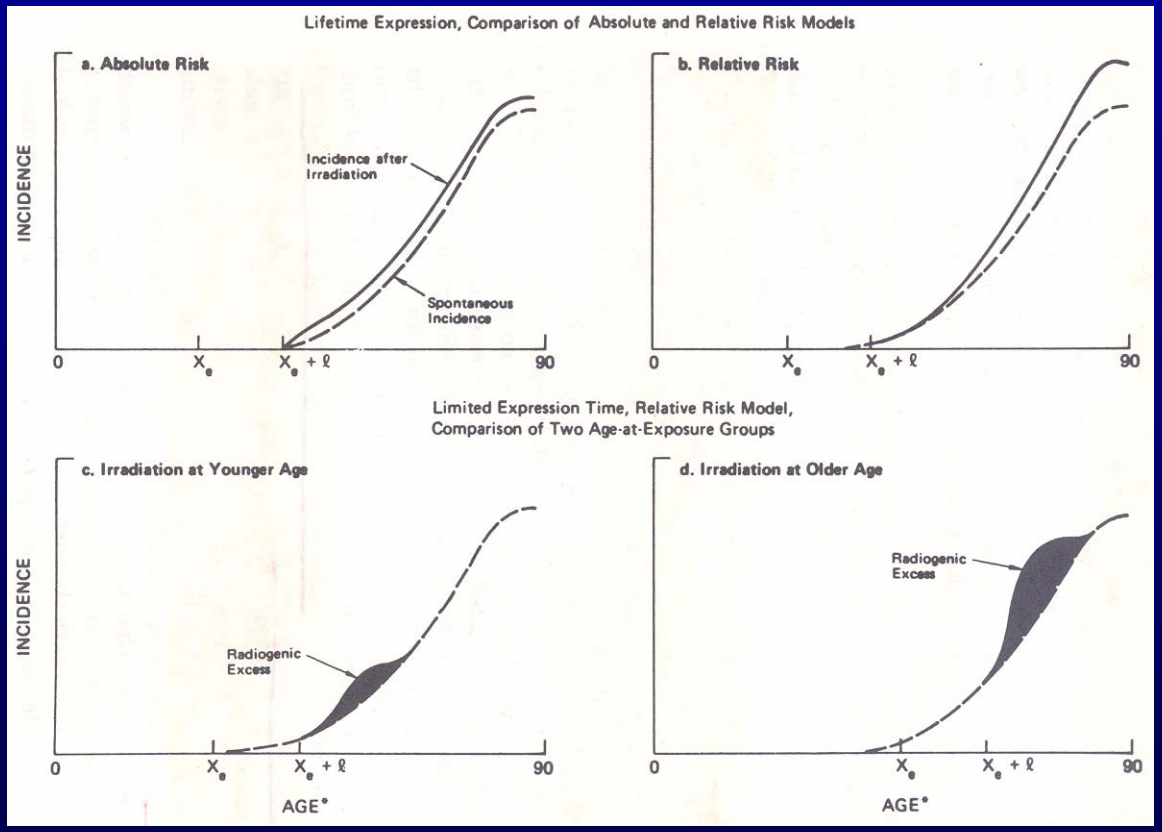
- Organ- or tissue-specific concentration of radionuclides
  - e.g., radioiodines in thyroid gland
- Biological effect depends on dose to critical (target) cells within a specific tissue
- Contrast with external exposure, for which dose to tissue is more uniform

Average Annual Dose (all sources)

0.15 to 0.20 rem = 0.0015 to 0.0020 Sv
= 1.5 to 2.0 mSv

Over 80-year lifetime: 120 to 160 mSv
(12 to 16 rem)

Possible Relations of Radiogenic Excess Cancer to Background



From: Boice et al. (1985), after BEIR (1980)

Characteristics of Ionizing Radiation

- Energetic
  - Sufficient to eject electron ⟶ ionization
- Penetrating

  … to a varying extent, depending on radiation type and energy (less so for α-particles)
  - Unaffected by cellular boundaries; all parts of cell equally vulnerable
- Energy deposition occurs randomly in tissue
- Capable of causing most types of cancer, and variety of other effects, immediate & delayed

Characteristics of UV Radiation

- Non-penetrating
- Insufficient energy per quantum (photon) to cause ionization (except for very short λ)
- Chemical change may result from molecular *excitations*
- Known skin carcinogen
- Also: erythema, cataracts, eye injury, possible effects on immune system

Long-wavelength Radiations (e.g., Microwaves, ELF)

- Penetrate tissue (extent inversely-associated with frequency)
- Biological effects primarily due to heating and induced fields and currents
- Direct genotoxic effects unlikely
- No clear evidence of carcinogenicity

Radiation vs. Chemical Carcinogens

- Radiation is more easily measurable & “dose” has precise meaning
  - Have much more quantitative information for radiation than for chemical carcinogens
- Mechanisms of cancer induction by radiation & some chemical carcinogens may be similar
- Radiation as a model for action of chemical carcinogens and mutagens at level of DNA?
  - e.g., free radicals

Radiation Chemistry

- Cells > 80% water $\rightarrow$ > 80% of energy will be deposited in water
- Radiation chemistry of water is important
- Radiation + water $\longrightarrow$ free radicals
- Enhanced by presence of O_2