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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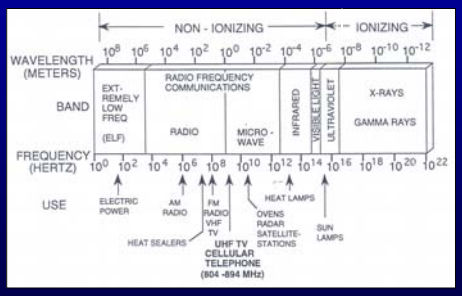
National Institutes of Health

Electromagnetic Spectrum



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

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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

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Linear Energy Transfer (LET)

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

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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

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Interaction of Ionizing Radiation with Tissue

charged particles
↓
electrical interactions
↓
ionization
↓
chemical changes
↓
biological effects

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

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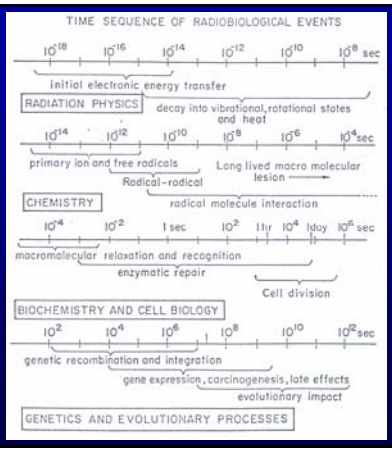

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Biological Effects of Ionizing Radiation

	Cellular Effects	Organismal Effects
x-rays → DNA	cell-killing	acute (& delayed) somatic effects, developmental effects
	malignant transformation	carcinogenesis
	mutations	genetic (hereditary) effects

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"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

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Erythema
(example of non-stochastic effect)

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

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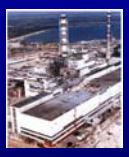
Sources of Radiation Exposure



Medical
Environmental
Occupation
Military

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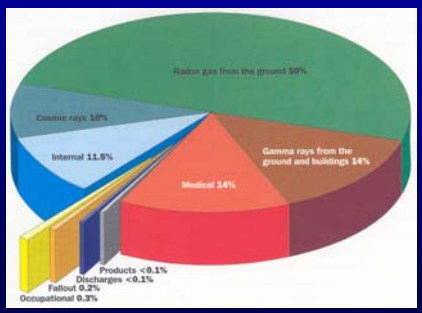
Sources of Radiation Exposure



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

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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

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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+)

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Development of Radiation Injury

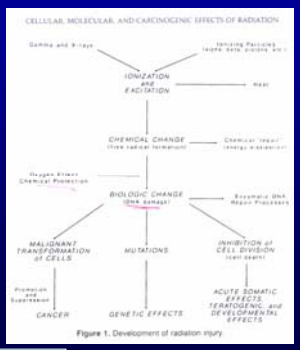

Figure 1. Development of radiation injury.

Little and Williams (1977)

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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

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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

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Applications of Radiation Epidemiology

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

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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

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Sources of Human Exposure to Ionizing Radiation

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

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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

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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

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Computed Tomography (CT) Scan

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

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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)

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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

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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

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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)

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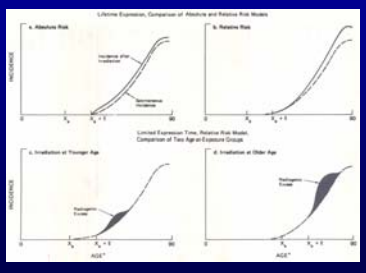
Possible Relations of Radiogenic Excess Cancer to Background



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

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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

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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

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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

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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

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Radiation Chemistry

- Cells > 80% water → > 80% of energy will be deposited in water
- Radiation chemistry of water is important
- Radiation + water ⟶ free radicals
- Enhanced by presence of O_2

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