U.S.NRC

UNITED STATES NUCLEAR REGULATORY COMMISSION

Protecting People and the Environment

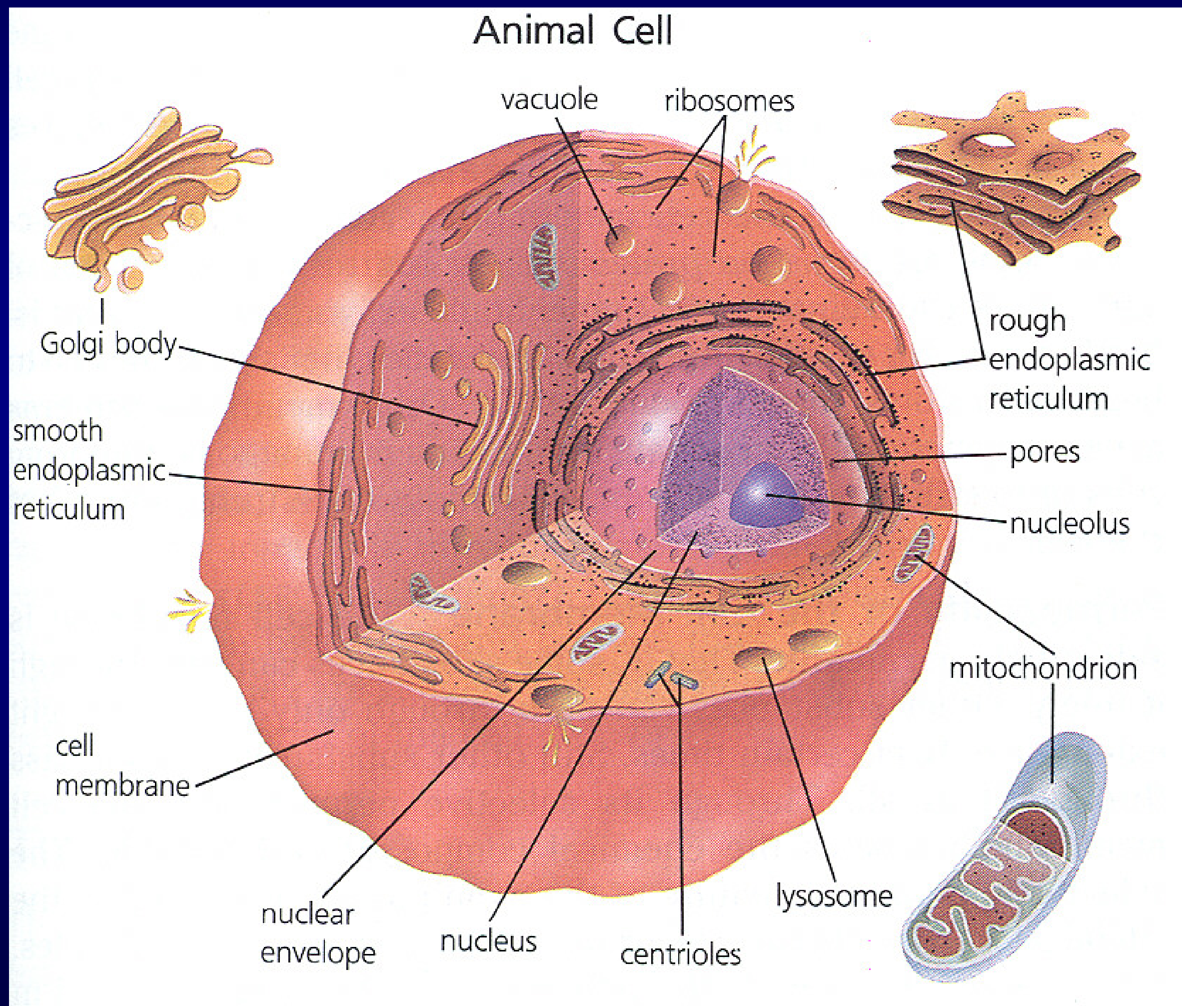
HRTD Human Resources Training & Development

BIOLOGICAL EFFECTS OF RADIATION

Topics

- Cell Kinetics
- DNA - Direct and Indirect Action
- Health Effects
- Acute Exposures
- Chronic Exposures

3-D Cell


Animal Cell
vacuole
ribosomes
Golgi body
smooth endoplasmic reticulum
cell membrane
nuclear envelope
nucleus
centrioles
lysosome
mitochondrion
rough endoplasmic reticulum
pores
nucleolus

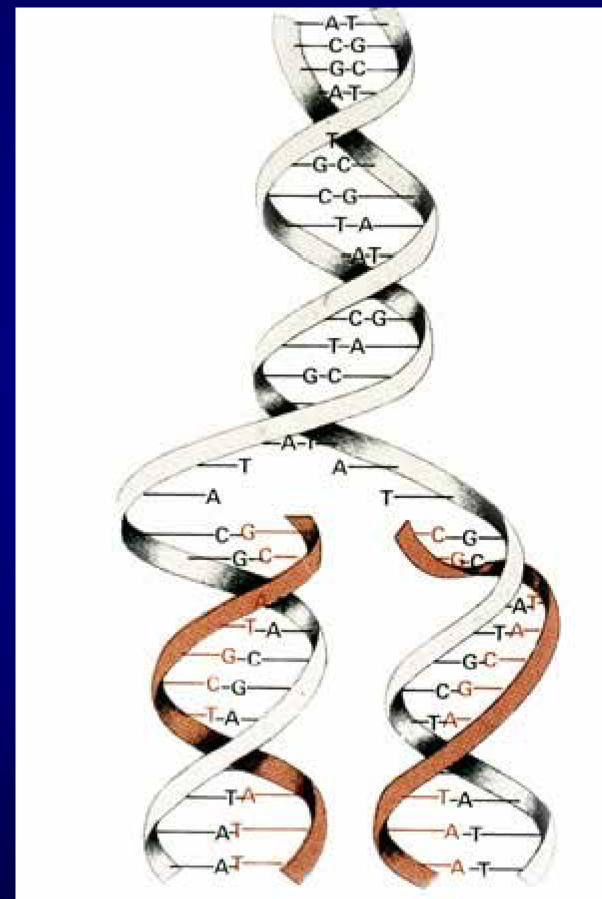
DNA

- DNA consists of a double helix of genetic material spiraled around each other
- Each strand consists of a sequence of bases (nucleotides) adenine, guanine, cytosine and thymine
- The two strands are connected at each base
  - Adenine bonds only with Thymine
  - Guanine bonds only with Cytosine

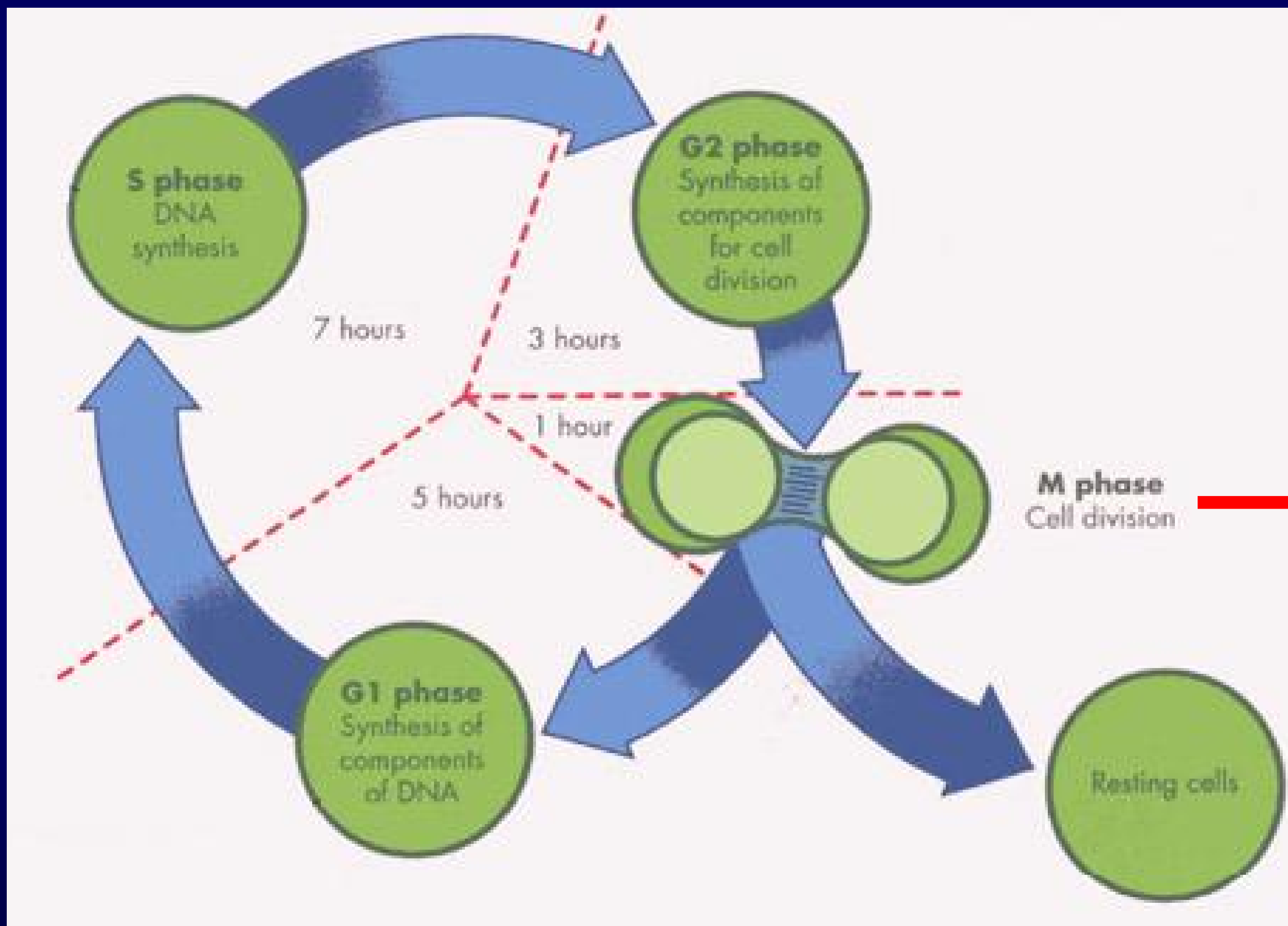
DNA

If the top strand is sequenced as indicated, the bottom strand will be sequenced appropriately matching "A" and "T", "G" and "C"

A - A - C - T - G - A - T - A - G - G - T - C
| | | | | | | | | | | |
T - T - G - A - C - T - A - T - C - C - A - G



Cell Cycle



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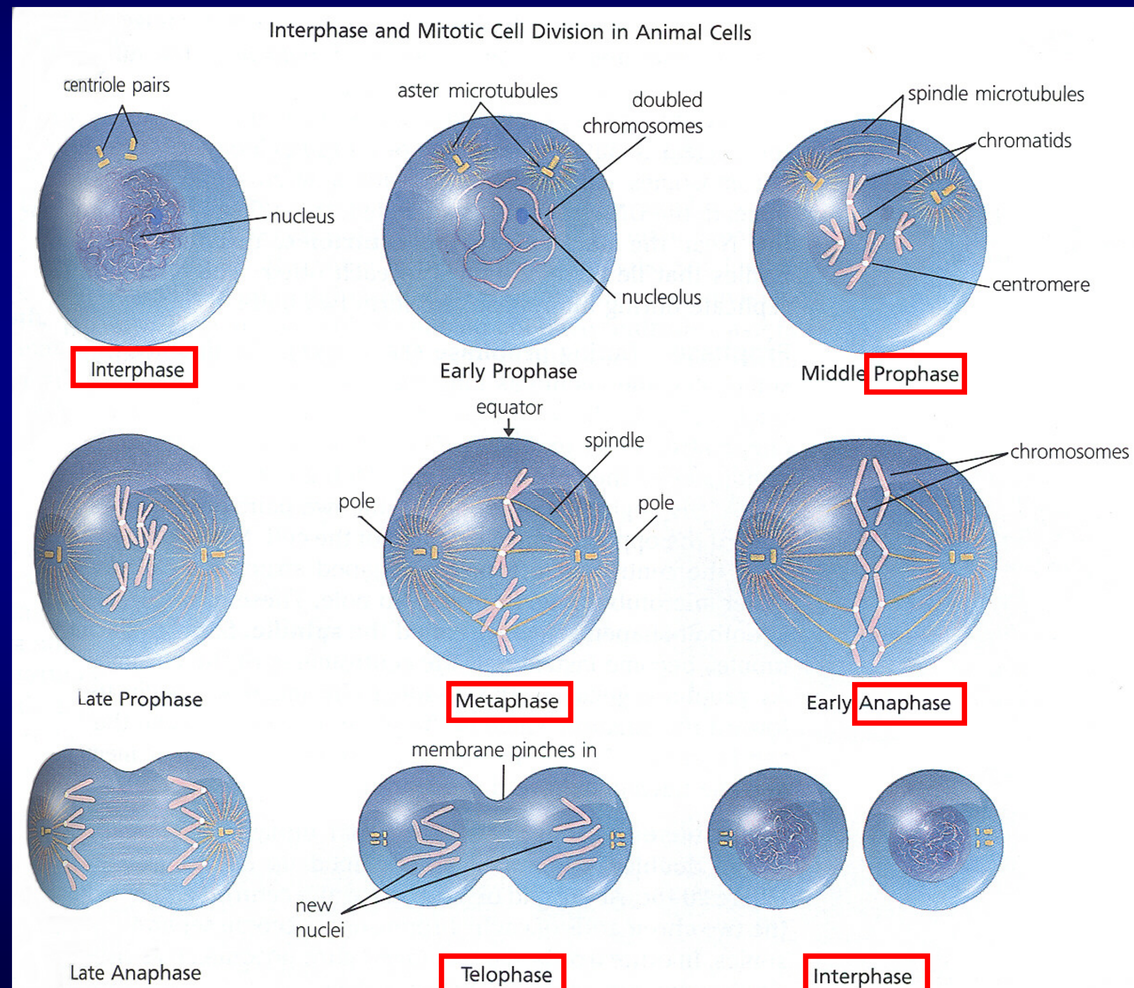
Mitotic Cycle

DNA strands separate

Each strand duplicates

Proteins verify an exact duplicate - correct errors

Mutations and deletions duplicated



Stem Cells

- Stem cells are cells which retain the information to either continue developing undifferentiated or to form specific tissues
- Function is to provide specialized cells while ensuring a means of reproducing additional stem cells if needed
- An example is the stem cells that form red blood cells

Health Effects and Mechanisms

- Damage to DNA from radiation can be direct or indirect

- Direct action: radiation damages DNA directly
  - Single strand breaks
  - Double strand breaks
  - Deletions

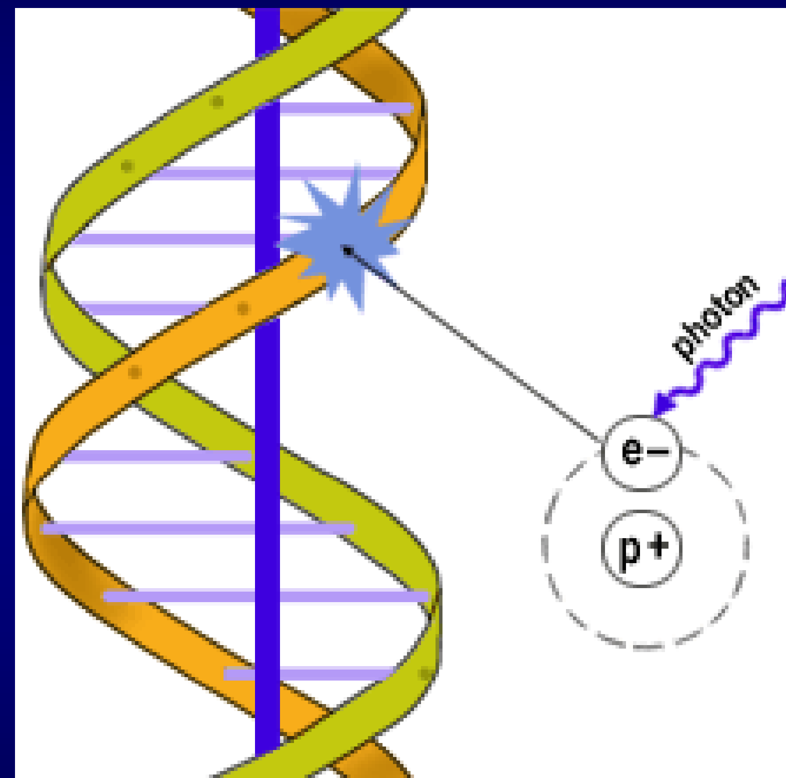
- Indirect action: radiation hydrolyzes water near DNA
  - OH^- radicals cause damage to DNA

Direct Effect

Radiation directly interacts with critical biological molecules in human cell

The nucleus is the most sensitive part of the cell to radiation

DNA within the cell nucleus is believed to be the critical biological target for radiation damage

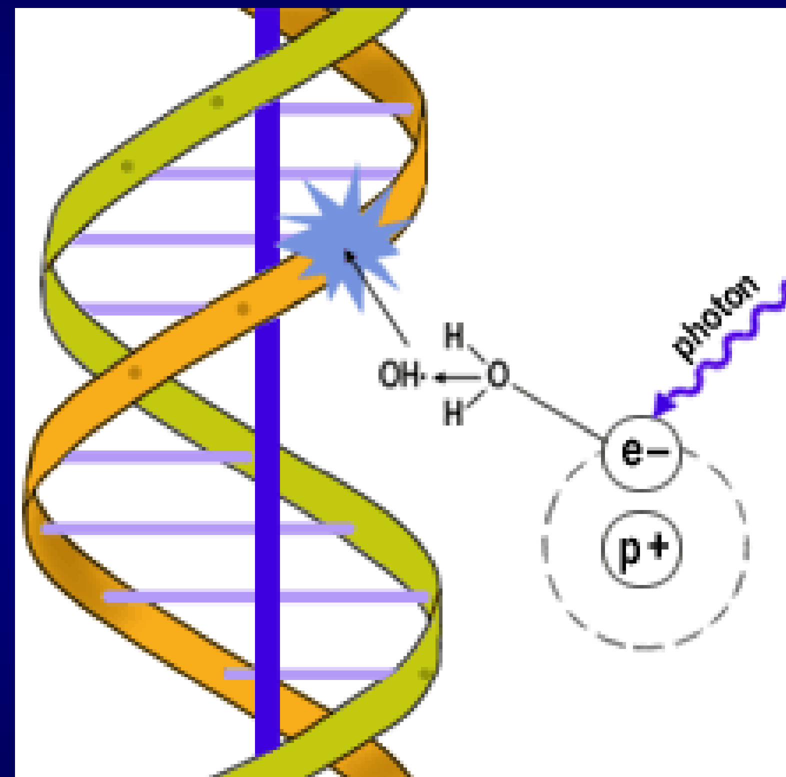


Indirect Effect

Radiation interacts with body water to produce toxic free radicals

A free radical is a chemical species with an unpaired electron (electrically charged) - a powerful oxidizing agent

Hydroxyl ions (OH*) can combine (OH* + OH* $\rightarrow$ H_2O_2) to form hydrogen peroxide a powerful oxidizing agent that can break molecular bonds

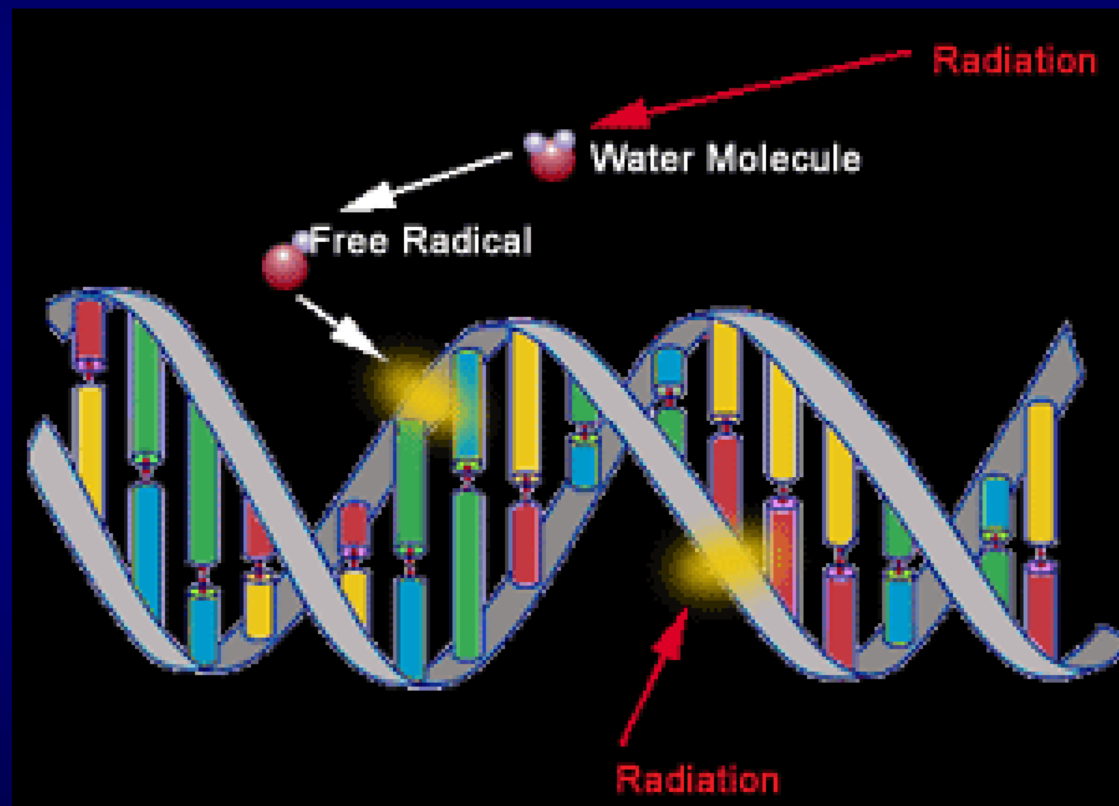


80% of all soft tissue in human body is water - thus the indirect effect is more likely to occur

Gamma Radiation
Direct and Indirect Action

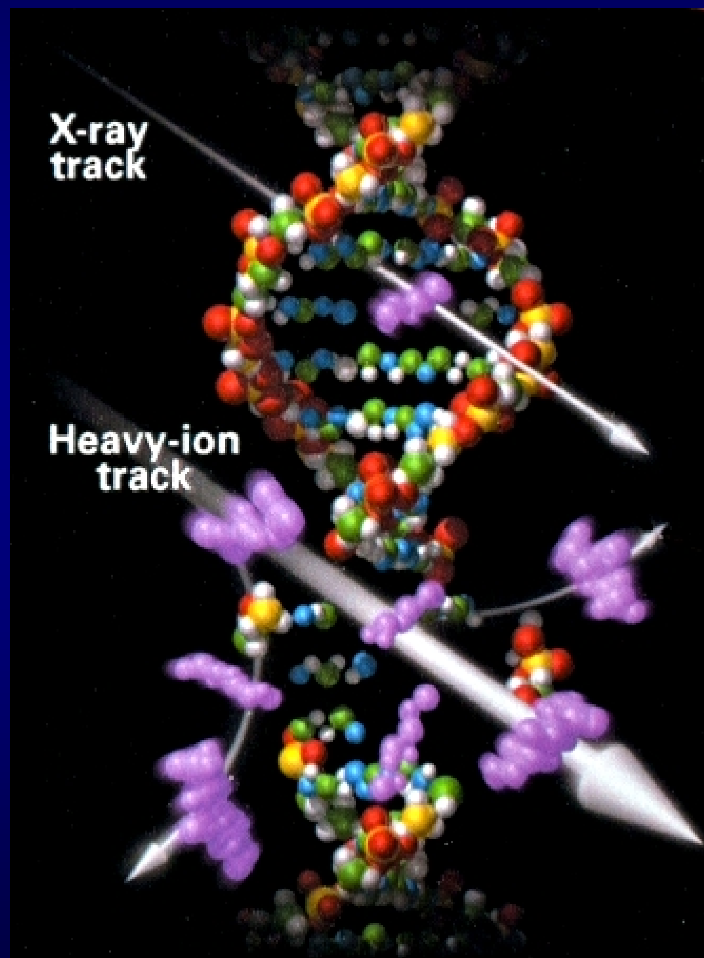
- 2/3 of photon interactions with DNA are through indirect action
- Free radicals travel 1-2 nm in their lifetime

Indirect Action



Direct Action

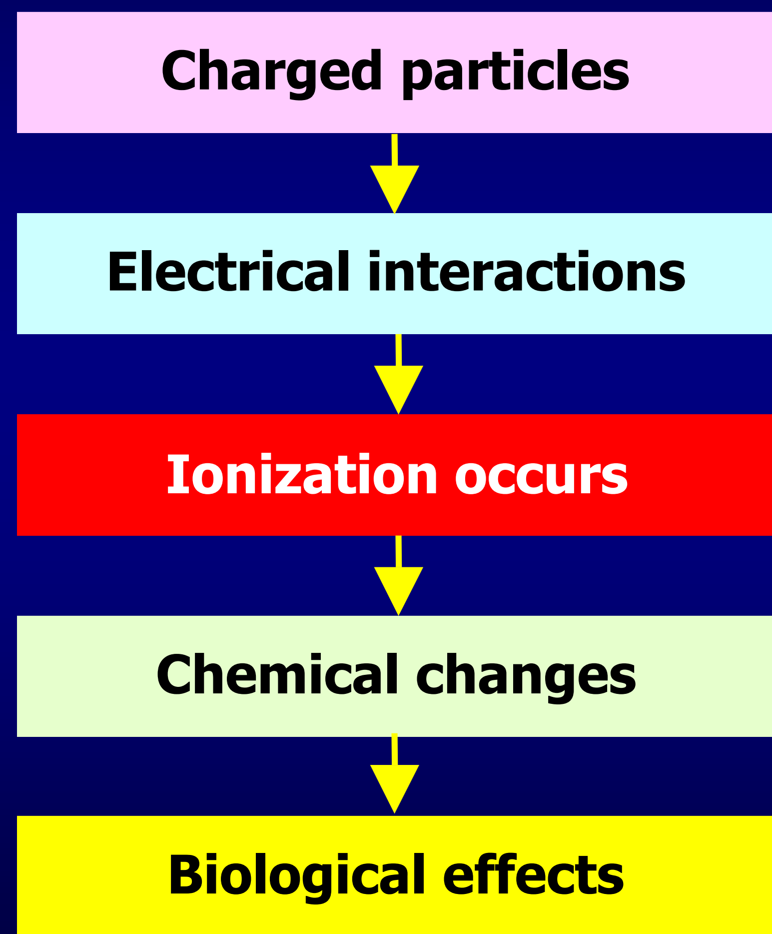
Low vs High LET



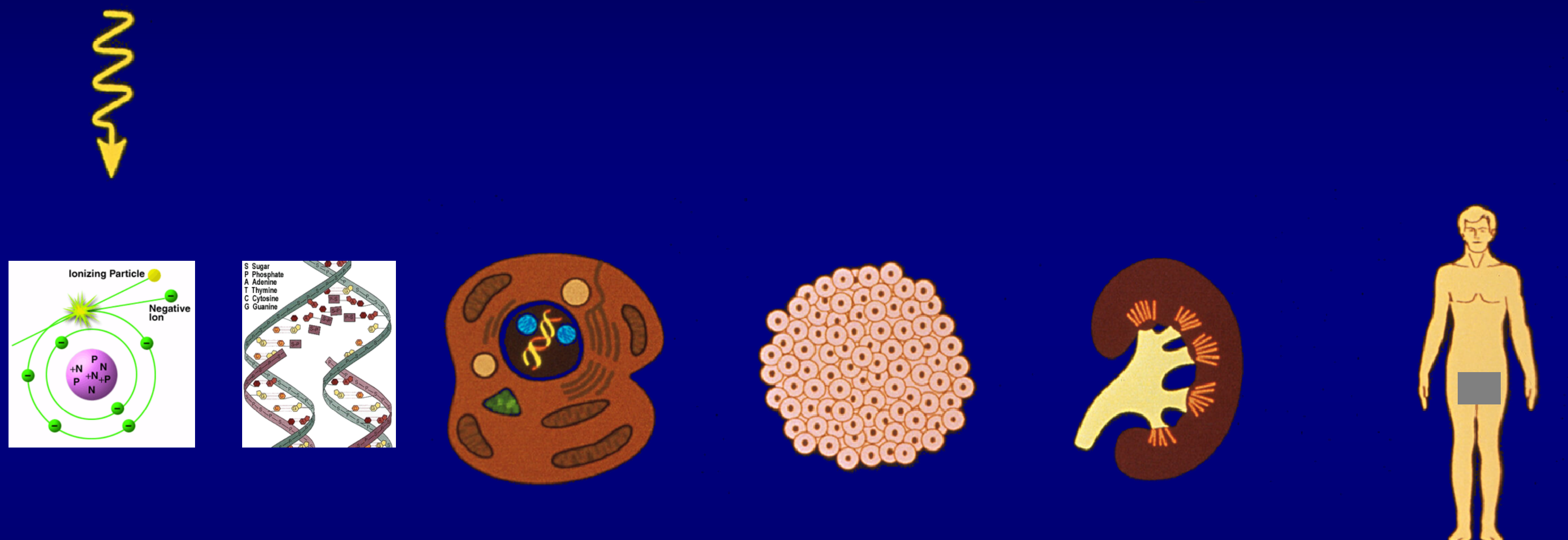
Interaction with Living Tissue

Ionization

Excitation



The Domino Theory



Atom Molecule Cell Tissue Organ Whole Body

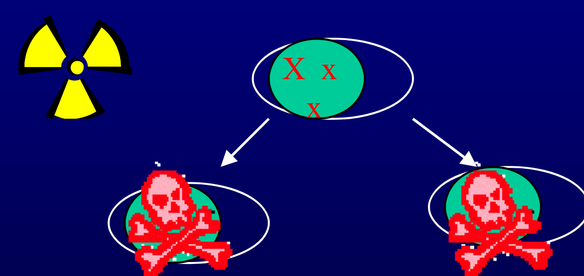
Radiation ionizes atoms
(knocks out electrons)

Four Possible Outcomes from Irradiation

- Cell not damaged - No lasting effects
- Cell damaged, dies during mitosis - No lasting effects
- Cell damaged, repairs correctly - No lasting effects
- Cell damaged, misrepairs causing a mutation:
  - If cell non-viable, cell dies - No lasting effect
  - If cell viable - cancer or hereditary effects - maybe

Cell Death From Irradiation

- As cells attempt to divide (mitotic death)
  - Rapid in tissues with rapid turnover
  - Slowly dividing tissues: long latent period and damaged expressed more slowly
  - Not necessarily at first post irradiation mitosis - may be up to 4 divisions later



Relative Biological Effectiveness (RBE)

- Comparison of dose from two different sources required to cause the same biological effect

$$\text{RBE} = \frac{\text{Dose of reference radiation to produce an effect}}{\text{Dose of other radiation to produce same effect}}$$

- RBE is endpoint dependent, i.e., it is different depending on the effect being compared (e.g., lethality, cataracts, etc.)

- Quality factors (Q) were derived from RBE's determined for various radiations from both animal and human data

Radiation Hormesis

- Theory that states that small doses of radiation can be beneficial
- Apparent benefits include: increased life span, increased growth and fertility, and reduction in cancer incidence
- Postulated that small doses of radiation stimulate the body's immune system, making it more resistant to disease
- NRC does not accept this theory and instead uses the linear, no-threshold theory

Health Effects of Exposure to Radiation

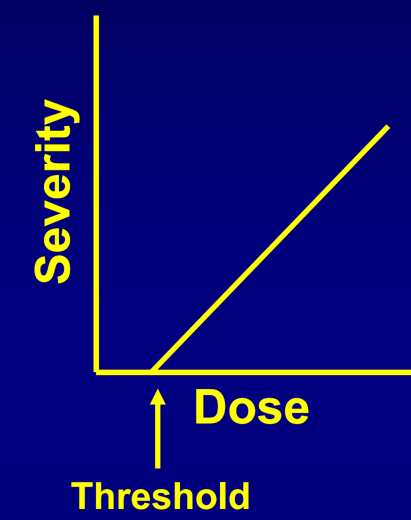
- Health effects range from no effect at all to death or diseases such as leukemia or bone, breast and lung cancer
- These effects have been observed in various groups studied such as medical radiologists, uranium miners, radium workers, radiotherapy patients, and the atomic bomb survivors

Acute vs Chronic Dose

- Acute - large dose in a short period of time (e.g., 50 rem or more over a 24 hour period)
- Chronic - small doses received over long time periods (e.g., doses within regulatory limits)
- Any radiation dose may cause delayed effects - only large acute doses cause early effects
- The sun as an example - an intense exposure can cause painful burning - repeated short exposures provide time for the skin to repair eliminating sunburn - some injury may not be repaired possibly resulting in skin cancer

Non-Stochastic or Deterministic Effect

- Has a well-defined threshold
- Severity of effect (injury) increases with dose
- Includes acute radiation syndrome, cataracts, skin damage and sterility
- Effects can be avoided altogether if dose is kept below the threshold



Body System Sensitivity

- Several body systems are sensitive to massive doses of radiation
- They include:
  - the blood forming organs and
  - the gastrointestinal (GI) tract

Blood Forming Organs

- Blood cells are formed in bone marrow
- They include:
  - red blood cells (carry oxygen to cells and carbon dioxide away)
  - white blood cells (fight infection)
  - platelets (form clots at the site of damage within the circulatory system)

GI Tract

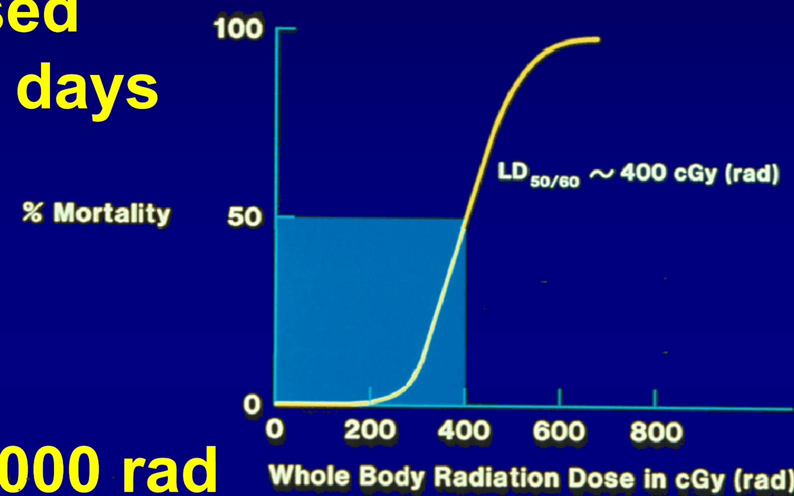
- Components of GI Tract:
  - stomach (digests food)
  - small intestine (where nutrients are absorbed)
  - large intestine and colon (where wastes are collected and voided)
- Small intestine is of greatest interest
- Epithelial lining susceptible to radiation damage
- Epithelial cells constantly replaced (rapidly dividing) by stem cells called crypts

Acute Radiation Syndrome

- Divided into three levels of effects:
  - Hematopoietic or blood syndrome
  - GI syndrome
  - Central Nervous System (CNS) syndrome

$LD_{50/30}$

- Dose at which 50% of exposed population will die within 30 days without medical treatment



- Acute doses above about 1,000 rad are usually fatal, even with medical treatment
- The $LD_{50/30}$ is sometimes written $LD_{50/60}$ indicating 50% death within 60 days instead of 30

Blood Syndrome

- Dose threshold is about 100 rad
- Chromosome aberrations could be seen at 20 rad but no overt clinical symptoms
- Organ at risk is bone marrow
- Death is possible within 2-8 weeks at doses > 400 rad
- Death is from infection, bleeding and anemia

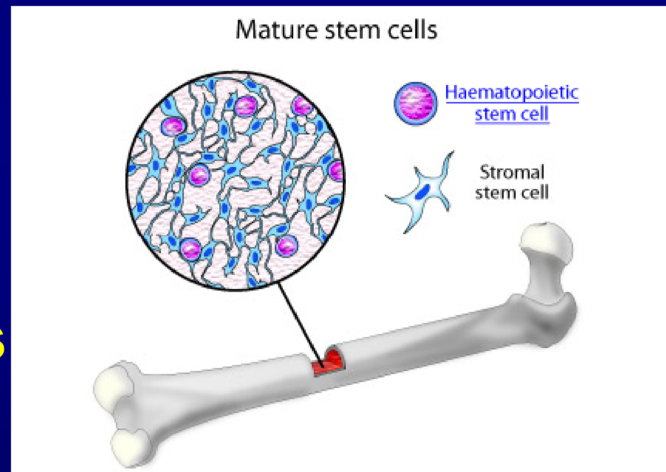
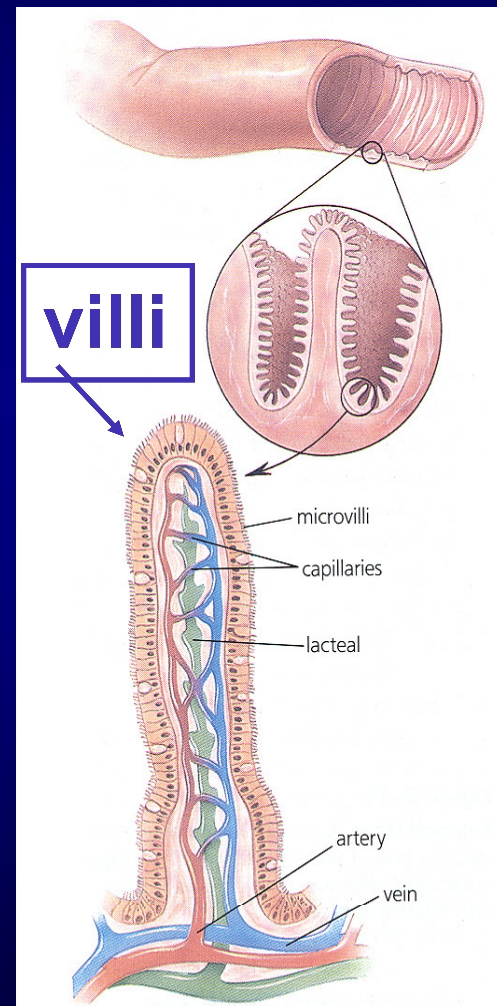


Illustration by Cell Imaging Core of the Center for Reproductive Sciences.

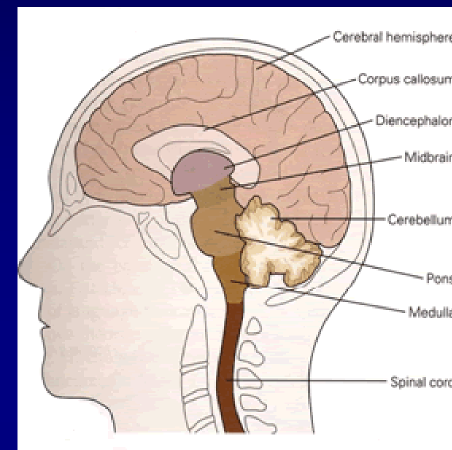
GI Syndrome

- Threshold of about 700 rad
- Organ at risk is epithelial lining of intestines
- Effects include nausea, vomiting, and diarrhea
- Death is likely within 3-14 days at doses over 1000 rad
- Causes of death include infection, bleeding, dehydration, electrolyte imbalance, and circulatory collapse



CNS Syndrome

- Threshold of about 2000 rad
- Organ at risk is brain
- Effects include lethargy, convulsions tremors, loss of muscle control, and coma (in addition to effects from other syndromes)
- Death is likely within 3 days for doses > 5000 rad
- Causes of death include respiratory and circulatory collapse



Range of High Dose Effects

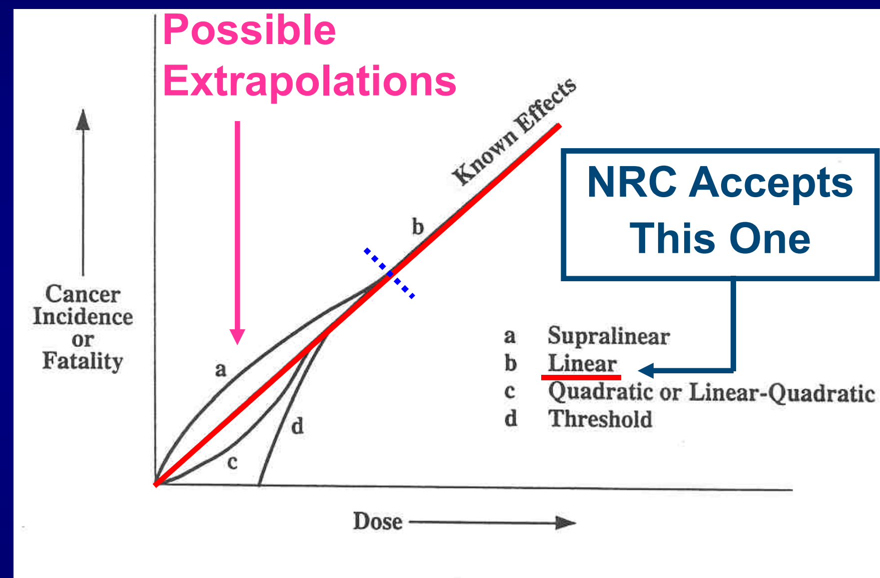
Dose (rem)	Effect
25-50	Changes in blood chemistry - No physical symptoms
100-300	Some physical changes seen - skin reddening, loss of hair - at the high end vomiting shortly after exposure
300-450	Vomiting is first symptom - unable to produce blood
450 ($LD_{50/30}$)	Death to 50% of the population within 30 days with no medical treatment
450-1,000	At upper end, bone marrow transplants needed - fatal within 1 month without medical care
1,000-5,000	Failure of GI system - fatal within 2 weeks
> 5,000	Central nervous system failure - death within days

Low Dose Effects

- Principal effects of doses < 10 rad are non-lethal cell mutations, principally cancer
- Low dose effects are called “stochastic” effects
- These effects take years to manifest themselves and are therefore called late effects

Stochastic Effects

- Occur randomly
- Probability of effect is proportional to dose
- Severity of effect is not a function of dose



- NRC assumes no threshold and a straight line

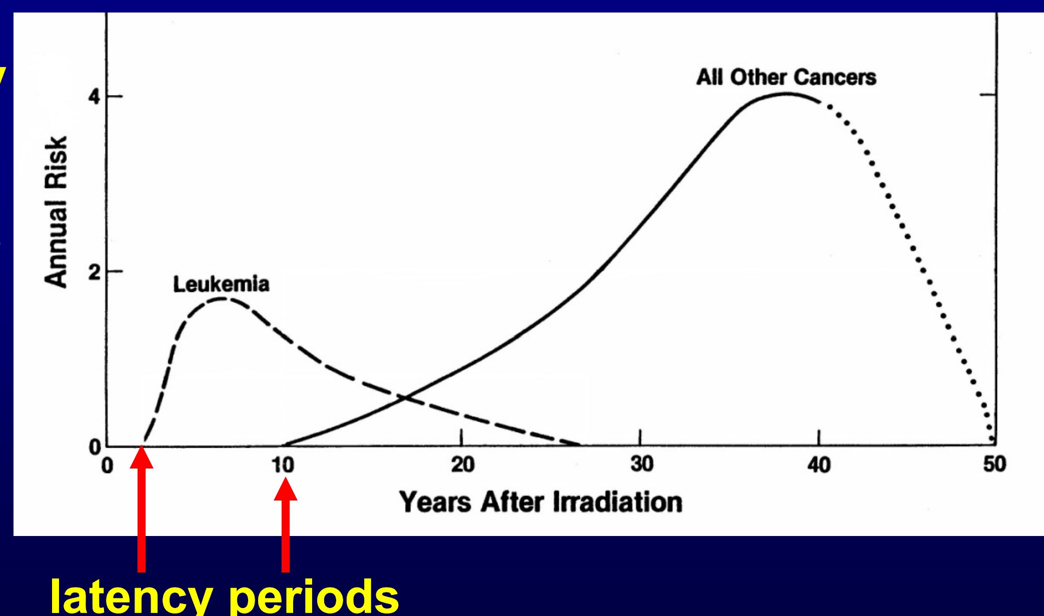
Categories of Low Dose Radiation Effects

- **Somatic** - effects in exposed individual (cancer)
- **Genetic** - effects in offspring of exposed individual
- **In utero** - effects in embryo/fetus

Somatic Effects

- Radiation induced cancer has been demonstrated in humans through epidemiological studies only at doses exceeding 5-10 rem delivered at high dose rates

- Leukemia has latency period of 2-3 years, whereas solid tumors have latency periods of 10 to 20 years

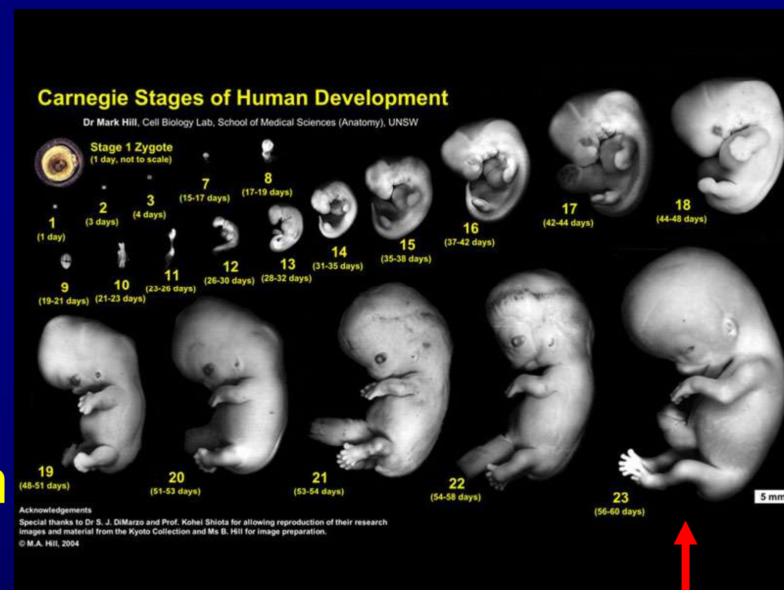


Genetic Effects

- Mutation of sex cells (sperm and egg) - effects passed along to offspring
- Radiation induced genetic effects have been observed in mice and fruit flies
- Never observed in human beings - Hiroshima data shows no increase in background mutation rate in offspring
- Radiation simply increases spontaneous mutation rate and does not cause new mutations - ~ 100 rem required to double the background mutation rate

Embryonic Development

- During this time, cells divide rapidly and are undifferentiated (i.e. stem cells - they can become any type of cell)
- Later, cells differentiate or become specialized (e.g. nerve cells, blood cells)
- Specific organs begin to form
- By 8th week, all body systems are present



56-60 days

Embryonic Development

- Stage of development when DNA changes occur is critical
- Changes have a greater probability of being expressed (e.g. in form of a defect) as development increases
- Cells can repair of portion of damage but some damage may be permanent
- Not all DNA damage is manifested as a disease or defect

In Utero Radiation Effects

- Principal effects of in-utero exposure are:
  - intrauterine death
  - growth retardation
  - mental retardation (maximum risk between 8 to 15 weeks gestation)
  - childhood cancer
  - developmental abnormalities

In Utero Radiation Effects

- First trimester of pregnancy is most critical
- Risk of all in utero effects is about 1-10 per 1,000 births per rem
- Normal risk of fetal abnormalities is about 5-30 per 1,000 live births
- Abnormalities more likely to have been caused by natural occurrence than dose of 1 rem during 9-month gestation

Cancer Incidence and Cancer Death Rates*

New Cancers

$$\frac{1.22 \times 10^6}{2.83 \times 10^8}$$

= 0.00431

= 431/100,000

State	All Sites
Nevada	8,300
New Hampshire	5,500
New Jersey	40,000
New Mexico	6,600
New York	81,500
North Carolina	35,700
North Dakota	3,000
Ohio	56,100
Oklahoma	16,100
Oregon	15,800
Pennsylvania	66,600
Rhode Island	5,400
South Carolina	18,000
South Dakota	3,500
Tennessee	27,300
Texas	76,100
Utah	5,100
Vermont	2,700
Virginia	29,300
Washington	23,600
West Virginia	10,500
Wisconsin	23,600
Wyoming	[illegible]
United States†	1,220,100

Cancers Deaths

= 170/100,000

State	Reported Death Rate per 100,000†
Nevada	184
New Hampshire	181
New Jersey	179
New Mexico	146
New York	169
North Carolina	175
North Dakota	155
Ohio	180
Oklahoma	170
Oregon	166
Pennsylvania	177
Rhode Island	178
South Carolina	178
South Dakota	155
Tennessee	181
Texas	168
Utah	122
Vermont	172
Virginia	177
Washington	162
West Virginia	184
Wisconsin	163
Wyoming	[illegible]
United States‡	170

* from all causes

Comparative Risks

Comparative Risks: One in a million chance of death

Situation	Cause of Death
2 mrem	cancer from radiation
traveling 700 miles by air	plane crash
crossing the ocean by air	cancer from cosmic rays
traveling 60 miles by car	car crash
living in Denver for two months	cancer from cosmic rays
living in a stone building	cancer from natural radiation
working in a factory for 1.5 weeks	work accident
working in a coal mine for 3 hours	work accident
smoking one to three cigarettes	lung cancer or heart disease
rock-climbing for 1.5 minutes	accidental fall
20 minutes being a man aged sixty	mortality from all causes
living in New York City for 3 days	lung cancer from air pollution

Somatic Risk Factor

- Risk factors include age at time of irradiation (adult worker or whole population) and relative severity of detriment

	Detriment (rem^{-1})			
Exposed Population	Fatal Cancer	Non-Fatal Cancer	Severe Hereditary Effects	Total
Workers	0.0004	0.00008	0.00008	0.00056
Whole Population	0.0005	0.00010	0.00013	0.00073

- The population factor is higher because it includes a much broader distribution of individuals than the worker population

Risk of Fatal Cancer from Radiation Exposure

From currently available data, the occupational risk value for a dose of 1 rem TEDE is 4 in 10,000 (0.04% or 0.0004) of developing a fatal cancer

We cannot rule out the possibility of higher risk, or the possibility that the risk may even be zero at low doses and dose rates

Under the L-N-T model, a worker who receives 5 rem in a year incurs 10 times as much risk as another worker who receives only 0.5 rem

Analogy for the Risk of Fatal Cancer from Radiation

- Odds of picking an ace of spades from a deck of cards is 1 in 52 $\approx$ 0.02
- If 1,000 people select one card from a full deck we should see about 20 aces of spades (1,000/52)
- No way to predict which of the 1,000 persons will actually draw an ace of spades - we might see 15 or possibly 25 or almost any number between 0 & 1000
- When a large number of people are exposed to radiation we can't predict who will or won't get cancer nor exactly how many if any

Sample Cancer Risk Problem

Assume that 100,000 people are exposed to a dose of 300 mrem (background levels) for one year. How many latent cancer fatalities would you expect?

ANSWER:

$$100{,}000 \text{ persons} \times 0.3 \text{ rem} \times \frac{5 \text{ cancer fatalities}}{10{,}000 \text{ person-rem}} =$$

$$100{,}000 \times 0.3 \times 0.0005 = 15 \text{ cancer fatalities}$$

Sample Cancer Risk Problem

Assume that 1 person is exposed to a dose of 300 mrem/year for a 70 year lifetime. What would you expect that individual's risk to be?

ANSWER:

$$1 \text{ person} \times 0.3 \frac{\text{rem}}{\text{year}} \times 70 \text{ years} \times \frac{5 \text{ cancer fatalities}}{10{,}000 \text{ person-rem}} =$$

$$1 \times 0.3 \times 70 \times 0.0005 = 0.011 \text{ cancer fatalities}$$

or we can express it as a risk for that individual of 1.1%

Sample Cancer Risk Problem

Assume a radiation worker receives the max allowed radiation dose every year for 40 years

ANSWER:

total dose is 40 years x 5 rem/yr = 200 rem

risk of fatal cancer is 200 rem x 0.0004/rem = 8%

death risk from cancer from all causes is about 20%

Sample Individual Latent Cancer Fatality (LCF)

Assumptions:

- **Peak dose to RMEI = 0.00002 mrem/yr**
- **Radiation risk coefficient for MOP = 5 x 10^{-4} LCF/rem**
- **Human lifetime = 70 yrs**

Table 5-6. Impacts for an individual from groundwater releases of radionuclides during 10,000 years after repository closure for the higher-temperature repository operating mode.

Individual	Mean: Peak annual individual dose (millirem)	Mean: Time of peak (years)	Mean: Probability of an LCF[a]	95th-percentile: Peak annual individual dose (millirem)	95th-percentile: Time of peak (years)	95th-percentile: Probability of an LCF[a]
At RMEI location[b]	0.00002[c]	4,900	6×10^{-10}	0.0001[d]	4,900	4×10^{-9}
At 30 kilometers[e]	~0[f]	NC[g]	~0	~0[f]	NC	~0
At discharge location[h]	~0[f]	NC	~0	~0[f]	NC	~0

a. LCF = latent cancer fatality; incremental lifetime (70 years) risk of contracting a fatal cancer for individuals, assuming a risk of 0.0005 latent cancer per rem for members of the public (DIRS 101856-NCRP 1993, p. 31).

b. The RMEI location is approximately 18 kilometers (11 miles) downgradient from the repository. The maximum allowable peak of the mean annual individual dose for 10,000 years at this distance is 15 millirem.

Sample Individual Latent Cancer Fatality (LCF)

Dose Calculation:

Individual LCF = 2×10^{-5} mrem/yr x 10^{-3} rem/mrem x 5×10^{-4} LCF/rem x 70 yr

Individual LCF = 7×10^{-10} LCF

(close to the value of 6×10^{-10} on the table on the previous slide)

THE END