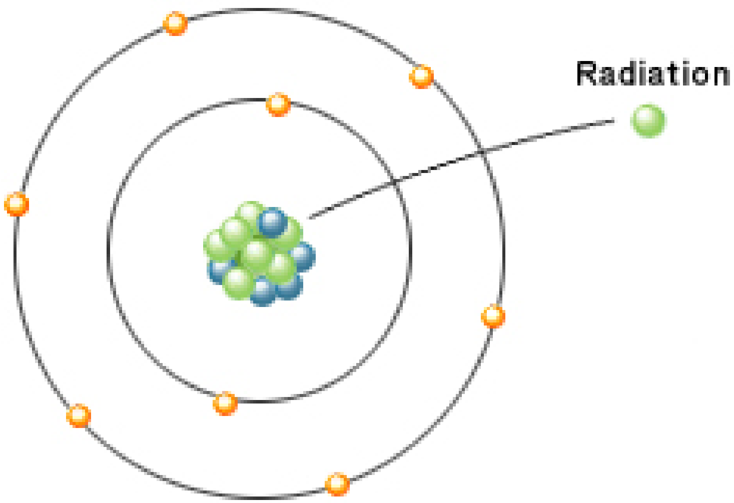
RADIATION RISK ASSESSMENT

EXPOSURE and TOXITY ASSESSMENT



Osipova Nina,
associated professor,
PhD in chemistry,
Matveenko Irina,
Associate professor,
PhD in philology
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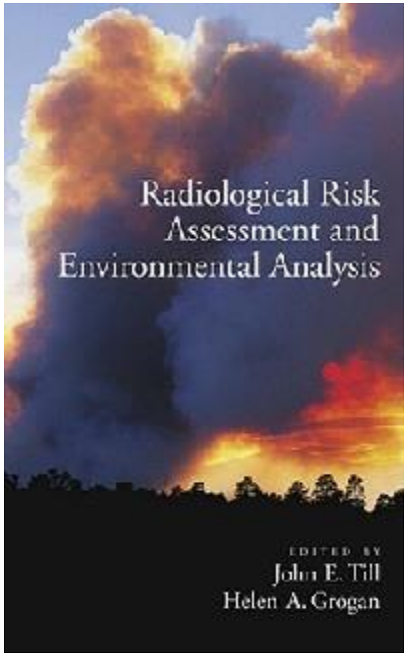


The contents

- 1.What is the mechanism of radiation damage?
- 2.Exposure assessment
- 3. TOXICITY ASSESSMENT

the four basic steps in the risk assessment process:

- 1. Data Collection and Evaluation
- 2. Exposure Assessment
- 3. Toxicity Assessment
- 4. Risk Characterization

Exposure Assessment

- is the process of estimating or measuring the magnitude, frequency and duration of **exposure** to an agent, along with the number and characteristics of the population **exposed**

ACRONYMS, SYMBOLS, AND UNITS

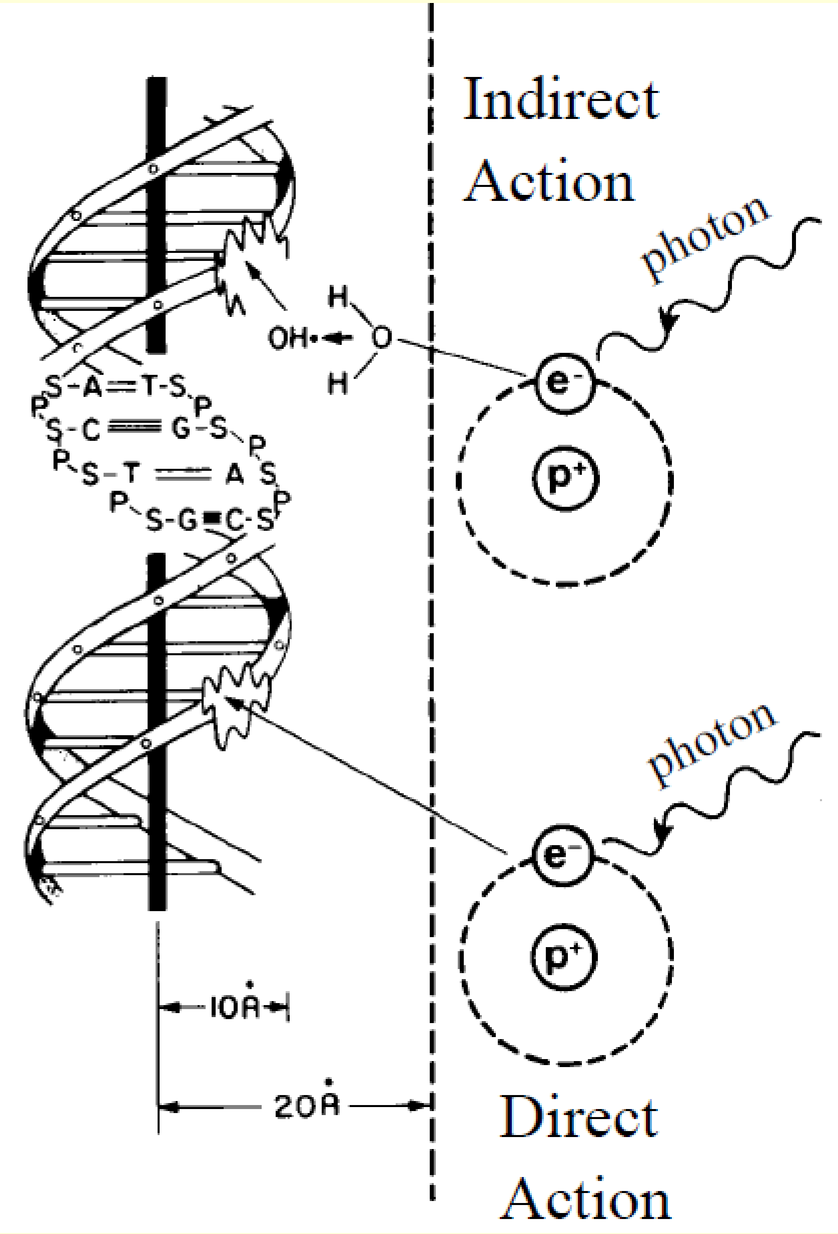
- A(t) = Activity at Time t
- Bq = Becquerel
- Ci = Curie
- D = Absorbed Dose
- DCF = Dose Conversion Factor Per Unit Intake
- HE = Effective Dose Equivalent

  HT = Dose Equivalent Averaged Over Tissue or Organ T

  HE,50 = Committed Effective Dose Equivalent Per Intake

  HT,50 = Committed Dose Equivalent Averaged Over Tissue T
- LET = Linear Energy Transfer
- LLD = Lower Limit of Detection
- MeV = Million Electron Volts

  pCi = PicoCurie (10-12 Ci)
- Q = Quality Factor in Definition of Dose Equivalent
- RBE = Relative Biological Effectiveness
- SI = International System of Units
- Sv = Sievert
- T = Tissue or Target Organs
- wT = Weighting Factor in the Definition of Effective Dose Equivalent and Committed Effective Dose Equivalent



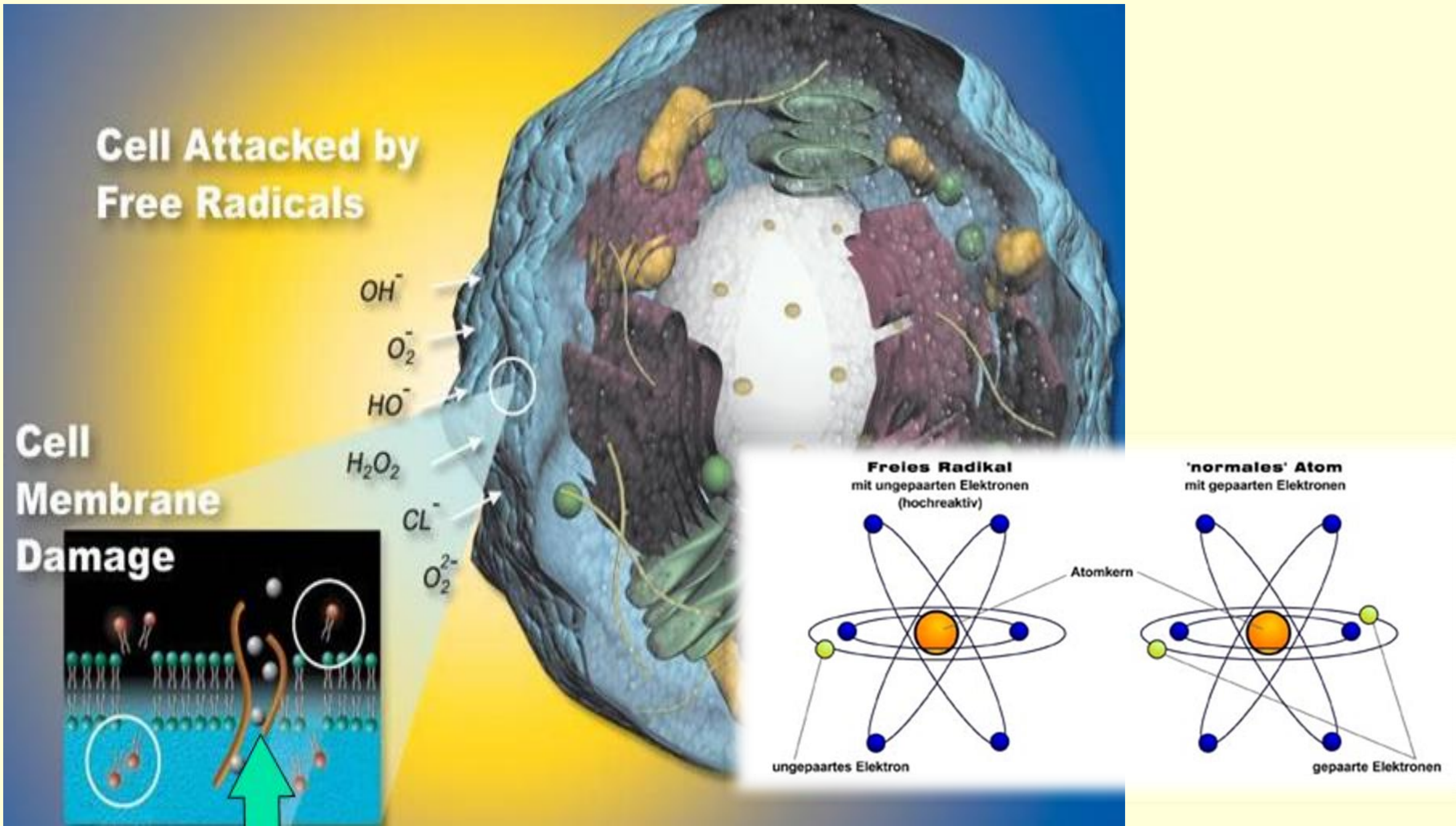
The absorption of energy from ionizing radiation produces damage to molecules by **direct** and **indirect** actions.

For **direct action**, damage occurs as a result of ionization of atoms on key molecules in the biologic system. This causes inactivation or functional alteration of the molecule.

Indirect action involves the production of reactive free radicals whose toxic damage on the key molecule results in a biologic effect.

A **free radical** is an electrically neutral atom with an unshared electron in the orbital position.

The radical is highly reactive.



Sequence of Effects

- **Physical:** less than seconds
- **Chemical:** seconds
- **Biological:** seconds to many years
  - Reactions with molecules and cells
  - Tissue changes
  - Cancer, leukemia

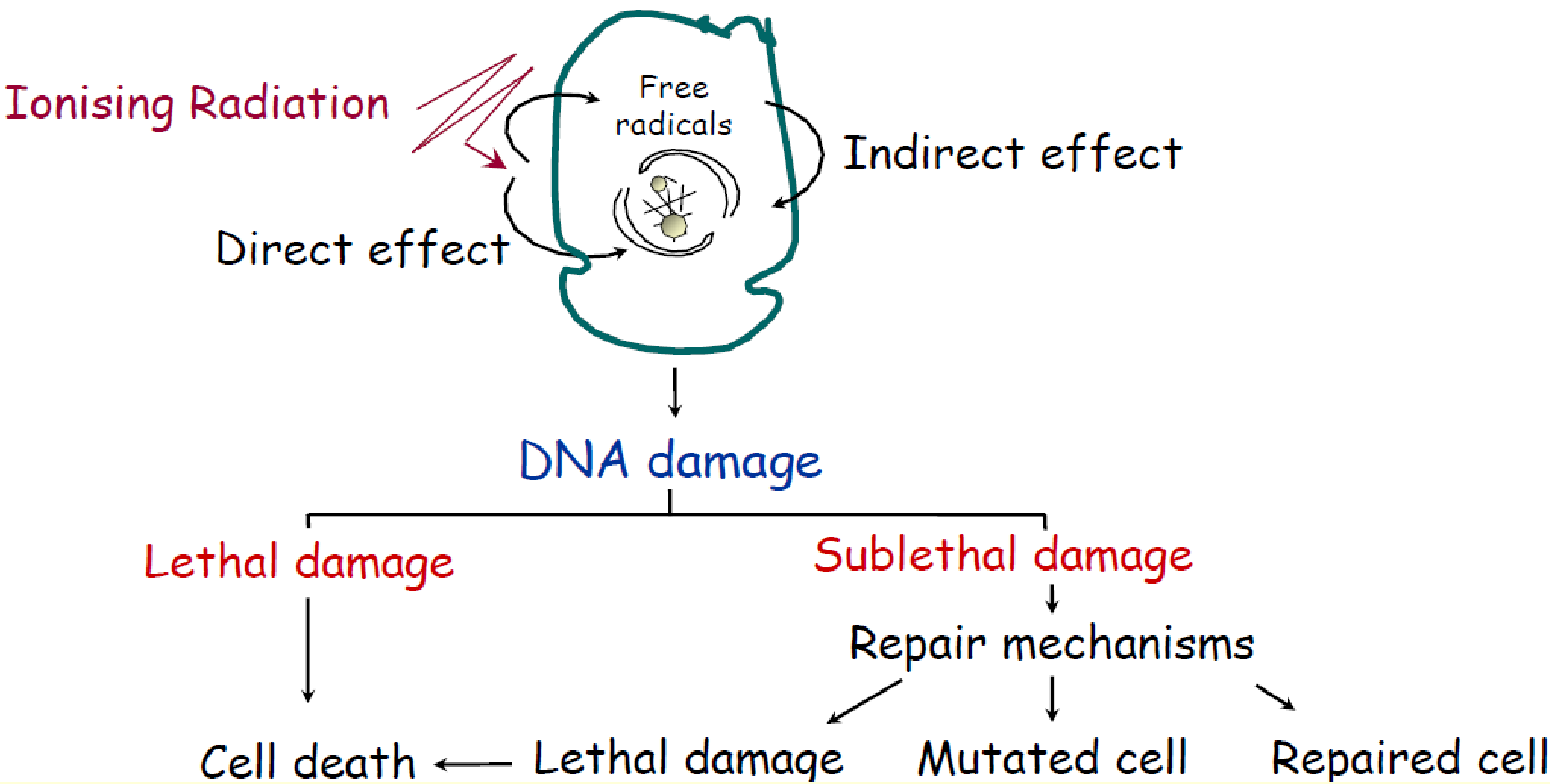
Physical phase

- Interactions of radiation with matter
- Direct ionization of atoms by charged particles
- Indirect ionization by neutral particles

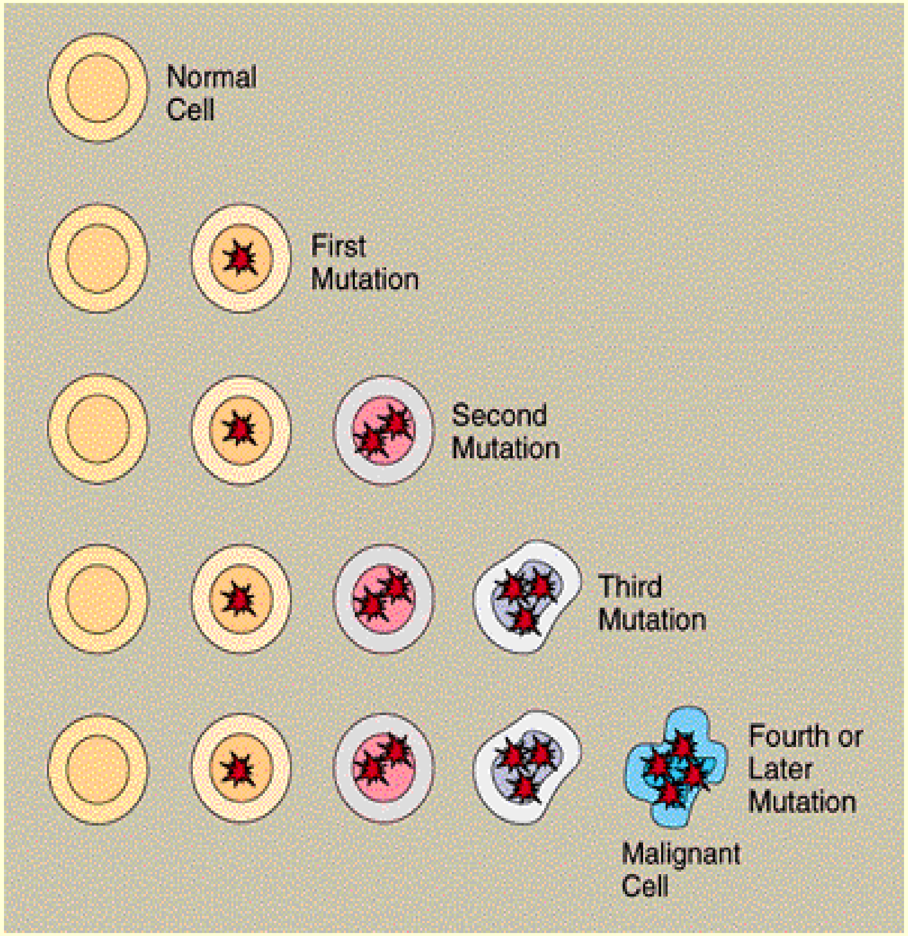
Chemical phase

- Chemical changes of biological molecules

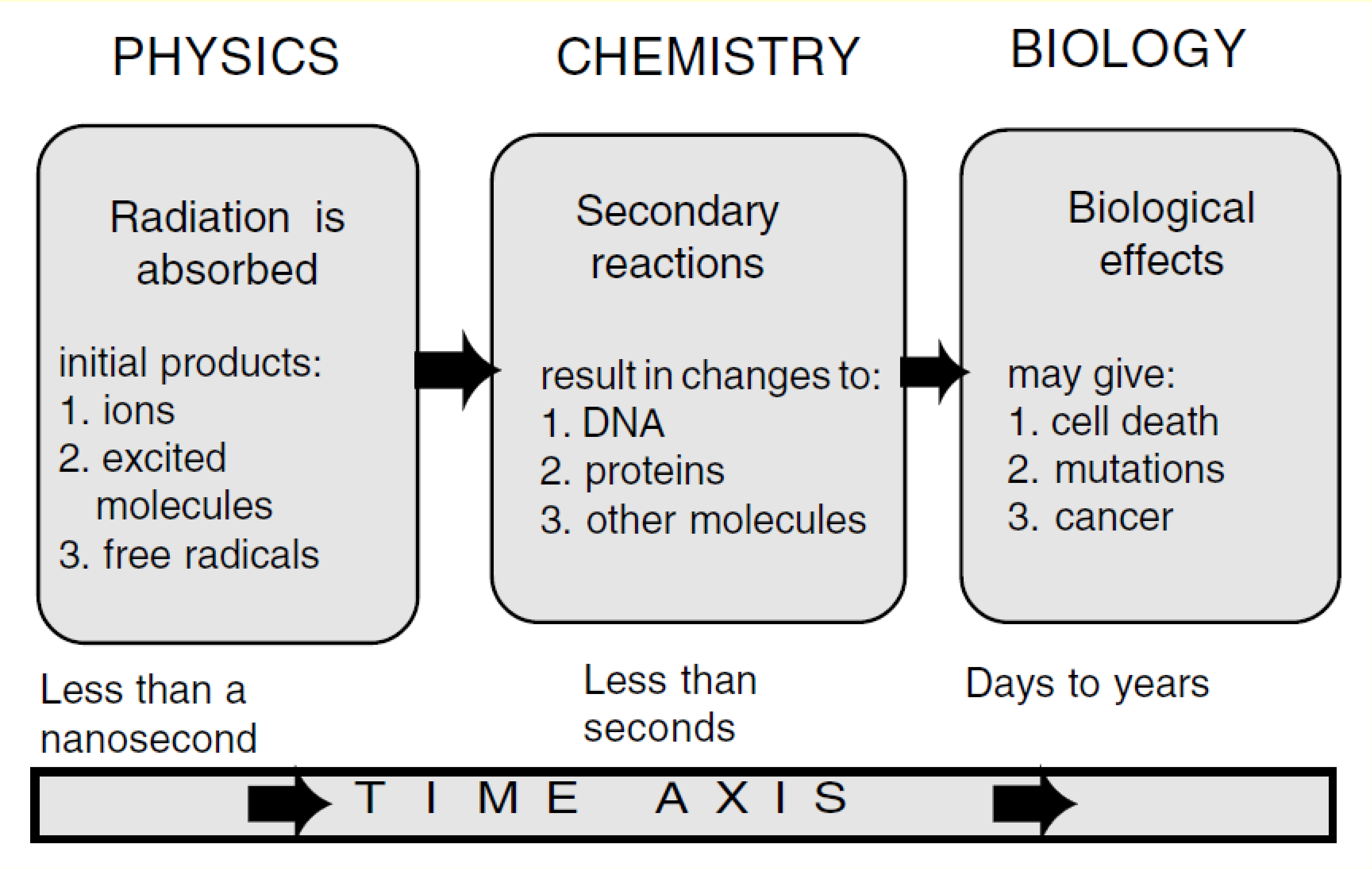
- **The rates of chemical effects are comparable with the rates of chemical reactions**.


Ionising Radiation
Free
radicals
Indirect effect
Direct effect
DNA damage
Lethal damage
Sublethal damage
Repair mechanisms
Cell death
Lethal damage
Mutated cell
Repaired cell

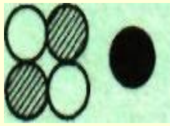
Biological phase



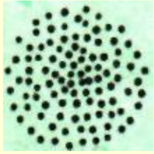
- A damaged cell may **die**.
- A damaged cell may be **mutated**.


PHYSICS
CHEMISTRY
BIOLOGY
Radiation is absorbed
initial products:
1. ions
2. excited molecules
3. free radicals
Secondary reactions
result in changes to:
1. DNA
2. proteins
3. other molecules
Biological effects
may give:
1. cell death
2. mutations
3. cancer
Less than a nanosecond
Less than seconds
Days to years
T I M E A X I S

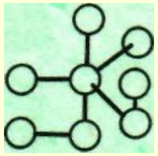
- The transfer of the free radical to a biologic molecule can be sufficiently damaging to cause **bond breakage** or inactivation of **key functions.**



- The *organic peroxy free radical* can transfer the radical form molecule to molecule causing damage at each encounter. Thus a **cumulative effect** can occur, greater than a single ionization or broken bond.

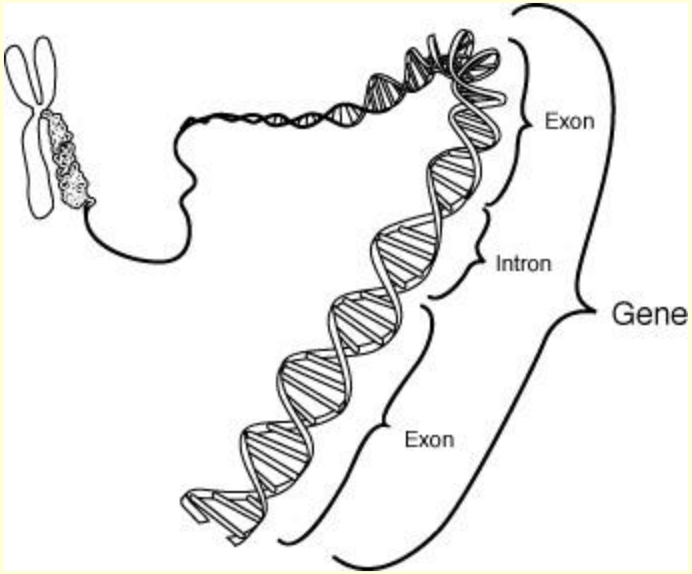


- DNA is the **primary target** for cell damage from ionizing radiation.

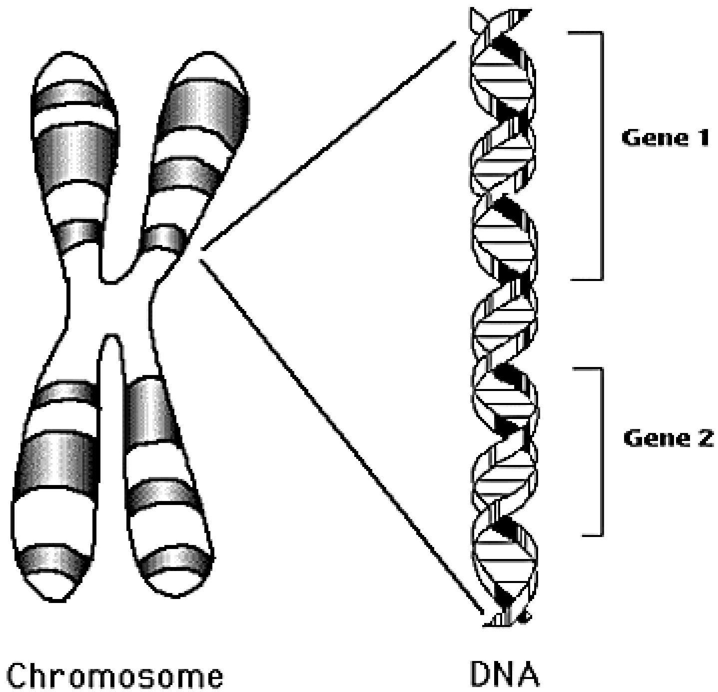


- Toxic effects at low doses to moderate doses (cell killing, mutagenesis, and malignant transformation) appear to result from damage to **cellular DNA**.

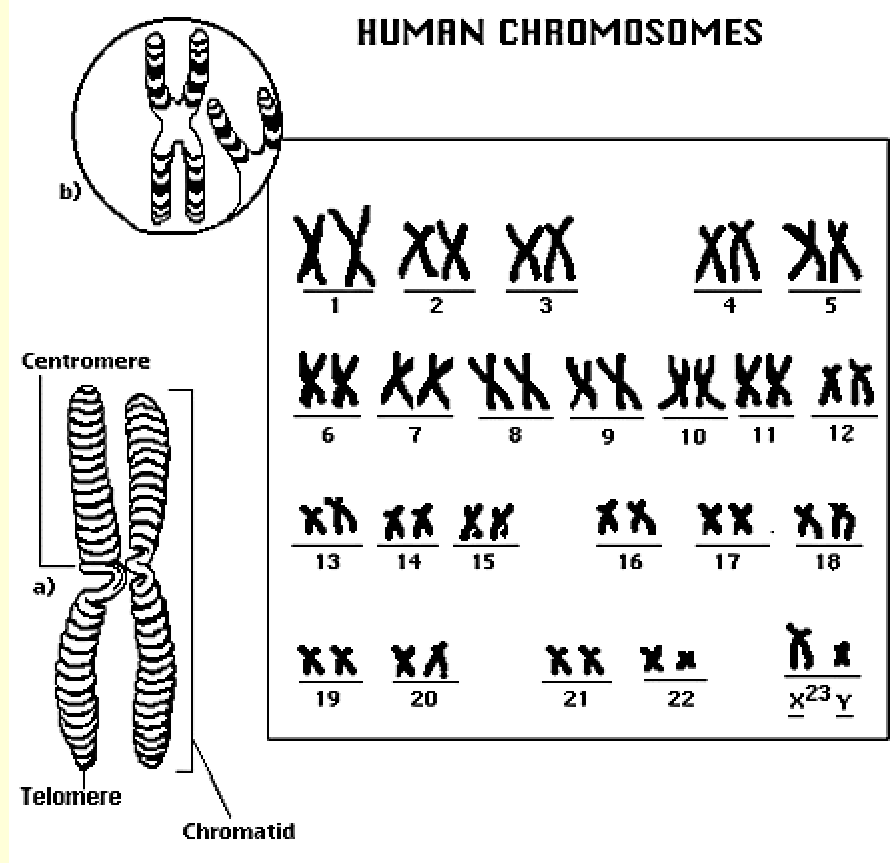
- Thus, ionizing radiation is a classical **genotoxic** agent.

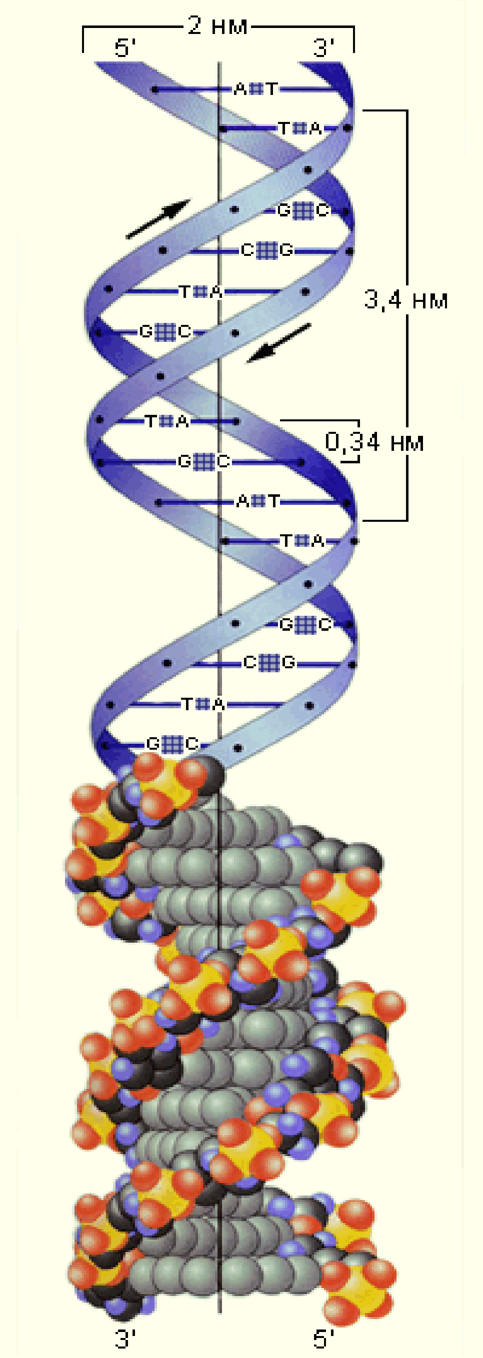


DNA is the most important material making up the chromosomes and serves as the master blueprint for the cell. It determines what **types of protein** that are produced in cell.



Genes

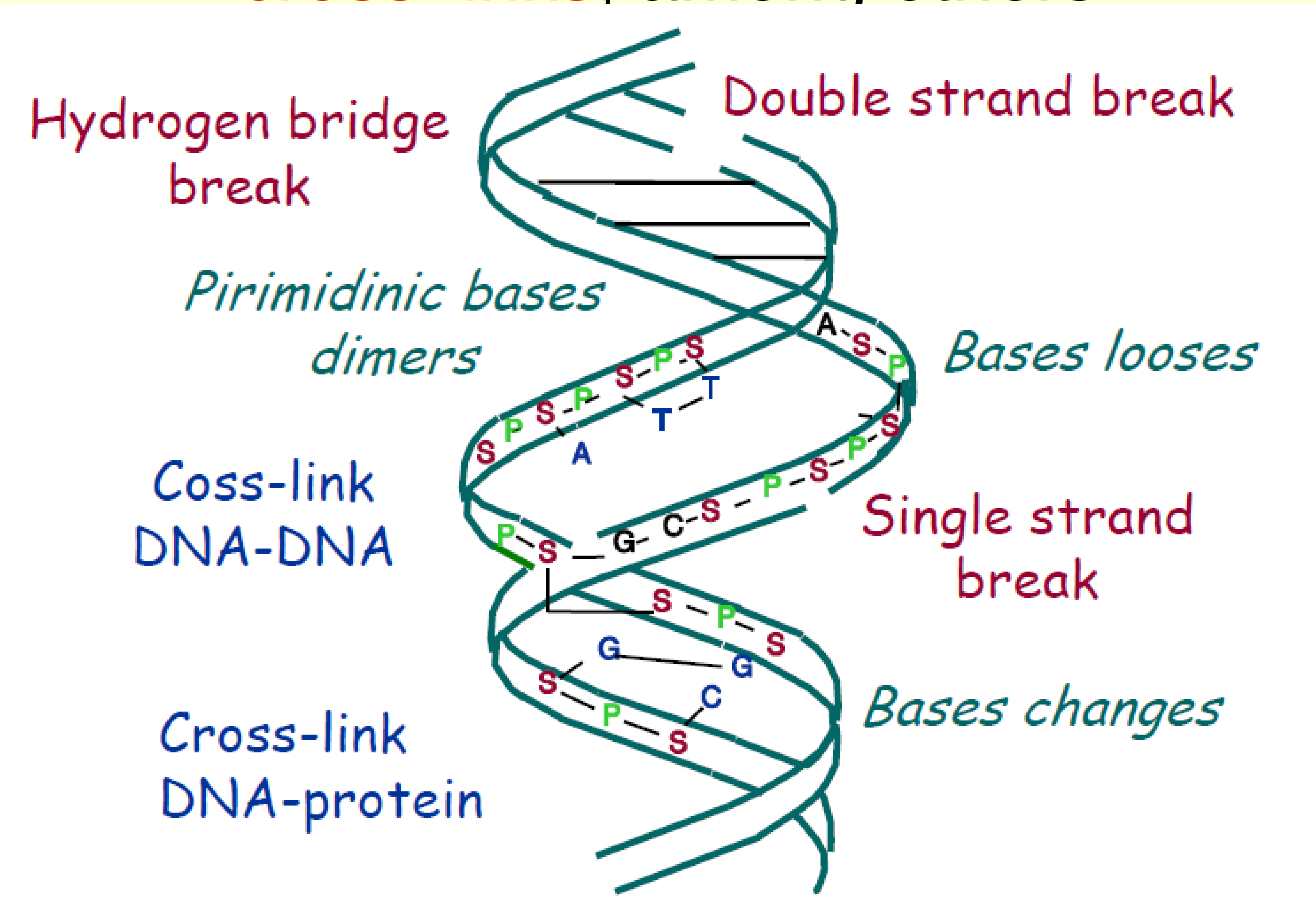




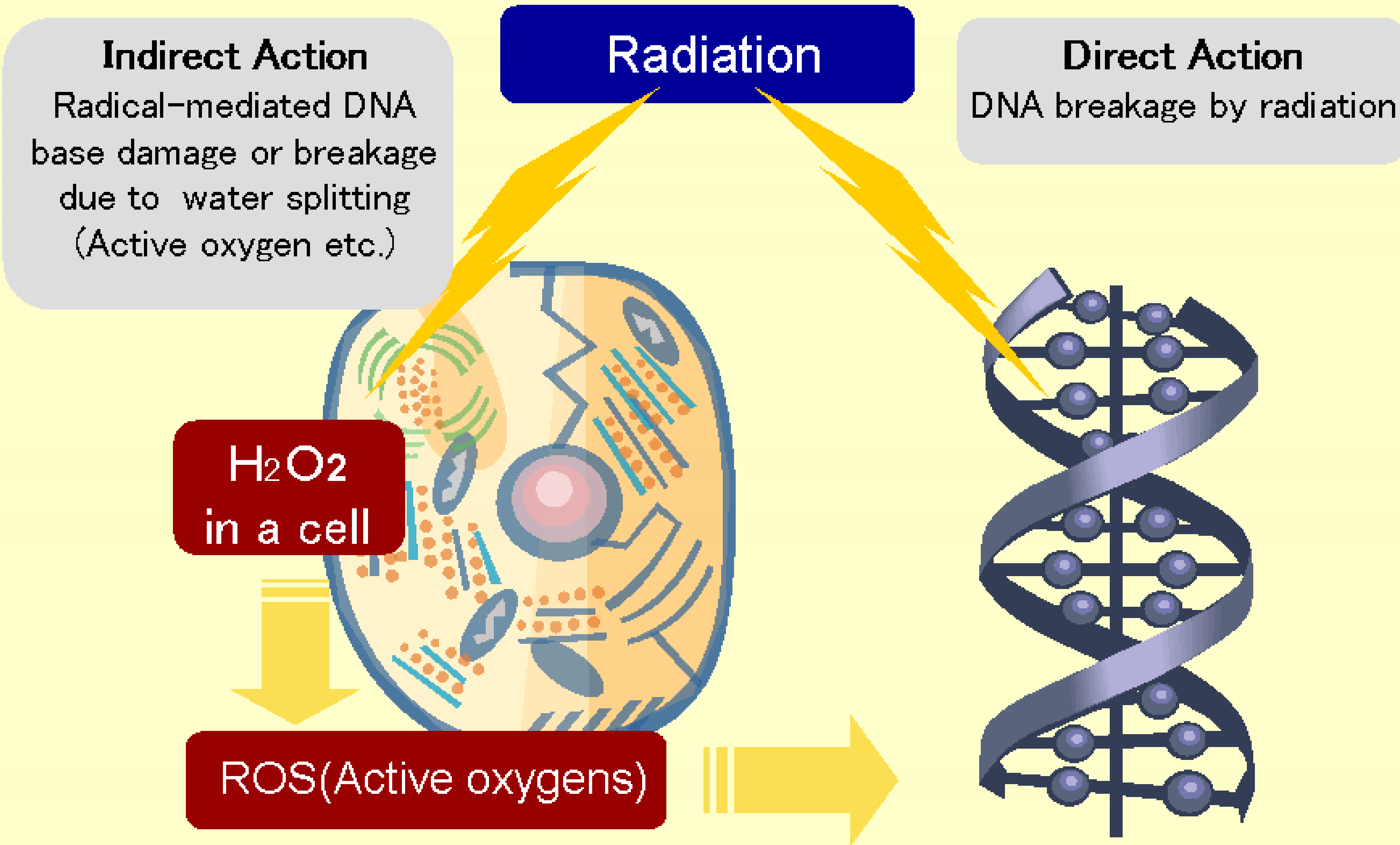
- The DNA molecule takes the form of a **double helix**.

- The sides of the chain are strands of alternating **sugar** and **phosphate groups**. Branching off from each sugar group is one of four **nitrogenous bases**: cytosine, thymine, adenine and guanine.
- This large molecule is **sensitive** to radiation damage.

Ionising radiation can induce a wide variety of DNA lesions: breaks, base changes or cross-links, among others



Action pathways of radiation on DNA



- Radiation emitted by radioactive substances can transfer sufficient localized energy to atoms to remove electrons from the electric field of their nucleus (ionization). In living tissue, this energy transfer can produce chemically reactive ions or free radicals, destroy cellular constituents, and damage DNA. Irreparable DNA damage is thought to be a major factor in carcinogenesis.

- While ionizing radiation may also cause other detrimental health impacts, only radiogenic cancer risk is normally considered in risk assessments

Influence of DNA damage ・・・

Irreparable Damage

- Not able to replicate genetic information
  - Stop cell growth
- Not able to transcribe genetic information
  - Stop protein synthesis

↓

Apoptosis

↓

- Leukocytopenia ・ infertility
- fetal anomaly
- cutaneous erythema・ acomia
- cataract

Defective Repair

- Wrong genetic information
  - Variant DNA

↓

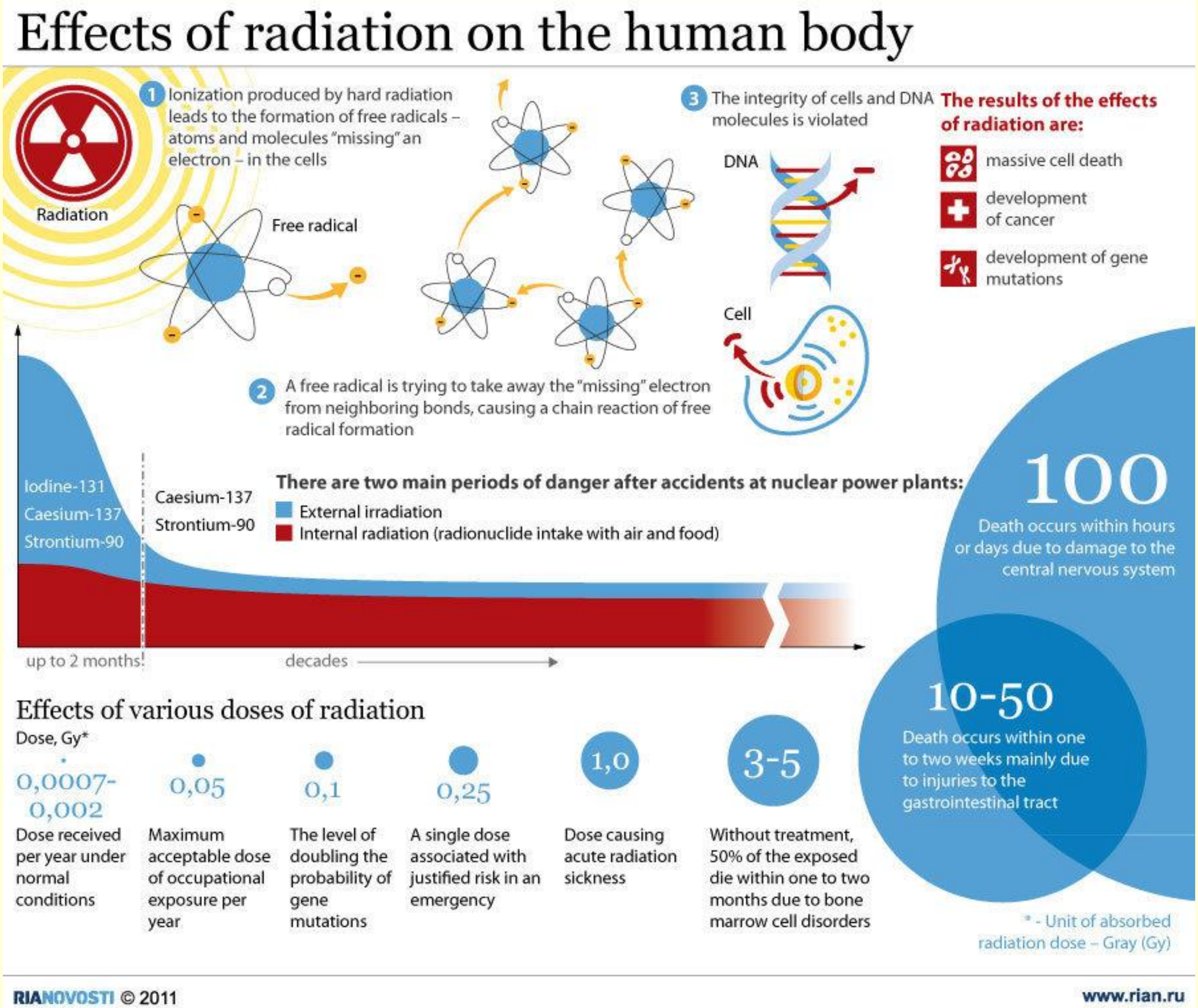
Mutation

↓

Cancer・genetic effect

low
linear energy transfer (LET) radiation (photons and electrons) and high-LET radiations (alpha particles and neutrons)

The type of ionizing radiation emitted by a particular radionuclide depends upon the exact nature of the nuclear transformation, and may include emission of alpha particles, beta particles (electrons or positrons), and neutrons; each of these transformations may be accompanied by emission of photons (gamma radiation or x-rays). Each type of radiation differs in its physical characteristics and in its ability to inflict damage to biological tissue. For purposes of radiation risk estimates, the various types of radiation are often categorized as low linear energy transfer (LET) radiation (photons and electrons) and high-LET radiations (alpha particles and neutrons)


Effects of radiation on the human body
Radiation
1 Ionization produced by hard radiation leads to the formation of free radicals – atoms and molecules "missing" an electron – in the cells
Free radical
2 A free radical is trying to take away the "missing" electron from neighboring bonds, causing a chain reaction of free radical formation
3 The integrity of cells and DNA molecules is violated
DNA
Cell
The results of the effects of radiation are:
massive cell death
development of cancer
development of gene mutations
There are two main periods of danger after accidents at nuclear power plants:
External irradiation
Internal radiation (radionuclide intake with air and food)
Iodine-131
Caesium-137
Strontium-90
Caesium-137
Strontium-90
up to 2 months
decades
100
Death occurs within hours or days due to damage to the central nervous system
10-50
Death occurs within one to two weeks mainly due to injuries to the gastrointestinal tract
Effects of various doses of radiation
Dose, Gy*
0,0007-0,002
Dose received per year under normal conditions
0,05
Maximum acceptable dose of occupational exposure per year
0,1
The level of doubling the probability of gene mutations
0,25
A single dose associated with justified risk in an emergency
1,0
Dose causing acute radiation sickness
3-5
Without treatment, 50% of the exposed die within one to two months due to bone marrow cell disorders
* - Unit of absorbed radiation dose – Gray (Gy)
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Low dose exposures

- Low dose exposures are not clinically detectable. That means that the long term effects can only be
- Estimated in statistical studies of whole populations. In this way, the estimated effects are compared to other
- common societal health risks (driving, flying, sports, alcohol, etc.) to look for the smallest discernible
- increased risk. This might mean that an increase of one additional case of cancer in a population of a million
- would be noted

Comparing Radiation Risk to Other Risks

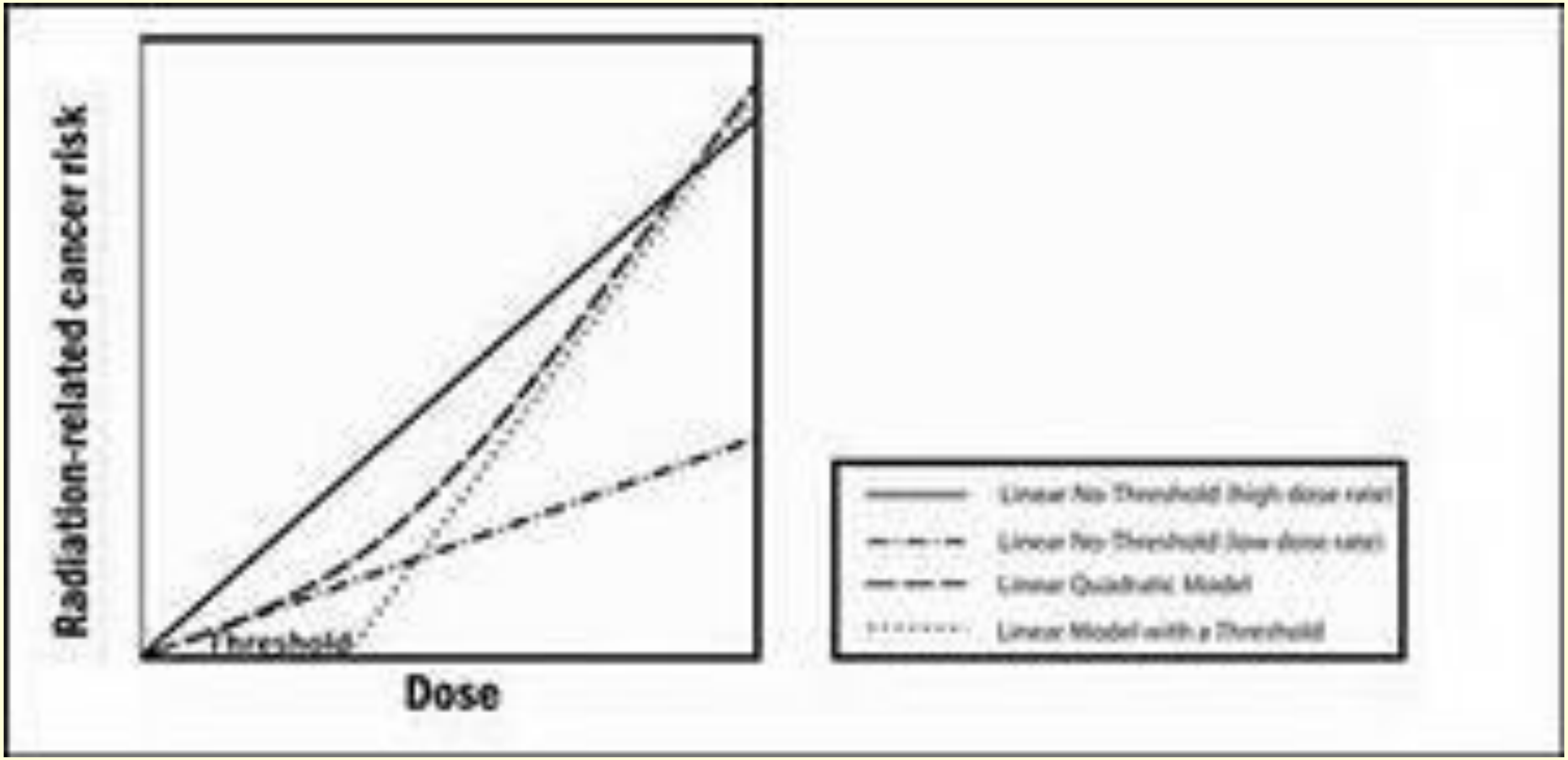
Comparing Radiation Risk to Other Risks

Estimated Loss of Life Expectancy from Health Risks	
Health Risk	**Average Days Lost**
Unmarried male	3500 (9.6 yr)
Smoking 20 cigarettes/day	2370 (6.5 yr)
Unmarried female	1600 (4.4 yr)
Overweight (by 20%)	985 (2.7 yr)
All accidents combined	435 (1.2 yr)
Auto accidents	200
Alcohol consumption (U.S. avg.)	130
Home accidents	95
Drowning	41
1000 millirem per year for 30 years*	30
Natural background radiation*	8
Medical diagnostic x-rays*	6
All catastrophes (earthquake, etc.)	3.5
1000 millirem occupational	1

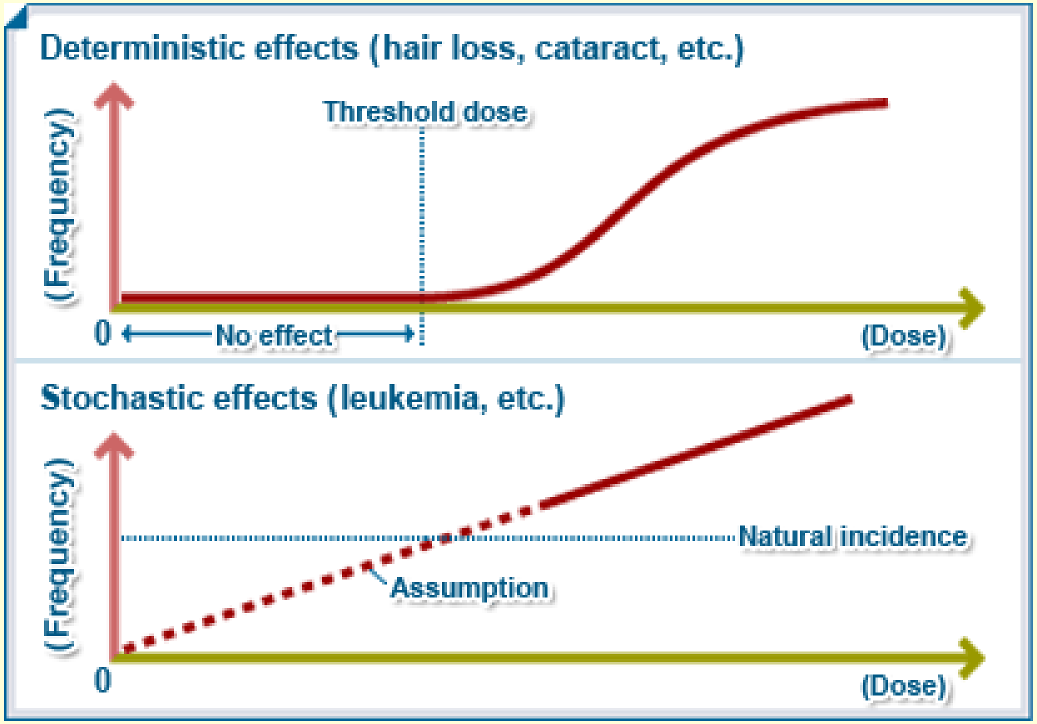
low exposure levels

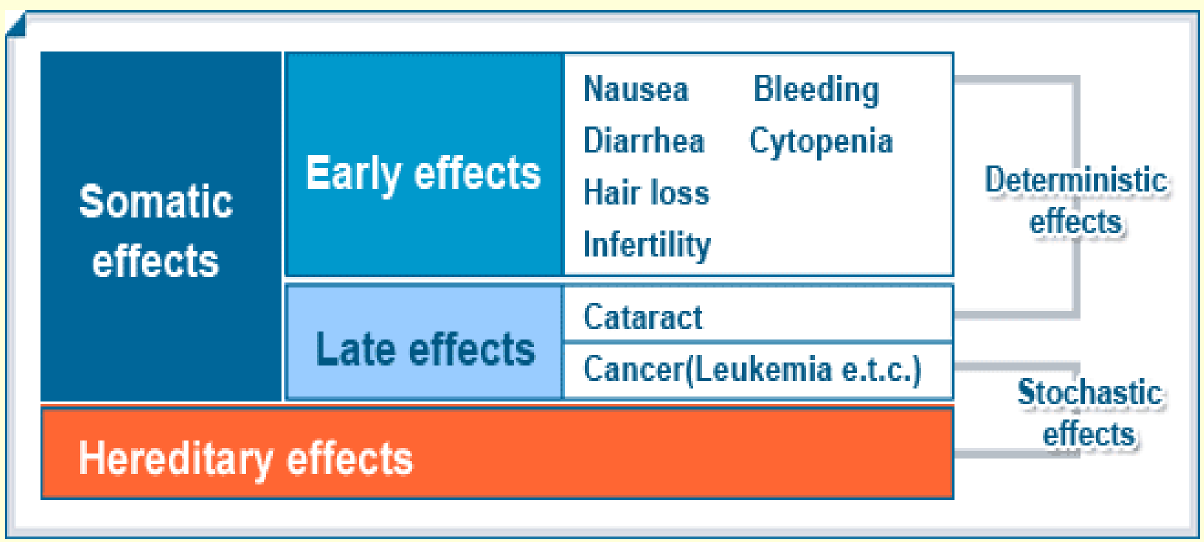
- Because of the inability to observe definite effects of low exposure levels in living tissue, the most con-servative approach is used when evaluating risks from radiation exposure. This approach is called the Linear No-Threshold Risk Model which assumes some minimal biological effect from any exposure even though it would only apply statistically to large populations — not to individuals

Linear No-Threshold Risk Model



- The biological effects of low doses can be divided into three categories:
- 1. Genetic Effects. Observed in offspring of exposed individuals resulting from egg or sperm cell muta-
- tions. As in the case of chemically (drugs) or biologically (viruses) related mutations, these effects
- usually result in nonviable organisms, but never in the “monsters” portrayed in movies or comics.
- 2. Somatic Ef fects. Observed in the exposed individuals. These might take the form of cancers similar
- to the effects of chemical agents (smoking or drinking alcohol) or biological agents (viruses).
- 3. In-Utero E ffects. Observed after birth due to exposure of the embryo. This is a sub-set of somatic
- effects, more serious in earlier stages of development, probably resulting in death, with diminishing
- consequences later in fetal development.


Deterministic effects (hair loss, cataract, etc.)
(Frequency)
Threshold dose
0
No effect
(Dose)
Stochastic effects (leukemia, etc.)
(Frequency)
Natural incidence
Assumption
0
(Dose)


Somatic effects
Early effects
Nausea
Bleeding
Diarrhea
Cytopenia
Hair loss
Infertility
Late effects
Cataract
Cancer(Leukemia e.t.c.)
Hereditary effects
Deterministic effects
Stochastic effects

Stochastic Effects

- Can occur after exposure to **moderate-low doses** of radiation.
- These effects occur **long-term after** irradiation.
- The **probability** of occurrence, but not the severity, increase with dose.

- **No threshold dose** exist for these effects.
- Can be **somatic** or **hereditary** (**genetic**).

acute doses

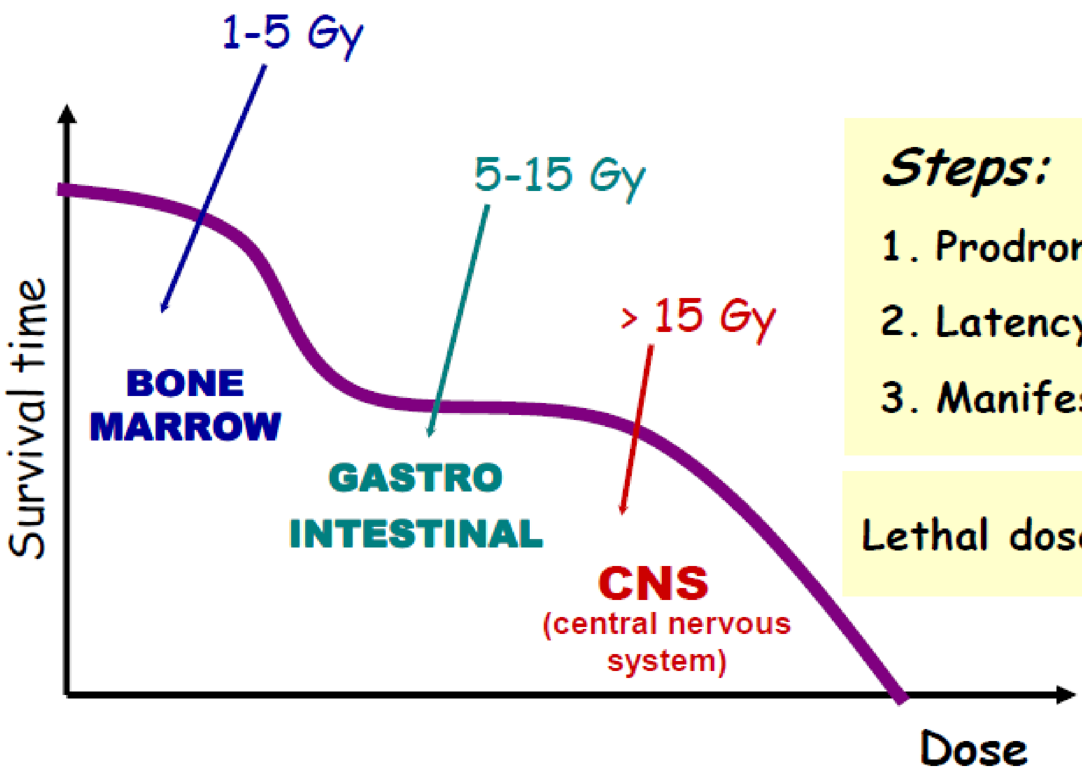
- In contrast to the low doses over long time, there have been occasions in which humans have received
- large doses in a matter of hours. These are called acute doses . In the cases of the atomic bombing of Hiroshi-
- ma and Nagasaki and the catastrophic release of radioactive material from the Chernobyl power plant in the
- former Soviet Union, the clinical effects were detectable. Cells were killed with resulting organ and whole
- body damage. Table 1 briefly describes the expected effects from acute doses.

Acute Radiation Dose Effects in Millirem

Radiation Doses

Acute Radiation Dose Effects in Millirem	
450,000.0	Acute dose, LD 50/60 (a lethal dose to 50% of a population within 60 days if no medical treatment)
100,000.0	Acute dose, radiation sickness, reduced blood count, recovery
25,000.0	Acute dose, reduced fertility, and temporary sterility
10,000.0	Minimum acute dose for which prompt effects are detectable

1 Acute irradiation syndrome



Steps:

1. Prodromic
2. Latency
3. Manifestation

Lethal dose 50/30

2 Chronic Irradiation syndrome

- Whole body clinic of a partial-body irradiation
- Mechanism: Neurovegetative disorder
- Similar to a sick feeling
- Quite frequent in fractionated radiotherapy

Syndromes of acute radiation sickness

	Dose (Gy)	Prodromic	Latency	Desease manifestation	Death
Bone marrow syndrome	1-5	Few hours	Some days - 3 weeks	Infections, haemorrhage, anaemia	30-60 days (>3Gy)
Gastrointestinal syndrome	5-15	Few hours	2-5 days	Dehydration, Malsnutrition, Infections	10-20 days
Central Nervous system syndrome	> 15	Minutes	Few hours	Convulsions, Ataxia, Coma	1-5 days

absorbed dose

- The average energy imparted by ionizing radiation per unit mass of tissue. The SI unit of absorbed dose is the joule per kilogram, also assigned the special name the Gray (1 Gy = 1 joule/kg); the conventional unit of absorbed dose is the rad
- (1 rad = 0.0 1 Gy).

What are radionuclide slope factors?

- **slope factors** are used for estimating incremental cancer risks resulting from exposure to radionuclides via inhalation, ingestion, and external exposure pathways.

Slope factors for radionuclides

- the probability of cancer incidence as a result of unit exposure to a given radionuclide averaged over a lifetime. It is the age-averaged lifetime excess cancer incident rate per unit intake (or unit exposure for external exposure pathway) of a radionuclide

Dose conversion factors (DCFs), or "dose coefficients"

- for a given radionuclide represent the dose equivalent per unit intake (i.e., ingestion or inhalation) or external exposure of that radionuclide. These DCFs are used to convert a radio- nuclide concentration in soil, air, water, or foodstuffs to a radiation dose. DCFs may be specified for specific body organs or tissues of interest, or as a weighted sum of individual organ dose, termed the effective dose equivalent

What is dose equivalent, effective dose equivalent, and related quantities

- "dose equivalent"is a measure of the energy absorbed by living tissues, adjusted for the relative biological effectiveness of the type of radiation present.

dose equivalent

dose equivalent =

the absorbed dose X Quality Factor (Q) or radiation weighting factor

Relative Biological Effectiveness

Radiation Type	Weighting Factor
X-rays & Gamma-rays	1
Protons	2
Neutrons	5-20 (according to energy)
Alpha particles	20

In vitro data suggest X-rays RBE > gamma-rays

– Difficult to assess in epidemiological studies

The "committed dose equivalent"

- is defined as the integrated dose equivalent that will be received by an individual during a 50-year period (based on occupational exposure) following the intake.

absolute excess risks of death in a cohort of people with cancer

- AER = ((O-E)/person-years) * 10,000

(the observed (O) and expected (E) deaths)

This gives us the excess risk per year per 10,000 persons. We have done this for various age groups and would like to use a test for trend to see whether there is a significant increase in the risk

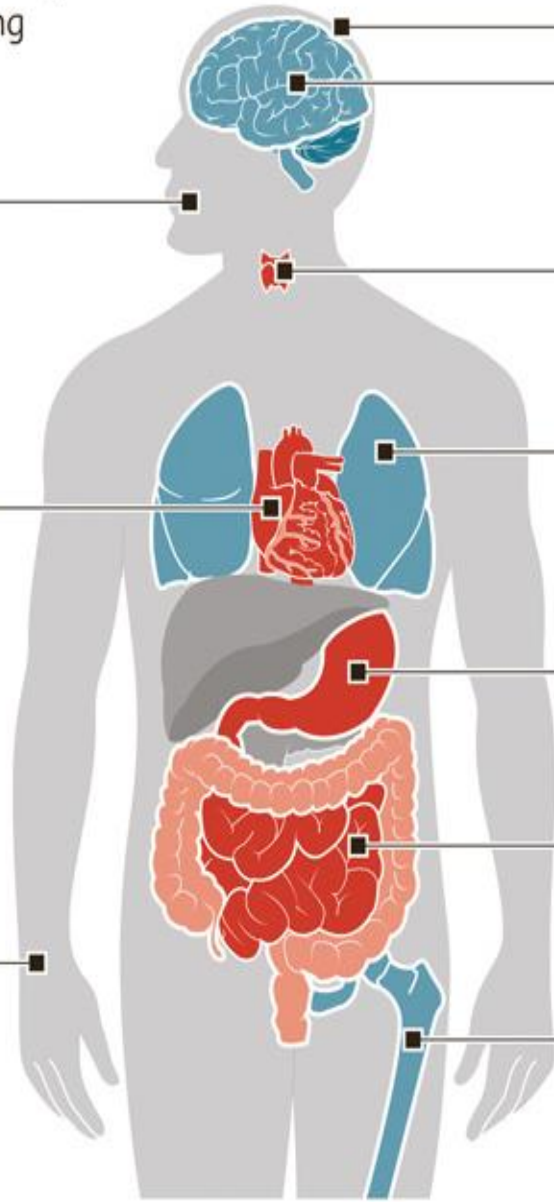
The "critical organ" is the organ that received the most dose for the radionuclide concerned

- Critical organ standards
- usually consist of a combination of whole body and critical
- organ dose limits, such as
- **25 mrem/yr to the whole body**,
- **75 mrem/yr to the thyroid,**

  25 mrem/yr to any critical organ other than the thyroid. When these standards were
- adopted, dose was calculated and controlled for each organ
- in the body and uniform radiation of the "whole body."
- The "critical organ" was the organ that received the most
- dose for the radionuclide concerned. With the adoption of
- the dose equivalent concept, the dose to each organ is
- weighted according to the effect of the radiation on the
- overall system (person).

» THE EFFECTS OF RADIATION ON THE BODY

Radiation can target many parts of the body. Symptoms vary, with severity depending on dosage or length of exposure.



HAIR LOSS

BRAIN
Headache, nausea, fatigue, fainting, weakness

MOUTH AREA
Inflammation of mouth/throat, ulcers, worsening of tooth or gum disease, bleeding

ENLARGED THYROID GLAND
Thyroid absorbs radioactive iodine-131, High cancer risk, espcially for children

LUNGS
Bronchitis, inflammation (pneumonitis) and scarring (fibrosis) causing shortness of breath and dry cough

HEART
Rapid heartbeat, inflammation of heart with chest pain

BLOOD
Hemorrhaging, anemia, bleeding spots under the skin, low platelet count

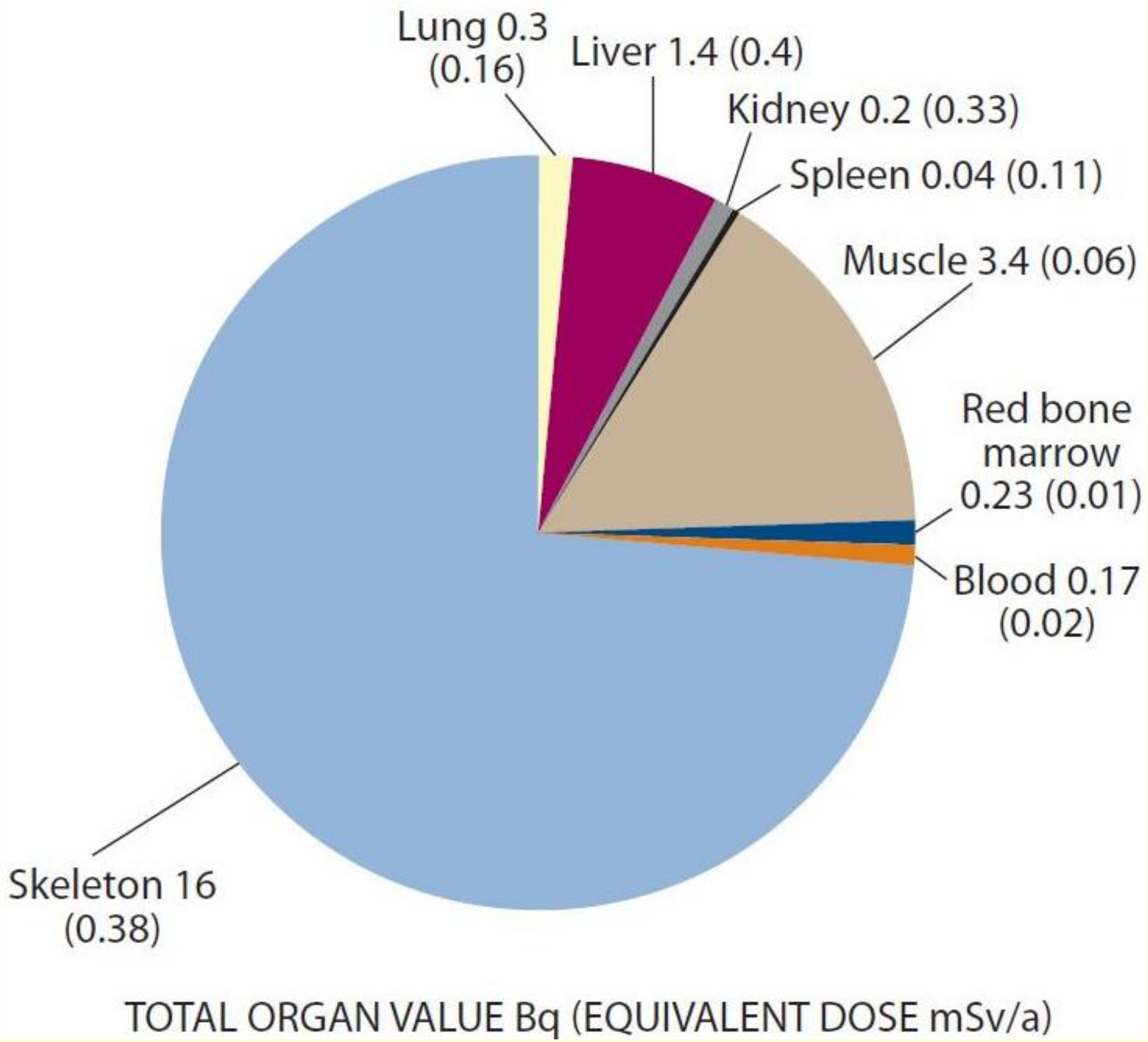
STOMACH
Nausea, ulcers, internal bleeding, vomiting, and diarrhea

SMALL/LARGE INTESTINE
Ulcers, internal bleeding, bloody stool, diarrhea

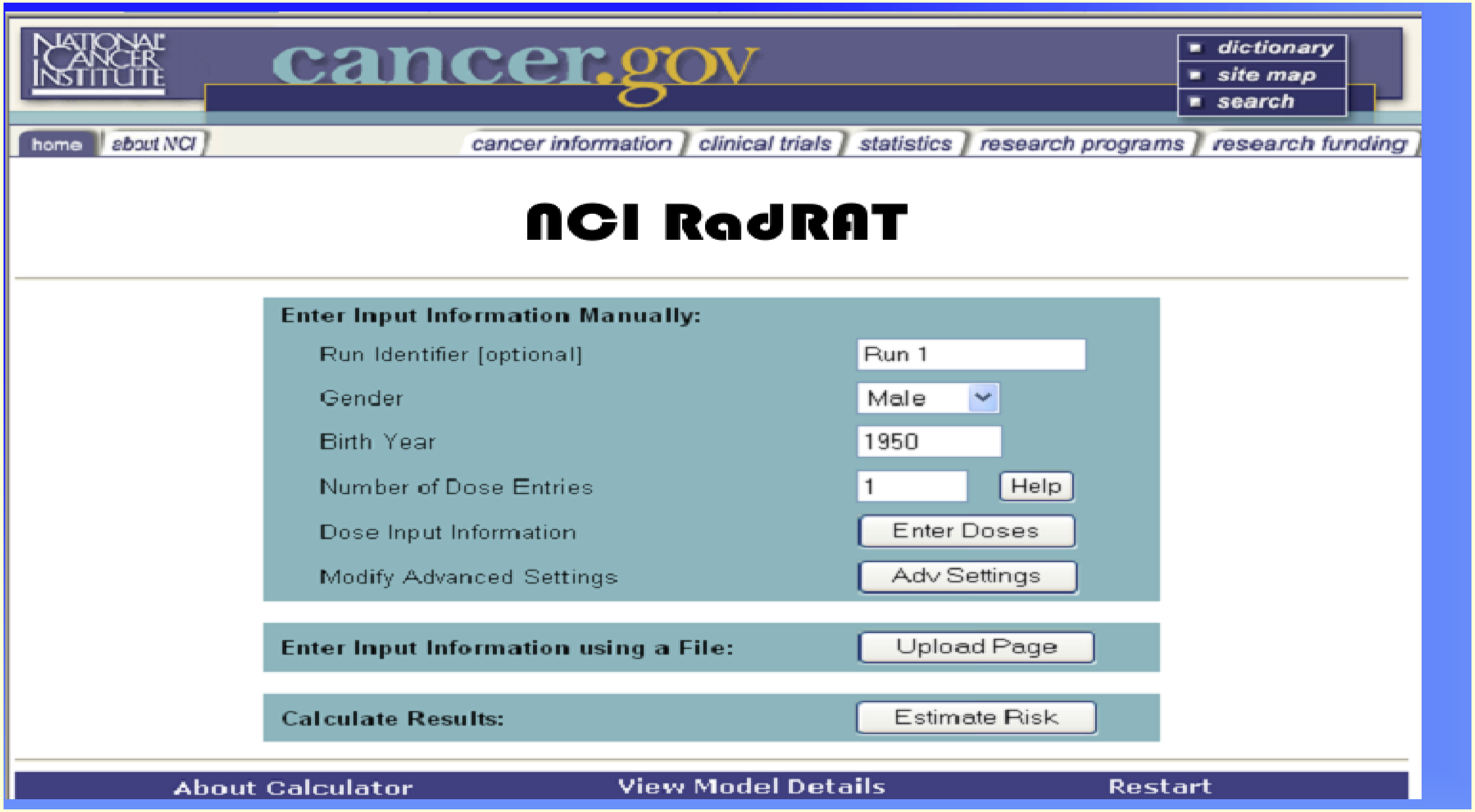
SKIN
Burning, inflammation, permanent skin darkening, bruising, open sores, sloughing, bleeding

BONE MARROW
Depletion of white blood cells – up to 50 per cent within 48 hours – leading to high infection risk

Distribution of **polonium-210** in human body organs after chronic ingestion of radionuclides of uranium and thorium series



Radiation Risk Assessment Tool



How should radionuclide slope factors and dose conversion factors be used?

- radionuclide slope factors are used to estimate the excess cancer risk resulting from exposure to radionuclides at radiologically contaminated sites for comparison with target risk range
-
    - 10-4-10-6 lifetime excess cancer risk
-

The incremental risk

- is calculated by multiplying estimates of the lifetime intake via inhalation and ingestion of each radionuclide of concern, and the duration and concentration in environmental media to which the receptor is exposed via the external exposure pathway, by the appropriate slope factor values for that exposure pathway and radionuclide.

The incremental risk

- lifetime intake x slope factor,
- where slope factor takes account of the duration and concentration in environmental media to which the receptor is exposed

Regulatory Limits

- Radiation worker:
  - 5 rem/yr = **50** mSv/yr
- Individual member of the general public:
  - 0.1 rem/yr = **1** mSv/yr

Compare to

- **natural background**: 0.06 rem/yr = **0.6** mSv/yr
- **average background**: 0.36 rem/yr = **3.6**

Levels of radiation exposure

The effects of radiation exposure at various doses:

Dose	Effect
6-7 Sv (600-700 rem)	a single dose is absolutely lethal
4.5 Sv (450 rem)	severe radiation sickness (kills 50% of people exposed)
1 Sv (100 rem)	earliest stage of mild radiation sickness
0.75 Sv (75 rem)	a short-term, insignificant change in blood content is caused by exposure at this level
0.3 Sv (30 rem)	exposure during a stomach x-ray
0.25 Sv (25 rem)	acceptable one-time exposure of personnel
0.1 Sv (10 rem)	acceptable one-time exposure of the population
0.05 Sv (5 rem)	acceptable exposure of nuclear power plant personnel in normal conditions over a year
0.03 Sv (3 rem)	exposure during a dental x-ray
5 mSv (500 mrem)	acceptable exposure of personnel under normal conditions
1 mSv (100 mrem)	background radiation over a year
10 mSv (1 mrem)	flight over a distance of 2400 km
0.005 mSv (0.5 mrem)	three hours of television viewing a day over a year

Radiation doses that can result in injury or death

Sievert (Sv) — a unit of equivalent radiation dose according to the SI system*

1 Sv = 100 rem**

* The International System of Units

** Rem - a unit of equivalent dose for any form of ionizing radiation

Common effects of short-term exposure

- **10,000 mSv (10 Sv) —** death within a few weeks
- **Between 2000 and 10000 mSv (2 - 10 Sv) —** acute and most likely fatal radiation sickness
- **1000 mSv (1 Sv) —** risk of cancer many years later

Normal background radiation is

3 mSv per year.

This comes from natural sources of ionizing radiation. Roughly two mSv per year come from radon in the air. These radiation levels are close to the minimum doses absorbed by all people on the planet

Normal background radiation

0.3 - 0.6 mSv / year -

man-made, mostly medical sources of radiation

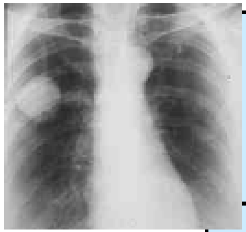
Background radiation

Safety standards call for 0.05 mSv per year around nuclear power plants. The actual dose near nuclear facilities is much less

Danger level	Radiation dose	Effect
	2 millisieverts per year (mSv/yr)	Typical background radiation experienced by everyone (average 1.5 mSv in Australia, 3 mSv in North America)
	9 mSv/yr	Exposure by airline crew flying New York-Tokyo polar route
	20 mSv/yr	Current limit (averaged) for nuclear industry employees
	50 mSv/yr	Former routine limit for nuclear industry employees. It is also the dose rate which arises from natural background levels in several places in Iran, India and Europe
	100 mSv/yr	Lowest level at which any increase in cancer is clearly evident.
	350 mSv/lifetime	Criterion for relocating people after Chernobyl accident
	400 mSv/hr	The level recorded at the Japanese nuclear site, 15 March

Radiation risks

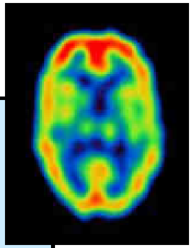
Effect	Population	Exposure period	Probability
Hereditary effects	Whole population	Lifetime	1 %/Sv (all generations)
Fatal cancer	Whole population	Lifetime	5 %/Sv
Fatal cancer	Working population	Age 18-65	4 %/Sv
Health detriment	Whole population	Lifetime	7.3 %/Sv
Health detriment	Working population	Age 18-65	5.6 %/Sv



RADIATION RISKS IN X-RAY EXAMINATIONS

Examination	Skin dose (mGy)	Effective dose (mGy)	Risk (%)
Urography	30	8	0.04
Lumbar spine	40	5	0.025
Abdomen	10	2.5	0.013
Chest	2	0.25	0.0013
Extremities	3	0.025	0.00013

RADIATION RISKS IN NUCLEAR MEDICINE



Examination	Radiopharmaceutical	Effective dose (mSv)	Risk (%)
Myocardium	Tl-201 chloride	23	0.12
Bone	Tc-99m MDP	3.6	0.018
Thyroid	Tc-99m pertechnetate	1.1	0.006
Lungs	Tc-99m MAA	0.9	0.005
Kidney clearance	Cr-51 EDTA	0.01	0.00005

Thank for your attention!