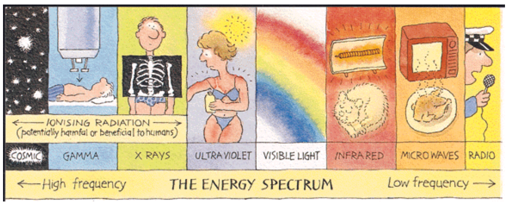
Ionising radiation

– radioactive damage of the cells – tissues - organism

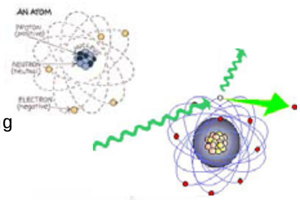
Radiation is energy travelling through space



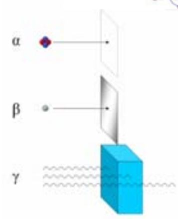
"Life on earth has developed with an ever present background of radiation. It is not something new, invented by the wit of man: radiation has always been there!"

Eric J Hall, Professor of Radiology, College of Physicians and Surgeons, Columbia University, New York, in his book "Radiation and Life"

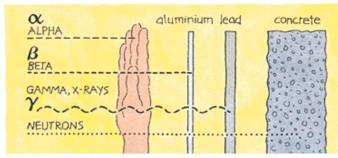
What is ionizing radiation ?



- Either **particle** radiation or **electromagnetic** radiation in which an individual particle/photon carries enough energy to **ionize** an atom or molecule by completely removing an electron from its orbit
- Ionising radiation produces electrically-charged particles called **ions** in the materials it strikes (= ionisation)
  - in the large chemical molecules of which all living things are made the changes caused may be biologically important
- Types:
  - α = α–particles (Helium atoms)
  - β = electrons or positrons
  - γ = electromagnetic (photons)
  - neutron



Penetration of ionizing radiation

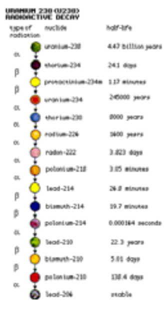


- Measures of ionizing radiation (units):
  - the amount of ionising radiation, or 'dose', received by a person is measured as **energy absorbed** in the body tissue, and is expressed in **gray** (Gy)
    - 1 Gy = 1 joule deposited per kilogram of mass (1 J/kg, formerly 100 rad)
  - equal exposure to different types of radiation expressed as gray do not produce equal biological effects (1Gy of α-radiation will have a greater effect than 1Gy of β-radiation) → radiation effect is expressed as **effective dose**, in a unit called the **sievert** (Sv).
    - regardless of the type of radiation, 1 Sv of radiation produces the same biological effect
    - example: 1Gy=1Sv for γ- or β-radiation, 1Gy=10Sv for neutrons and 1Gy=20Sv for α-radiation
  - for radioactive substances **rate of radioactive decay** is expressed in **becquerel** (Bq)
    - 1 Bq is one atomic decay per second)

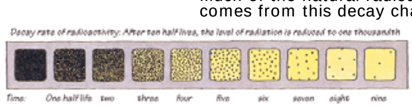
Unstable atoms

- Most atoms are stable: carbon-12 or oxygen-16 atoms remains the same forever
- Certain atoms eventually disintegrate into a totally new atoms
  - they are said to be "unstable" or "radioactive"
    - an unstable atom has excess internal energy, with the result that the nucleus can undergo a spontaneous change towards a more stable form = "**radioactive decay**"
  - when an atom of a radioisotope decays, it gives off some of its **excess energy as radiation** in the form of γ-rays or fast-moving sub-atomic particles
    - unit: becquerel (1 Bq is one atomic decay per second)

Radioactive decay

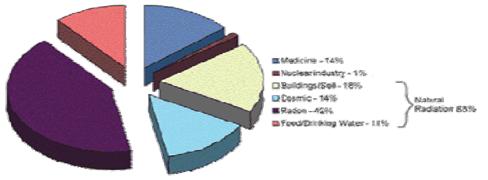


- Atoms in a radioactive substance decay in a random fashion but at a characteristic rate
  - the length of time this takes, the number of steps required and the kinds of radiation released at each step are well known
  - the **half-life** is the time taken for half of the atoms of a radioactive substance to decay (range from less than a millionth of a second to millions of years depending on the element)
    - after one half-life the level of radioactivity of a substance is halved, after two half-lives it is reduced to one quarter, after three half-lives to one-eighth and so on
- All uranium atoms are mildly radioactive
  - figure for uranium-238 shows the series of different radioisotopes it becomes as it decays, the type of radiation given off at each step and the 'half-life' of each step on the way to stable, non-radioactive lead-206
- Much of the natural radioactivity in rocks and soil comes from this decay chain



Sources of ionizing radiation

- Natural radiation
  - cosmic
    - positively charged ions from protons to Fe-nuclei
    - energy of this radiation can far exceed energies that humans can create even in the largest particle accelerators
      - the dose rate from cosmic radiation on airplanes is so high that, according to the United Nations UNSCEAR 2000 Report airline workers receive more dose on average than any other worker, including nuclear power plant workers
  - solar
    - all extremely hot objects (sun produces ultraviolet and γ-radiation)
      - most solar radiation is electromagnetic radiation, although the sun also produces particle radiation (mostly protons with relatively low in energy (10-100 keV)
  - non-radon terrestrial sources
    - radiactive decay of natural isotopes (γ-ray emitters) in the rocks and soil – mainly potassium, uranium and thorium
  - Radon
    - Radon-222 is produced by the decay of Radium-226 which is present wherever uranium is
    - Radon is a gas, it seeps out of uranium-containing soils found across most of the world and may concentrate in well-sealed homes
    - the single largest contributor to an individual's background radiation dose and is certainly the most variable from location to location
    - Radon gas is the second largest cause of lung cancer in America, after smoking
- Man-made radiation
  - medicine
    - diagnostic, therapeutic, sterilisation
  - commercial
    - smoke detectors (americium-241)
  - industrial
    - nuclear power plants (nuclear fission or nuclear fusion)
    - scientific – particle accelerators
    - food preservation
    - agriculture (fertilising, increasing genetic variability)
    - insect control
    - water resources
    - analysing pollutants
    - industrial tracers

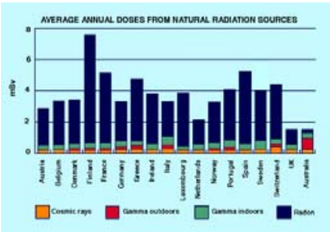


Radioactivity of some natural and other materials

1 adult human (100 Bq/kg)	7000 Bq
1 kg of coffee	1000 Bq
1 kg superphosphate fertiliser	5000 Bq
air in a 100 m^2 Australian home (radon)	3000 Bq
air in many 100 m^2 European homes (radon)	30 000 Bq
1 household smoke detector (americium)	30 000 Bq
radioisotope for medical diagnosis	70 million Bq
radioisotope source for medical therapy	100000 000 million Bq
1 kg 50-year old high-level nuclear waste	10 000 000 million Bq
1 kg uranium	25 million Bq
1 kg low level radioactive waste	1 million Bq
1 kg of coal ash	2000 Bq
1 kg of granite	1000 Bq

Background radiation

- Naturally and inevitably present in our environment
- Levels can vary greatly
  - people living in granite areas or on mineralised sands receive more terrestrial radiation than others, while people living or working at high altitudes receive more cosmic radiation
- A lot of our natural exposure is due to radon (gas seeps from the earth's crust and is present in the air we breathe)



Uses of ionizing radiation

- diagnostic
  - X-ray, computer tomography (CT), positron emission tomography (PET)
  - RIA (radioimmunoassay)
  - scintigraphy - technetium-99m (skeleton, heart, circulation)
- therapeutic
  - whole body/localised irradiation
    - external sources - γ-rays from a cobalt-60 source
    - internal sources - using a small dose of γ- or β-radiation (pleural cavity, intravaginal, ...)
  - selective destruction by radioisotopes
    - thyroid cancer – iodine-131
    - head and breast cancer – irridium-192
    - bone metastases – samarium-153
- sterilisation
  - medical hardware, food

Protection from radiation, standards, regulation

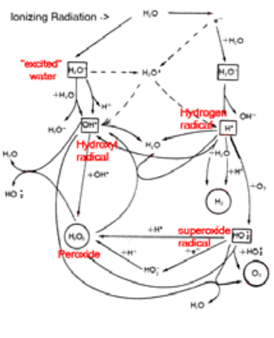
- Limiting time:
  - for people who are exposed to radiation in addition to natural background radiation through their work, the dose is reduced and the risk of illness essentially eliminated by limiting exposure time
- Distance:
  - the intensity of radiation decreases with distance from its source
- Shielding:
  - barriers of lead, concrete or water give good protection from penetrating radiation such as gamma rays
  - radioactive materials are therefore often stored or handled under water, or by remote control in rooms constructed of thick concrete or lined with lead
- Containment:
  - radioactive materials are confined and kept out of the environment - radioactive isotopes for medical use, for example, are dispensed in closed handling facilities
  - nuclear reactors operate within closed systems with multiple barriers which keep the radioactive materials contained - rooms have a reduced air pressure so that any leaks occur into the room and not out from the room
- Radiation protection standards are based on the conservative assumption that the risk is directly proportional to the dose, even at the lowest levels, though there is no evidence of risk at low levels
  - this assumption, called the '**linear no-threshold (LNT) hypothesis**', is recommended for radiation protection purposes
  - it cannot properly be used for predicting the consequences of an actual exposure to low levels of radiation
    - for example, it suggests that, if the dose is halved from a high level where effects have been observed, there will be half the effect, and so on. This could be very misleading if applied to a large group of people exposed to trivial levels of radiation and could lead to inappropriate actions to avert the doses
  - practically, **"As Low As Reasonably Achievable"** (ALARA)"
- Much of the evidence which has led to today's knowledge and standards derives from the atomic bomb survivors in 1945, uranium miners, industrial catastrophes (e.g. Chernobyl) animal experiments etc. who were exposed to high doses incurred in a very short time

Radiation injury

- Types
  - external irradiation
  - external contamination with radioactive materials followed by or transdermal absorption
  - internal contamination by inhalation or ingestion with incorporation of radiologic materials into the body's cells and tissues
- These 3 types of exposure can occur in combination and can be associated with thermal burns and traumatic injuries
- Example: nuclear detonation
  - heat (~35% of total energy)
    - heat and light cause thermal injury, including flash burns, flame burns, flash blindness (due to temporary depletion of photopigment from retinal receptors), and retinal burns
  - blast (~50% of total energy)
    - blast wave results in fractures, lacerations, rupture of viscera, and pulmonary hemorrhage and edema
  - radiation (~15% of total energy)
    - radiation causes the acute radiation syndrome (radiation sickness)

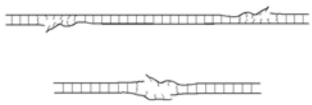
Biological effect of ionizing radiation

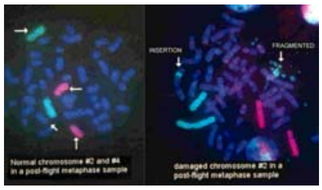
- Direct ionization of macromolecules
  - ionized macromolecules almost never function properly, due to the fact that their function is largely controlled by their shape and therefore by their charge distribution
  - breakage of disulfide bonds produces radicals
- Indirectly through the ionization ("radiolysis") of water (~60% of body!!)
  - ionization of water produces "free radicals" - hydrogen and hydroxyl radicals - which are very reactive, leading very quickly to the breakage of bonds in a biological molecule (again, the macromolecule is rendered ineffective)
- Three outcomes – cellular/molecular level:
  - cell cycle block → cell death
    - interphasis (lymphocytes)
    - mitosis or post-mitotic (other proliferating cells)
  - cell/DNA mutation (gene or chromosome)
    - reparation resulting in no residual damage
    - cells incorrectly repair themselves resulting in a biophysical change



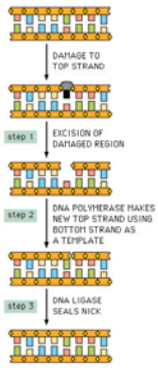
Fatal × non-fatal DNA lesions

- point mutations
- single strand breaks (SSB)
  - reparation
- double strand breaks (DSB)
  - lethal (apoptosis)
  - homologous recombination
  - non-homologous end-joining
    - translocation
    - insertion





DNA repair

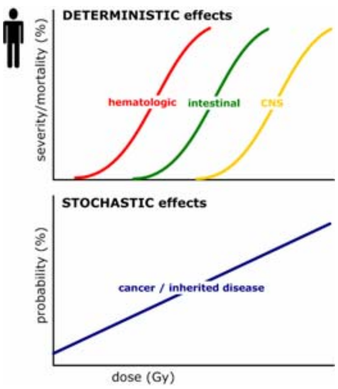


- (*in situ* repair)
- excision repair
  - inter-individual variability in its capacity – individual radiosensitivity/susceptibility to damage

Character of biological effects

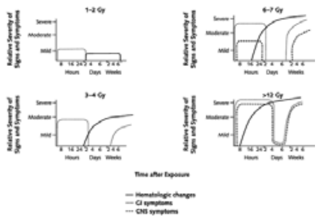
- **Deterministic**
  - **severity dependent** ("determined") **on the dose**
  - manifestation **specific**
  - effect only when exposure **exceeded threshold**
  - damage of **large amount of cells**
  - onset rather close to the exposure (**short latency**)
  - types:
    - acute radiation syndrome
    - chronic post-radiation syndrome
      - cataract, radiation dermatitis,
    - damage of the foetus *in utero*
    - sterility
- **Stochastic**
  - **probability increases with the dose** (not the severity!)
  - manifestation **non-specific**
  - gradual increase of the risk **without "safe" threshold**
  - damage of the **single cell** enough to cause effect
  - **manifestation delayed** (typically years)
  - types:
    - somatic mutation - cancer
      - leukemias, thyroid, lung, breast, bones
    - germinative mutation (oocyte, sperm cell) – inherited genetic disease

Overview effect types



Acute radiation syndrome

- Clinical components of the acute radiation syndrome include the **hematopoietic**, **gastrointestinal**, and **cerebrovascular** syndromes
- The time course and severity of symptoms for the component syndromes are different at different dose ranges – i.e. **deterministic** effect!!!
  - from few hours after exposure until few months following a radiation exposure



Acute radiation syndrome

- Haematopoietic syndrome
  - lymphopenia, granulocytopenia (immunodeficiency), thrombocytopenia (bleeding), anemia
- GIT syndrome
  - early (hrs) - nausea, vomiting, diarrhea
  - later (days) - loss of intestinal integrity
    - malabsorption, dehydration, toxemia/sepsis, ileus, bleeding)
- Cerebrovascular syndrome
  - headache, impaired cognition, disorientation, ataxia, seizures, prostration, and hypotension
- Cutaneous syndrome
  - erythema, burns, edema, impaired wound healing
  - epilation (damage to hair-root cells → hair loss)

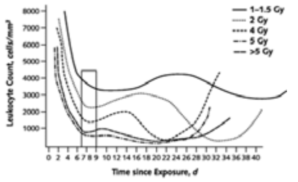
Table 1. **Phases of Radiation Injury***

Dose Range, *Gy*	Prodrome	Manifestation of Illness	Prognosis (without Therapy)
0.5–1.0	Mild	Slight decrease in blood cell counts	Almost certain survival
1.0–2.0	Mild to moderate	Early signs of bone marrow damage	Highly probable survival (>90% of victims)
2.0–3.5	Moderate	Moderate to severe bone marrow damage	Probable survival
3.5–5.5	Severe	Severe bone marrow damage; slight GI damage	Death within 3.5–6 wk (50% of victims)
5.5–7.5	Severe	Pancytopenia and moderate GI damage	Death probable within 2–3 wk
7.5–10.0	Severe	Marked GI and bone marrow damage, hypotension	Death probable within 1–2.5 wk
10.0–20.0	Severe	Severe GI damage, pneumonitis, altered mental status, cognitive dysfunction	Death certain within 5–12 d
20.0–30.0	Severe	Cerebrovascular collapse, fever, shock	Death certain within 2–5 d

* Modified from Walker RI, Cerveny RJ, eds. (21). GI = gastrointestinal.

The hematopoietic syndrome

- Irradiation (>1Gy) of bone marrow stem and progenitor cells at increasing doses results in exponential cellular death - **hematologic crisis**
  - hypoplasia or aplasia of the bone marrow + peripheral pancytopenia (predisposition to infection, bleeding, and poor wound healing, all of which contribute to death)
- While most bone marrow progenitors are susceptible to cell death after sufficiently intense radiation doses, subpopulations of **stem cells** or accessory cells are selectively **more radioresistant**, (presumably because of their largely non-cycling (G_0) state)
  - play an important role in recovery of hematopoiesis after exposure to doses as high as 6 Gy, albeit with a reduced capacity for self-renewal
- Anemia is delayed due to long life-span of erythrocytes (~120 days)!
- Massive **stress reaction** (glucocorticoids release) partly contributes to lymphopenia (due to their cytolytic action) and paradoxically delayed granulocytopenia (due to release of additional granulocytes from spleen)



Embryo, foetus, germinative cells - summary

- Pregnancy - damage of the foetus *in utero*
  - <3 weeks (blastogenesis)
    - "all or nothing"
      - ☛ gene and chromosomal mutation usually lead to abort
  - 3 – 8th week (organogenesis)
    - growth retardation
    - teratogenic - congenital deformalities
      - ☛ microceohlay, microphtalmia, spina bifida, cleft palate, ...
  - 8 – 15th week (eraly foetal period)
    - mental retardation
    - cancer susceptibility in born children (leukemias)
  - later
    - rather resistant
- Sterility
  - spermatogenesis - temporary sterility in males
  - ovaries - much higher doses required to induce sterility in females
- Germinative mutations
  - inborn abnormalities

Psychological impact of radiation exposure

- Approx. 75% of individuals exposed to nuclear weapon detonations or industrial accidents (victims as well as participants in radiation cleanup) exhibit some form of psychological symptoms
  - inability to sleep, difficulty concentrating, social withdrawal
- In addition, exposed individuals and their families have a high rate of post-traumatic stress disorder
  - symptoms include anxiety disorders, depression, a recurrent sense of re-experiencing the traumatic event, outbursts of anger, an exaggerated startle response, and increased irritability
    - post-traumatic stress disorder can be diagnosed when these symptoms persist for more than 1 month

Medical management of ARS

- blood transfusions
- cytokine therapy
  - granulocyte macrophage colony-stimulating factor (GM-CSF)
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- bone marrow and stem-cell transplantation
- antibiotics and chemoterapeutics
- prevention of thyroid cancer
  - potassium iodide (reduction of radioiodine uptake when present) by saturating the thyroid gland with non-radioactive iodine