Radioactivity

Lecture 8

Biological Effects of Radiation

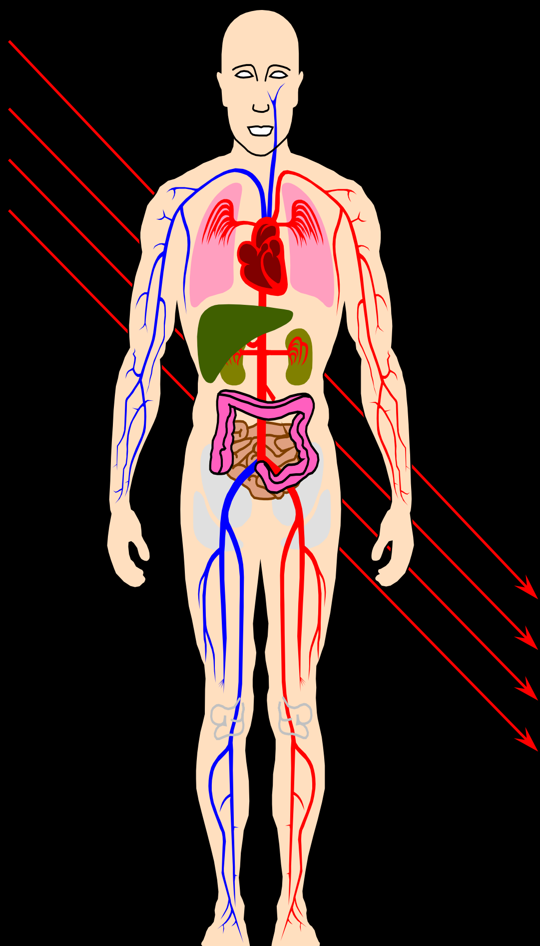
Studies of impact of ionizing radiation on the human body - Hiroshima -

US-Japanese teams medical tests, autopsies, human organ analysis, on-site radioactivity measurements ...

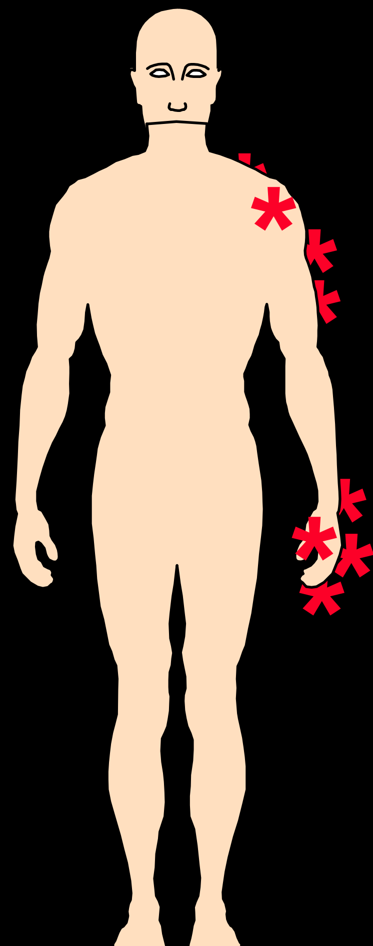
autopsy

Radiation Exposure Types

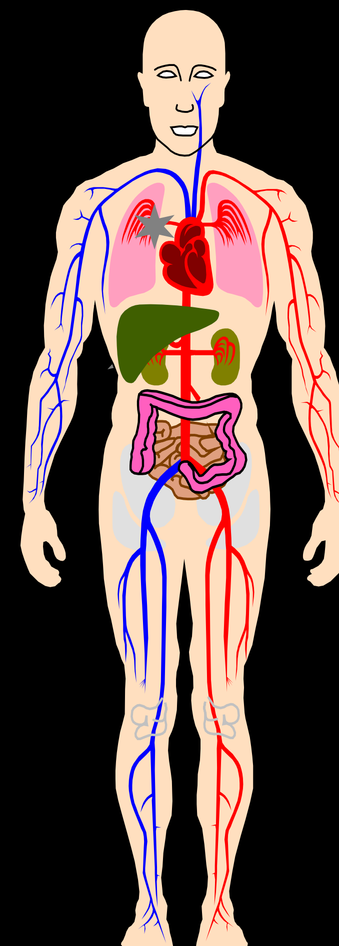
Irradiation



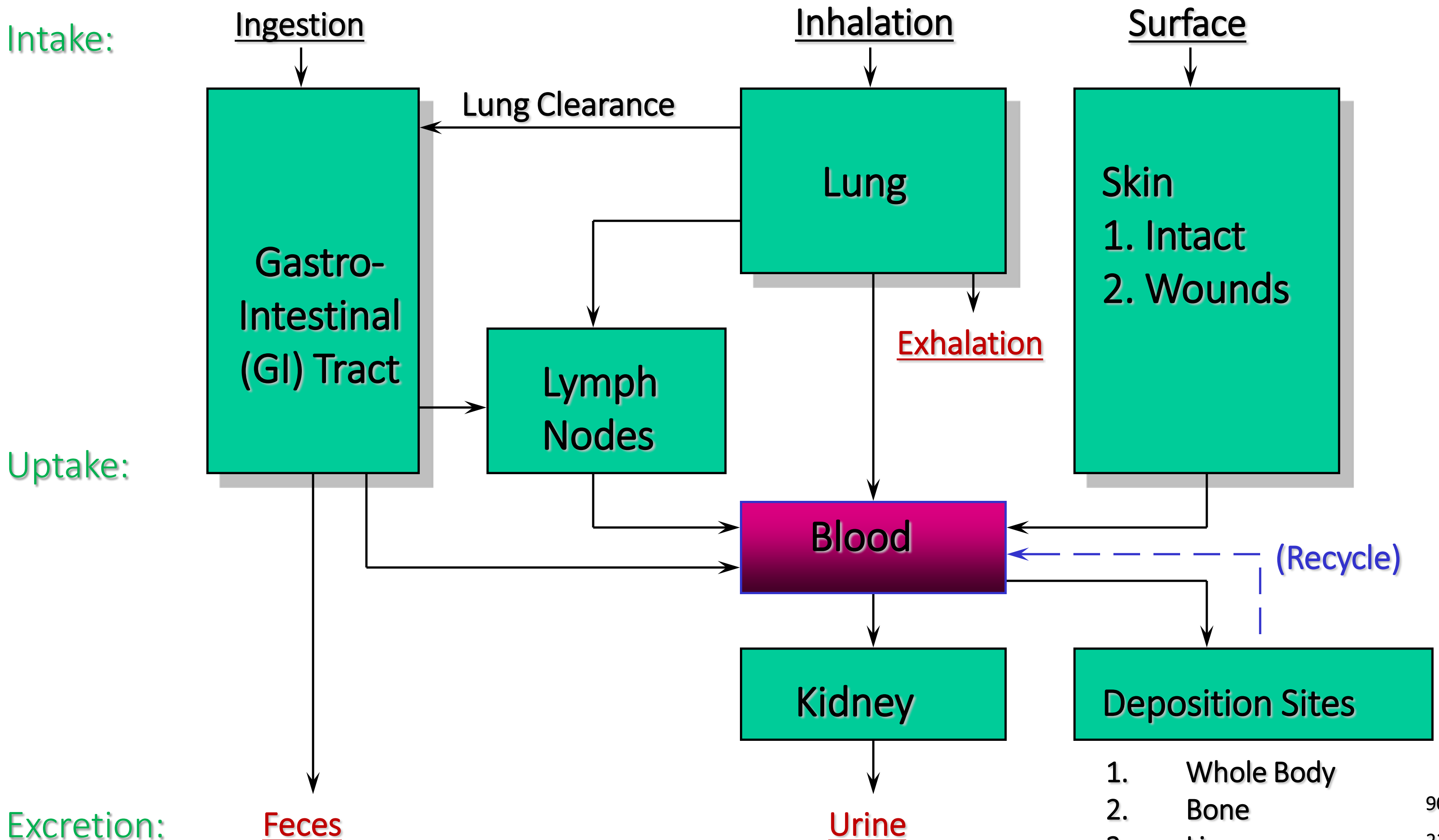
External Contamination



Internal Contamination



Schematic Model of Radionuclide Uptake

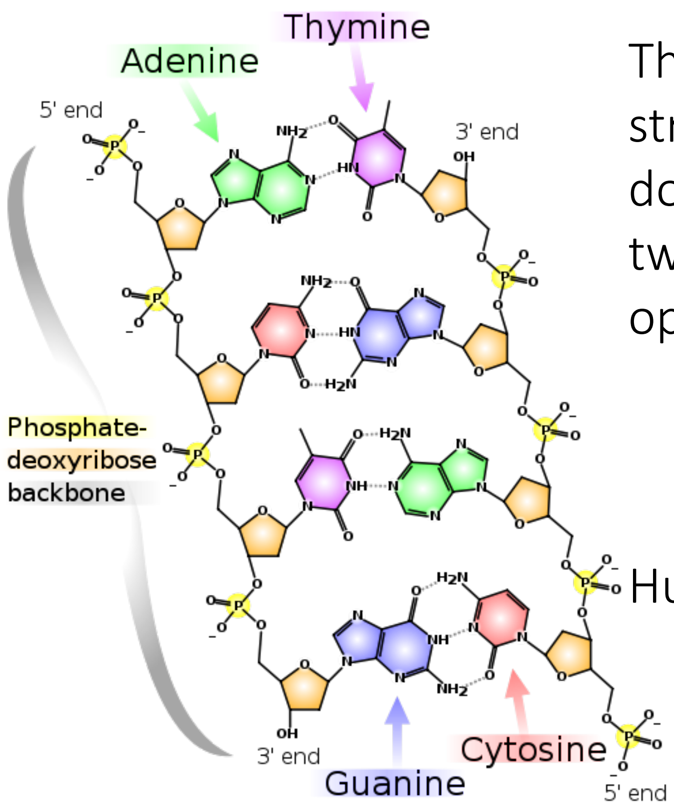


1. Whole Body
2. Bone ^{90}Sr
3. Liver ^{232}Th
4. Muscle ^{137}Cs
5. Thyroid ^{131}I

Deposition depends on chemical characteristics of isotopes

Basic DNA structure

Genetics is the science of heredity and variation in biological systems! It is based on the gradual change of the gene structure in the DNA Deoxyribonucleic acid, which contains the genetic code & instructions for the biological system in the sequence of the four A, S, G, T types of nucleotides

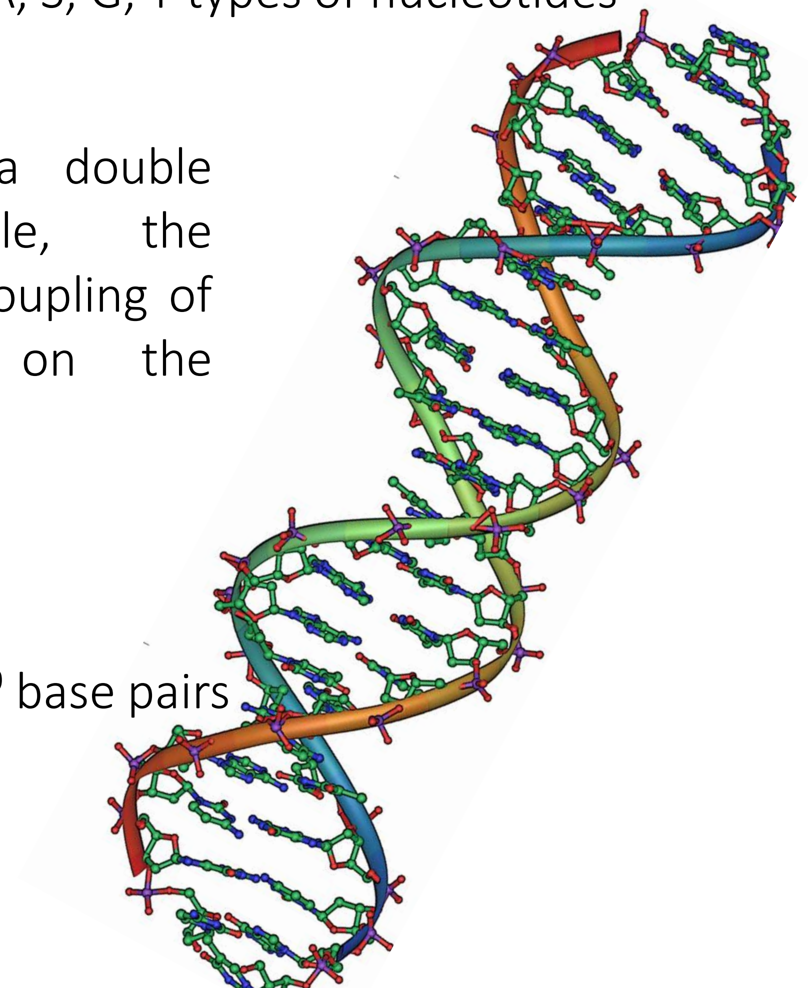


The DNA forms a double stranded molecule, the double helix. Pair coupling of two nucleotides on the opposite strand :

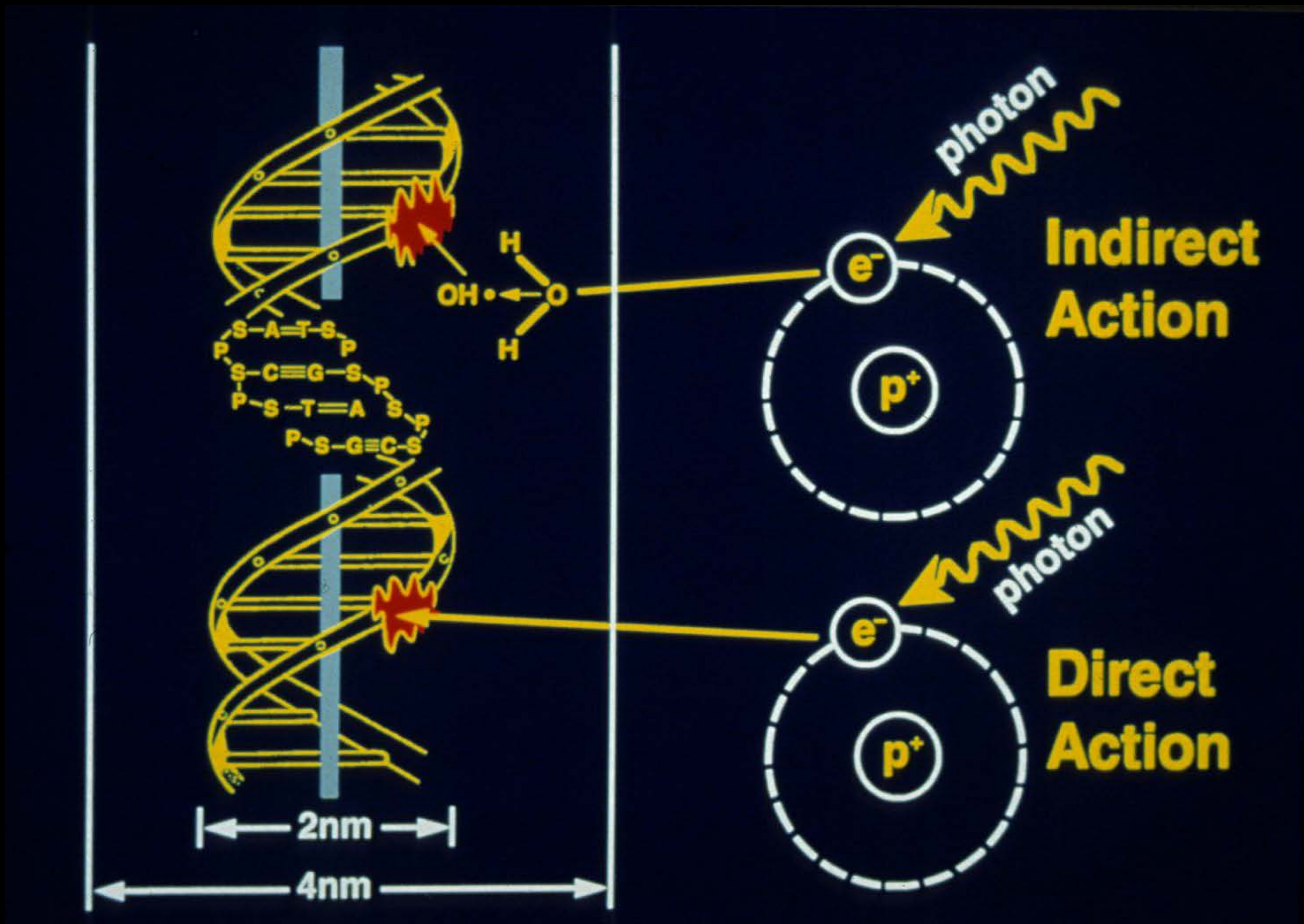
A with T,

G with C.

Humans have ~$3 \cdot 10^9$ base pairs

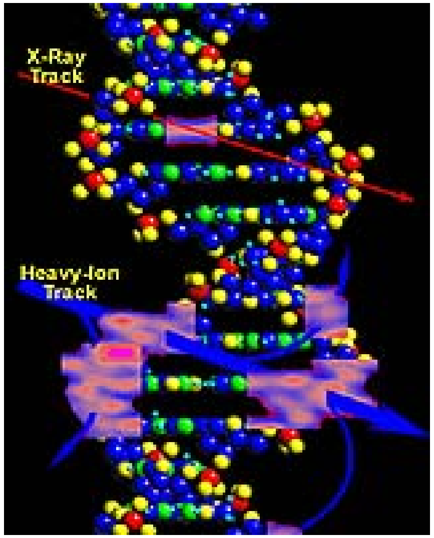


Radiation interacting with cell molecules



Sequence of Events in Indirect Action

$T_{1/2}$ in sec — Incident X-ray photons



$\downarrow$

10^{-15} — Fast electrons

$\downarrow$

10^{-5} — Ion radicals

$\downarrow$

10^{-5} — Free radicals

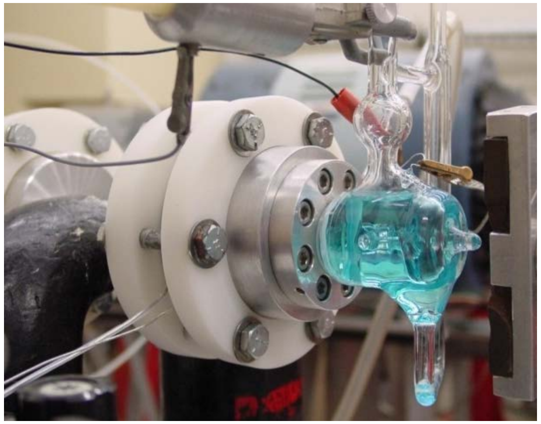
$\downarrow$

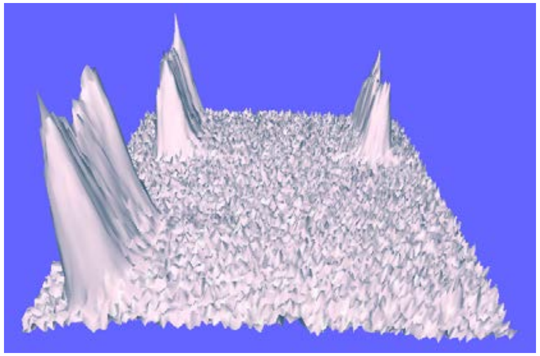
Macromolecular changes from breakage of chemical bonds

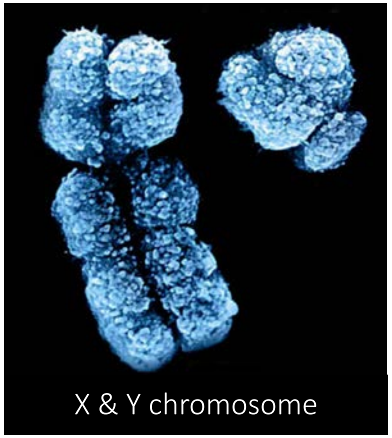
$\downarrow$

Possible biological effects

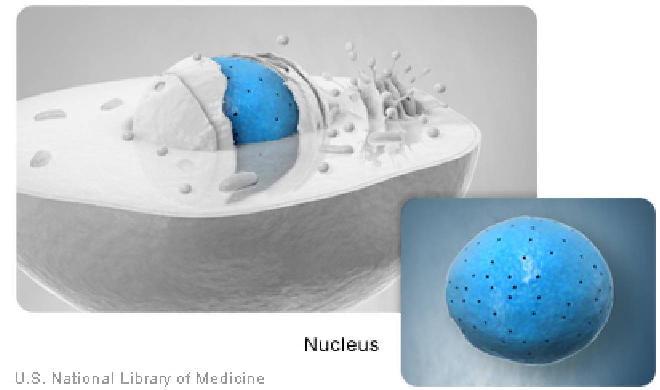
days	- cell killing
generation	- mutation
years	- carcinogenesis





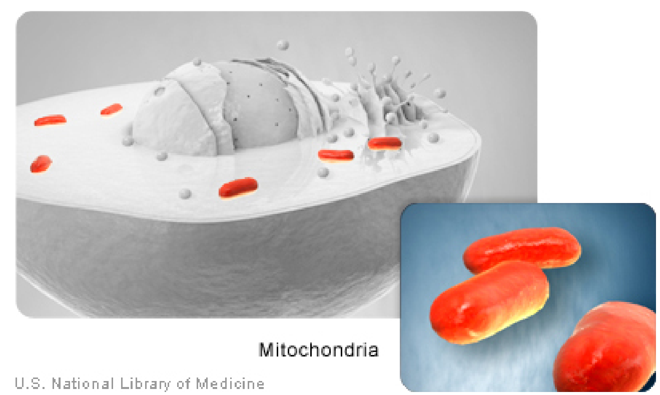


Three types of DNA ...

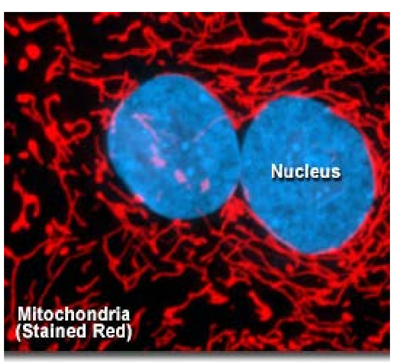


Nuclear DNA (blue print of body structure...)
inherited by cell division from parents

Y chromosome DNA (determines the male sex)
inherited from father to son
(male XY chromosome, female XX chromosome)



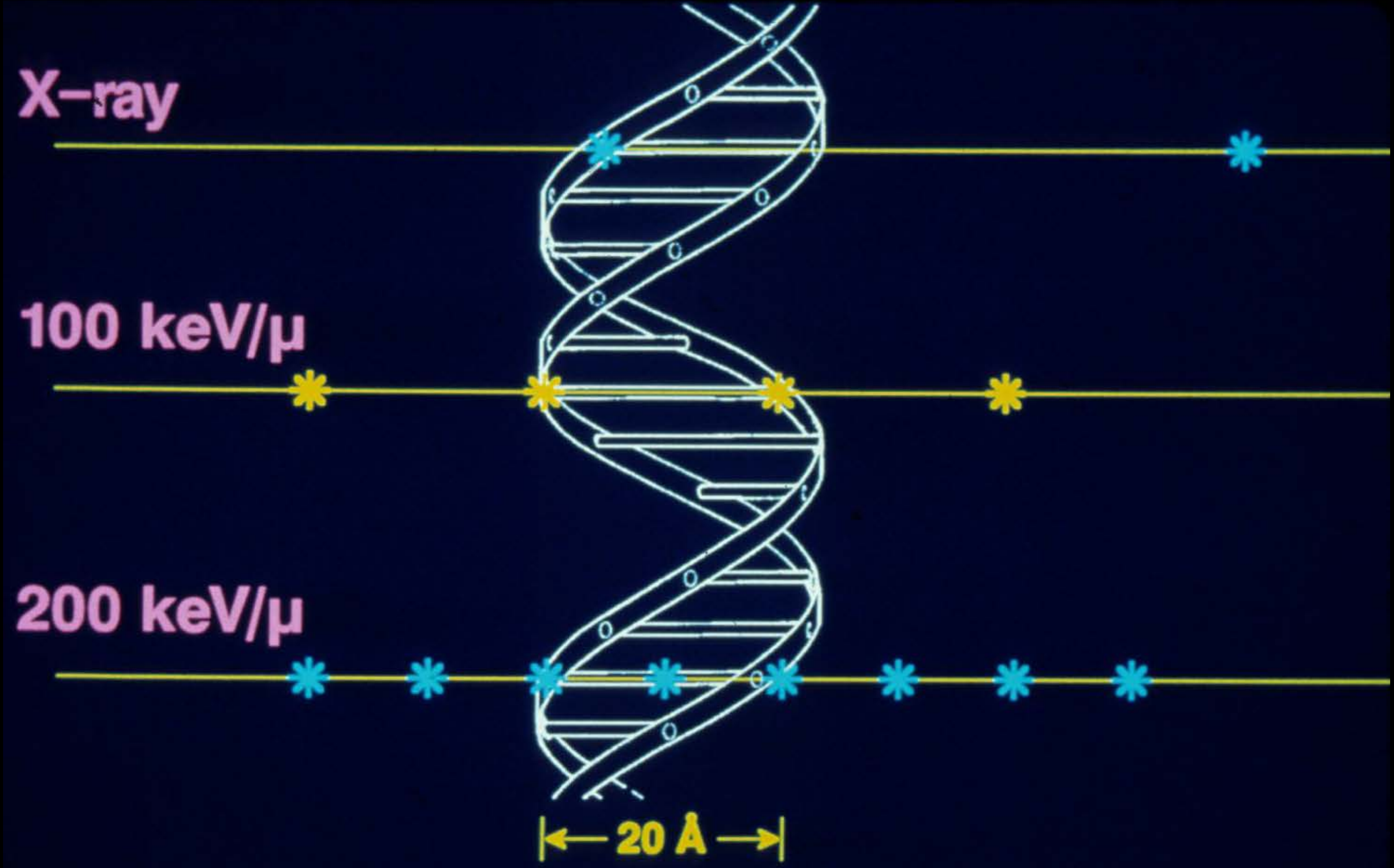
Mitochondrial DNA (outside the cell nucleus)
inherited from mother to children



Damage could cause cancer of body organ or impact genetic information for next generation,

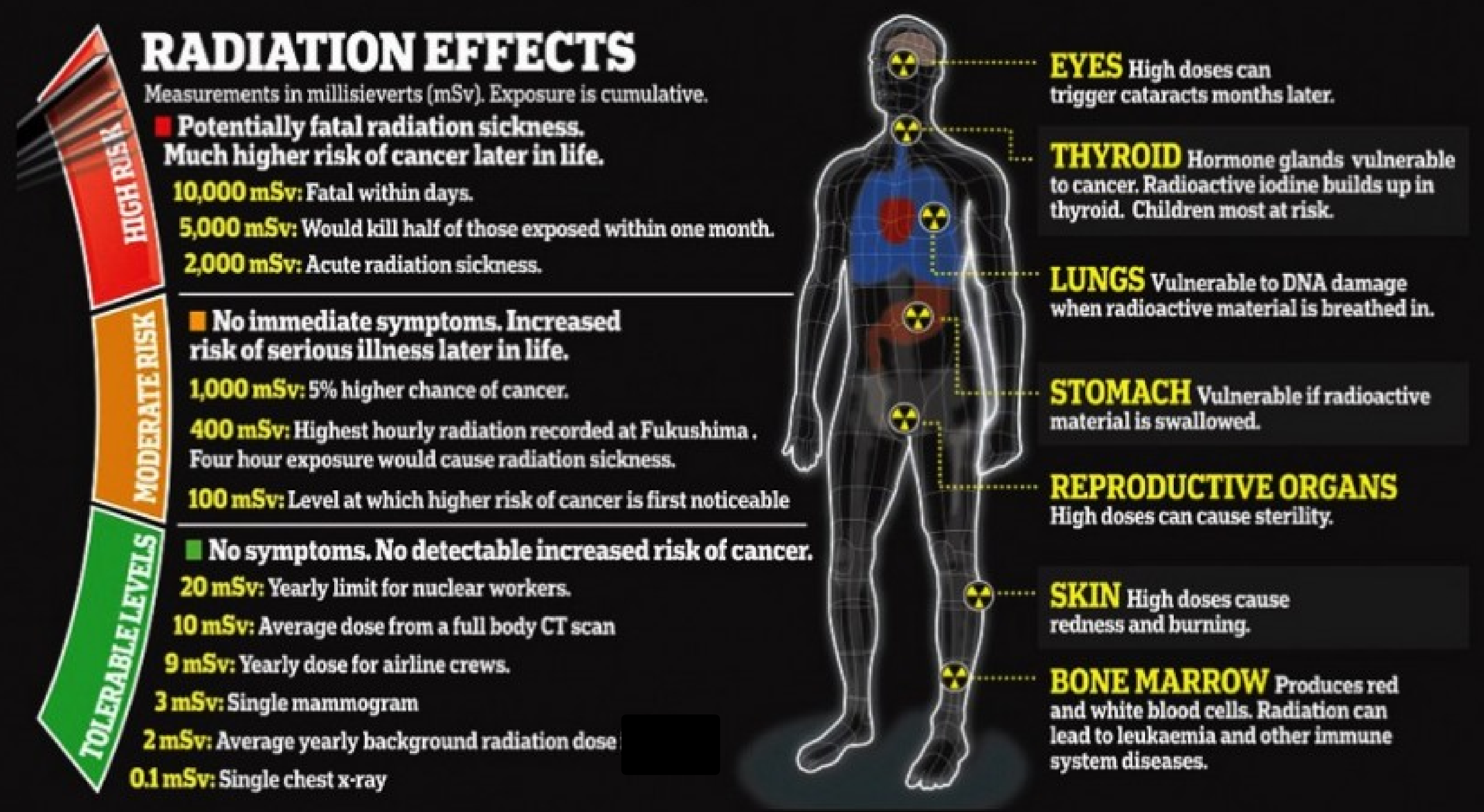
$\Rightarrow$ mutation!!!

Energy dependence of radiation damage



Linear energy transfer (LET): amount of energy deposited per unit track length

What are the high level radiation effects?



Acute Radiation Syndrome Recognition

- Signs and symptoms experienced by individuals exposed to acute whole body irradiation.
- Data collected largely through Japanese atomic bomb survivors at Hiroshima and Nagasaki.
- Limited number of accidents at nuclear installations.
- Clinical radiotherapy.
- Well-characterized animal data base.
- Lethal Dose is $\geq$ 8 Gy = 800 rad.
- LD_{50} dose of human is ~4.5 Gy = 450 rad.

Early Lethal Effects

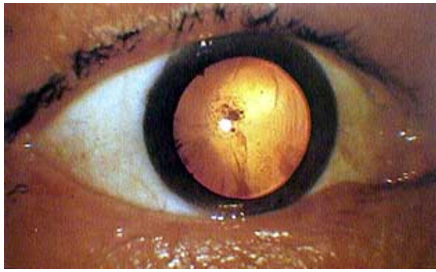
Hematopoietic **syndrome**:

- Hair loss (Epilation) and radiation sickness >2 Gy
- Purpura, or bleeding under the skin.
- Suppresses normal bone marrow and spleen functions.
- Lens opacity, blindness
- Symptoms associated with hematopoietic syndrome are: chill, fatigue, hemorrhages, ulceration, infection and anemia. Death at D>8 Gy unless receive bone marrow transplant.

Gastrointestinal **syndrome:**

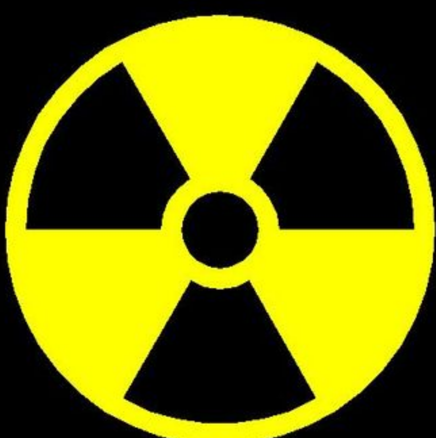
- Occurs at dose >10 Gy of gamma-rays or its equivalence.
- Death usually occurs within 3 to 10 days.
- Symptoms due largely to depopulation of the epithelial lining of the GI tract by radiation.
- No human has survived radiation dose >10 Gy.
- Clinical symptoms include nausea, vomiting, and prolong diarrhea, dehydration, loss of weight, complete exhaustion, and eventually death.

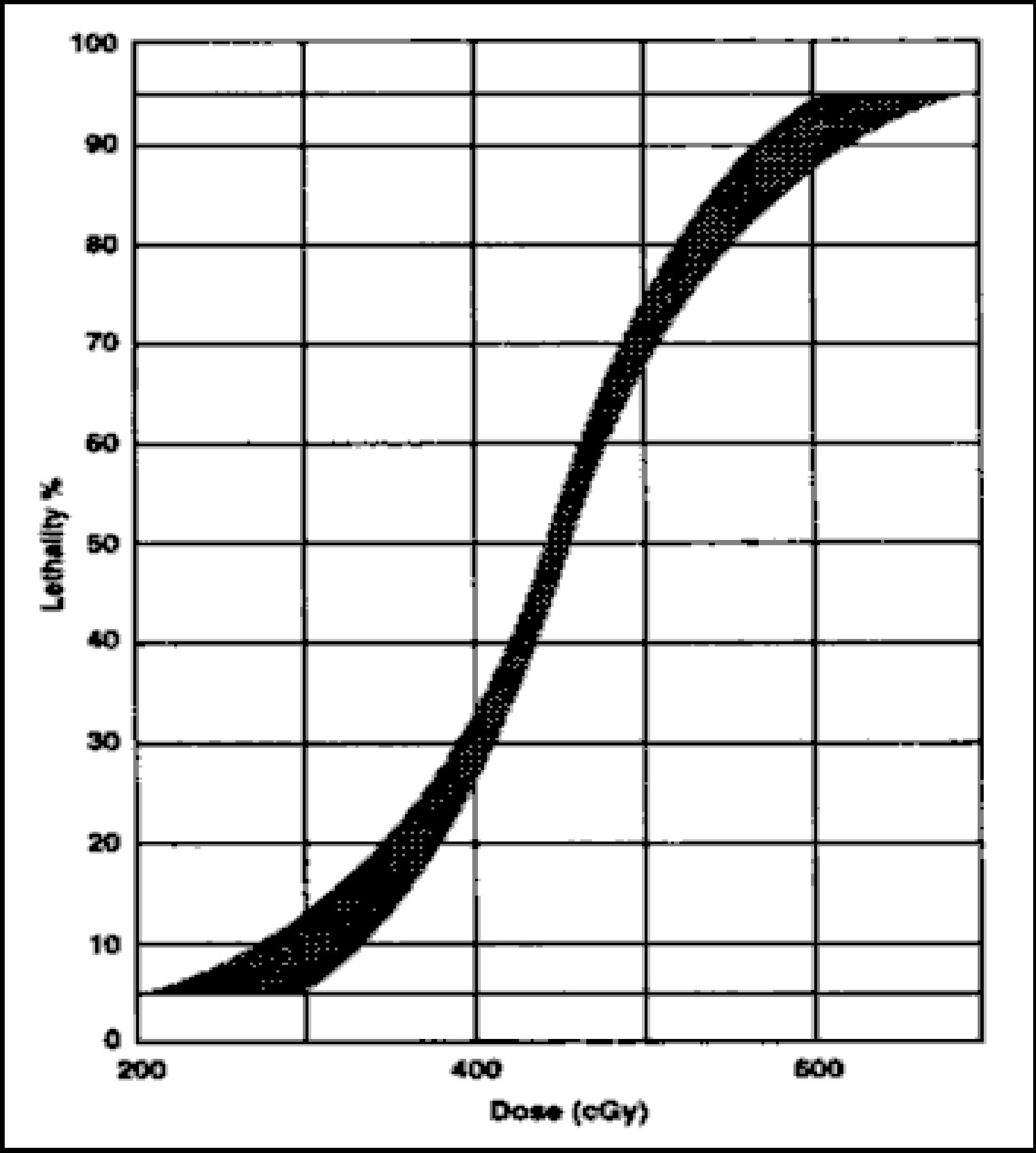





Human lethality as function of dose

A 50% lethality is reached with an accumulated dose of 450 cGy = 450 rad=4.5 Gy. A dose of 100 rad dose is survivable. A 800 rad dose is lethal.





Alexander Litvinenko

Litvinenko died on radiation poisoning by a small amount of ^{210}Po after 22 days. ^{210}Po is an alpha emitter that has a half-life of 138.4 days; it decays directly to its stable daughter isotope, ^{206}Pb. The alpha particles have an energy of 5.307 MeV. Calculate the minimum amount of ^{210}Po Litvinenko must have eaten.

(1 MeV = $1.6 \cdot 10^{-13}$ Joule)
(1 Gy=1 J/kg)

$$A = \lambda \cdot N = \frac{\ln 2}{T_{1/2}} \cdot N = 5 \cdot 10^{-3} \cdot N \left[d^{-1}\right]$$

$$210\, g = 6.022 \cdot 10^{23}\ particles \qquad N = m[g] \cdot 2.87 \cdot 10^{21}\ particles$$

$$D = \frac{E}{m} \cdot A \cdot t = \frac{5.307 MeV}{80 kg} \cdot A \cdot t = \frac{4.25 \cdot 10^{-15}\ J}{80 kg} \cdot N \cdot t \qquad t = 22d$$

$$D = 1.17 \cdot 10^{-15} Gy \cdot N = 3.35 \cdot 10^{6} \cdot m[g] Gy$$

$$m[g] = \frac{8\ Gy}{3.35 \cdot 10^{6}} = 2.4 \cdot 10^{-6} g \qquad A = 3.43 \cdot 10^{13}\ d^{-1} = 4 \cdot 10^{9}\ s^{-1} = 4 \cdot 10^{9} Bq$$

Yasser Arafat

Measurements suggest small amounts of about 2 pico-gram (1 pg = 10^{-12}g) of ^{210}Po in the body of Yasser Arafat. Our natural amount of ^{210}Po corresponds to 60 Bq. By how much did Yasser Arafat exceed this limit?

$$N = \frac{2\cdot 10^{-12}}{60}\cdot 6.022\cdot 10^{23} = 2\cdot 10^{10}\quad {}^{210}Po\ atoms$$

$$A = \lambda\cdot N = \frac{\ln 2}{T_{1/2}}\cdot N = \frac{0.69}{138.4\cdot 24\cdot 3600}\cdot 2\cdot 10^{10}\ s^{-1}$$

$$A \approx 1170 Bq \quad D = 5.3\cdot 10^{-17} Gy\cdot A\cdot t = 6.2\cdot 10^{-14}\cdot t$$

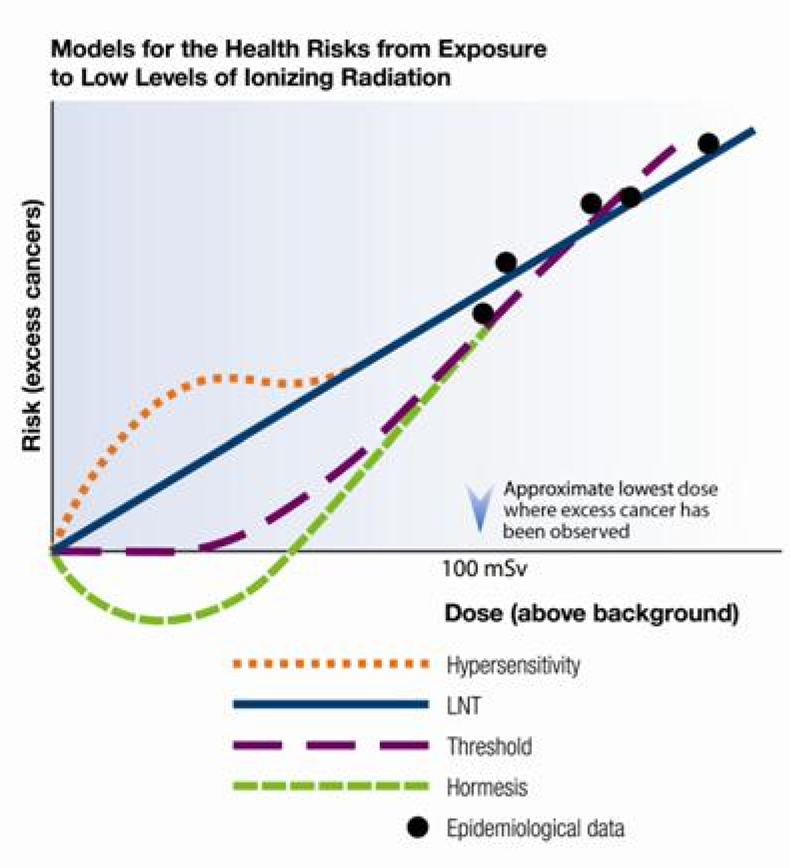
$$t = 2y = 6.3\cdot 10^{7} s \qquad D \approx 4\mu Gy$$

About a factor of 20 higher than the natural ^{210}Po activity of the human body! High uncertainties in these data because of the two year time period between death and exhumation. The detected amount is only 3% of the original ^{210}Po amount.

Improving forensic investigation for polonium poisoning.
Froidevaux P., et al. Lancet. 2013 Oct 12;382(9900):1308.

$$\frac{N}{N_0} = e^{-\lambda t} = e^{-\frac{\ln 2}{138.4}\cdot 712} = 0.03$$

What are the low level radiation effects?



LNT Definition

- The LINEAR NO-THRESHOLD MODEL (LNT) is a model used in radiation protection to estimate the long-term, biological damage caused by ionizing radiation
- It assumed that the damage is directly proportional ("linear") to the dose of radiation, at all dose levels
- Radiation is always considered harmful with no safety threshold

Fierce arguments due to lack of data and statistical interpretation!

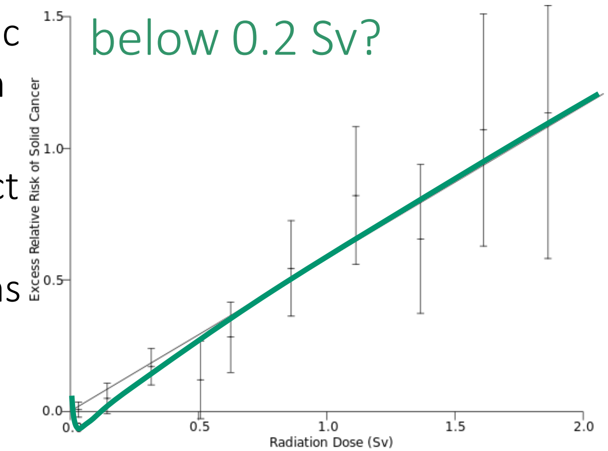
Pro: BEIR and UNSCEAR

Against: medical and radiological experts

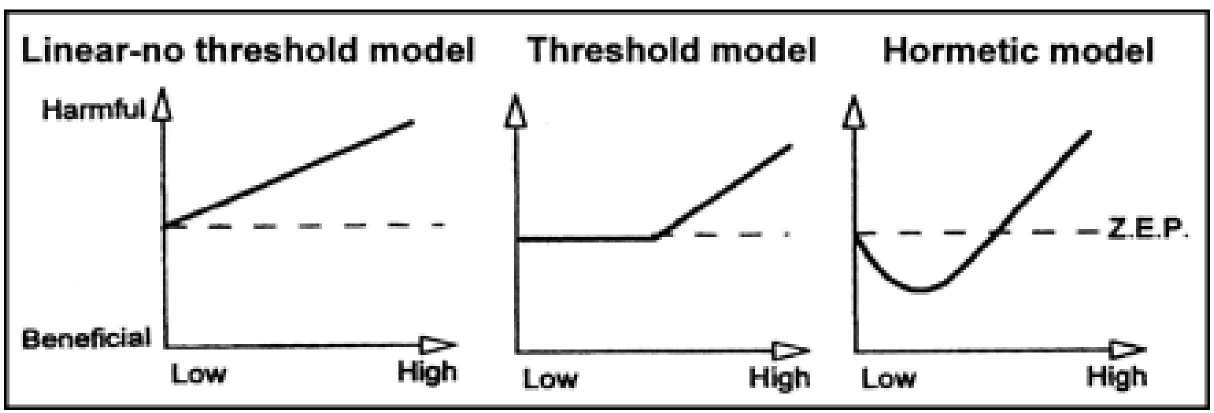
Hormesis or Linear No Threshold model

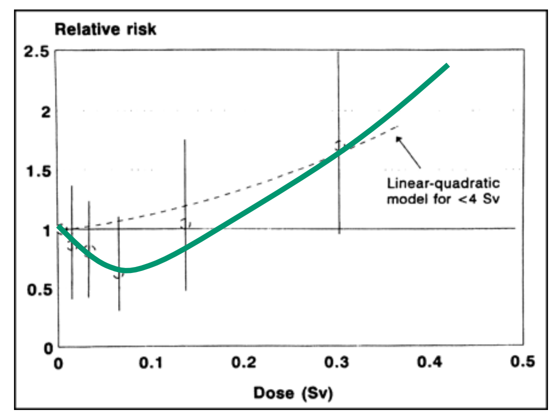
The LNT model is the recommended model for extrapolating cancer probability form known high dose exposures to unknown low-dose regions of exposure. It is the recommended approach by the Atomic Energy Commission. This approach is questioned by some radiation experts who claim that low level radiation may have beneficial effects, stimulating the activation of repair mechanisms that protect against disease. This phenomenon is observed for many poisonous substances. A number of compensatory and reparatory mechanisms are activated in response to the damage caused by ionizing radiation. These include up-regulation of antioxidant responses, scavenging of damaged cells that may undergo tumorigenesis, activation of enzymatic DNA repair mechanisms, and activation of the immune system to help recognize and transform mutated cells.

Possible hormesis effect below 0.2 Sv?



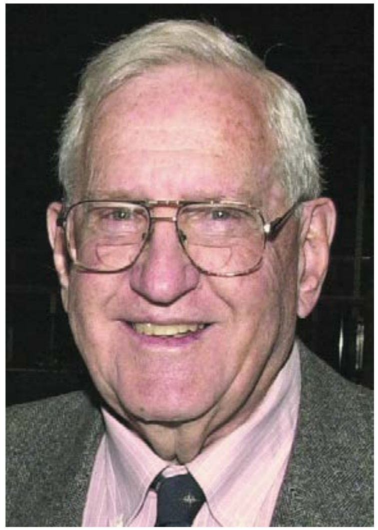
Increased risk of solid cancer as function of dose in atomic bomb survivors.





Incidence of leukemia as function of dose in atomic bomb survivors in Japan.

Hormesis defenders

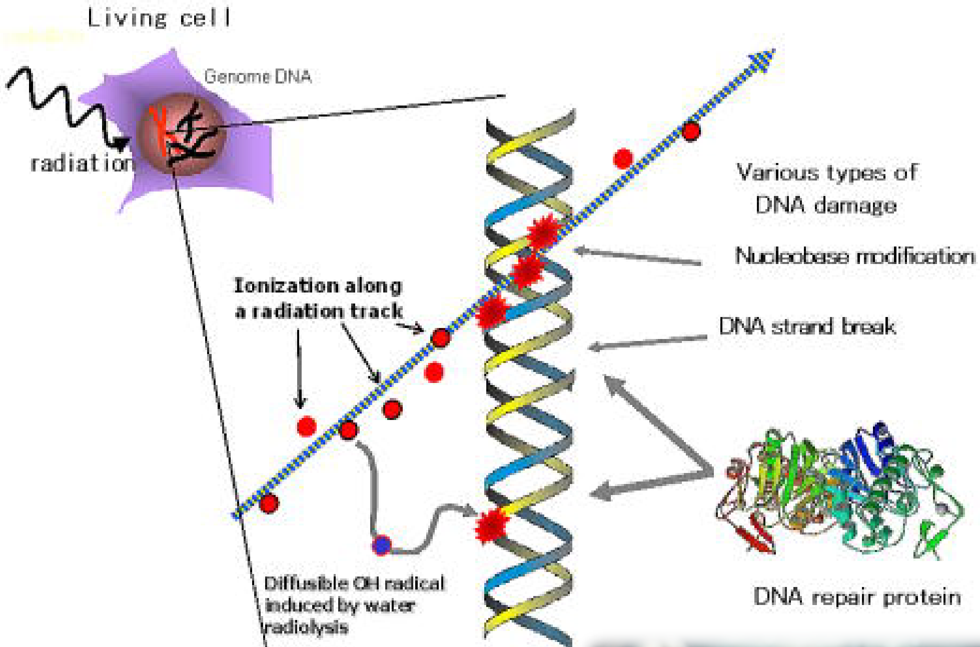
Harold Agnew (1921-2013)


Edward Teller (1908-2003)

Miskolc Tapolca, Hungary

Bad Gastein, Germany

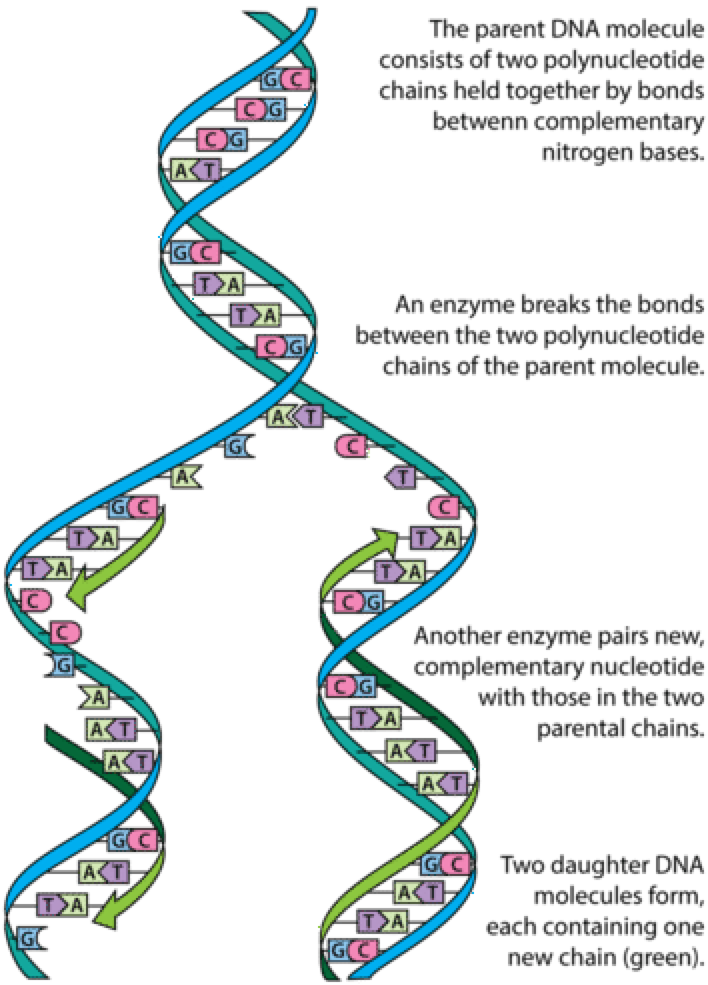
Enzymatic Repair Mechanisms



The capability of repair depends on the kind of radiation, the extent of damage , the capability of enzymes to identify and chemically neutralize aggressive radicals (OH^-). Also important is the cycle time for cell division. In fast cycles less time for repair. Fast cycling blood cells are more prone to radiation damage, but fast growing cancer cells are more vulnerable to radiation bombardment.

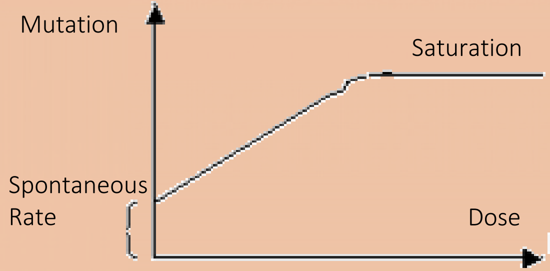
The repair mechanism by enzymes is based on copying the damaged sequence from the identical sequence in the second helix strand. In case of larger damage, whole sections are newly synthesized, based on secondary information carriers. If those are not around, the repair is made on enzyme guesswork. This can cause changes in information work, causing mutation. Unfavorable mutations are naturally eliminated. Favorable ones lead to evolution!

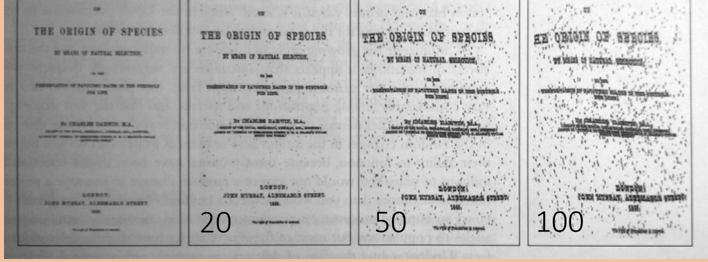
DNA Division and Copying



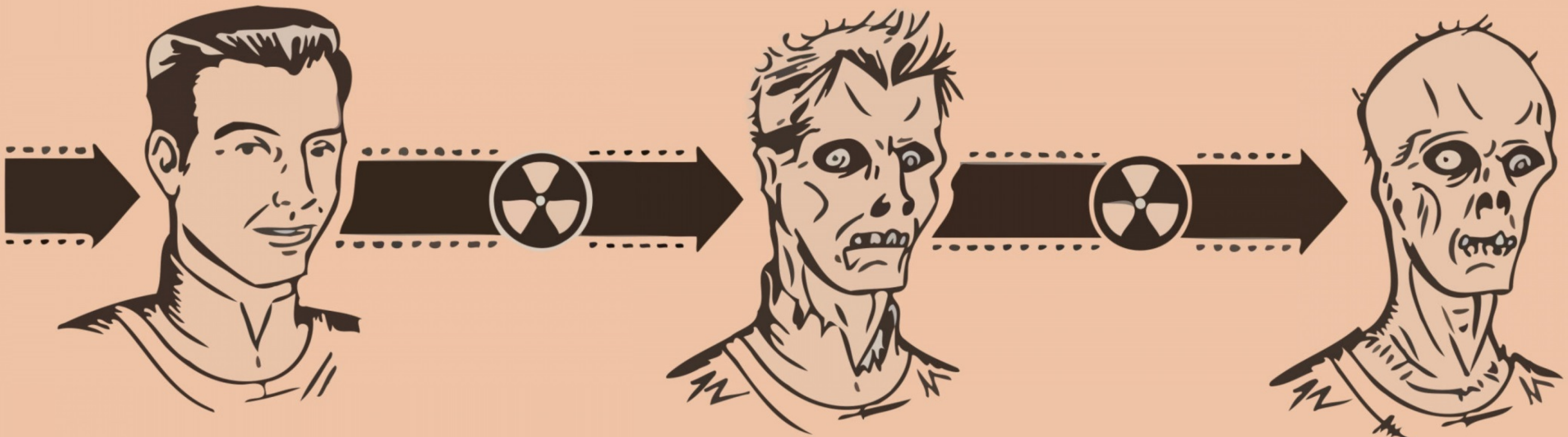
DNA divisions happen continually with cell divisions. Each of the new cells must contain identical DNA structure and information. The DNA division produces replica of the original DNA molecule using each of the strands as a template! The frequency of the cell division depends on cell. Blood cells have high replication rates, so have cancer cells! Changes in DNA information happens during the division causing a mutation of the cell information. This mutation can be spontaneous or induced depending on the cause for the error in replication!

Mutation





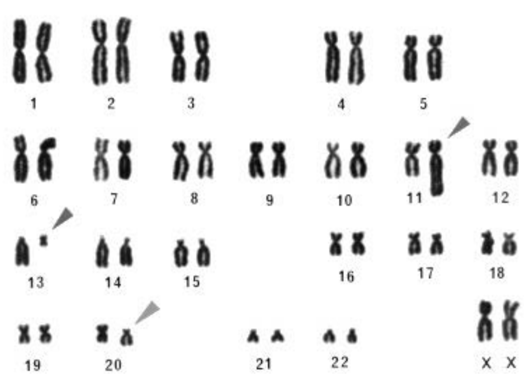
A mutation is any alteration of a genome. It includes substitutions, insertions, and deletions causing a change in the information transfer during cell division. There are 23 pairs of chromosomes in the human genome. There are a total of six billion places where a mutation can happen.

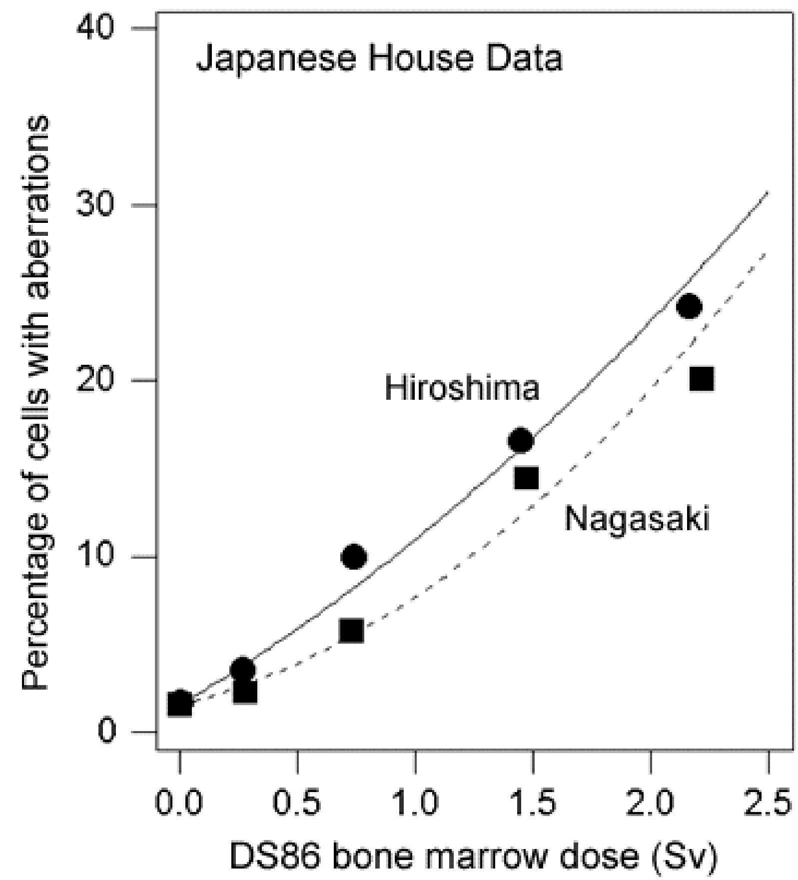


Natural mutation rate is characterized as balance between spontaneous mutation and natural selection and is about $2 \cdot 10^{-10}$ Mutationen per generation and base. With $3 \cdot 10^{9}$ bases per genom one anticipates ~5 mutations per genom and generation. With about 400 cell divisions generations for an adult male we get 2000 mutations. The natural mutation rate is spontaneous, while a radiation induced mutation is deterministic and increases linearly towards higher doses. **But how is the dose dependence at low dose?**

Long range genetic effects

Chromosomes observed during cell division. Abnormal ones are marked by grey arrow.

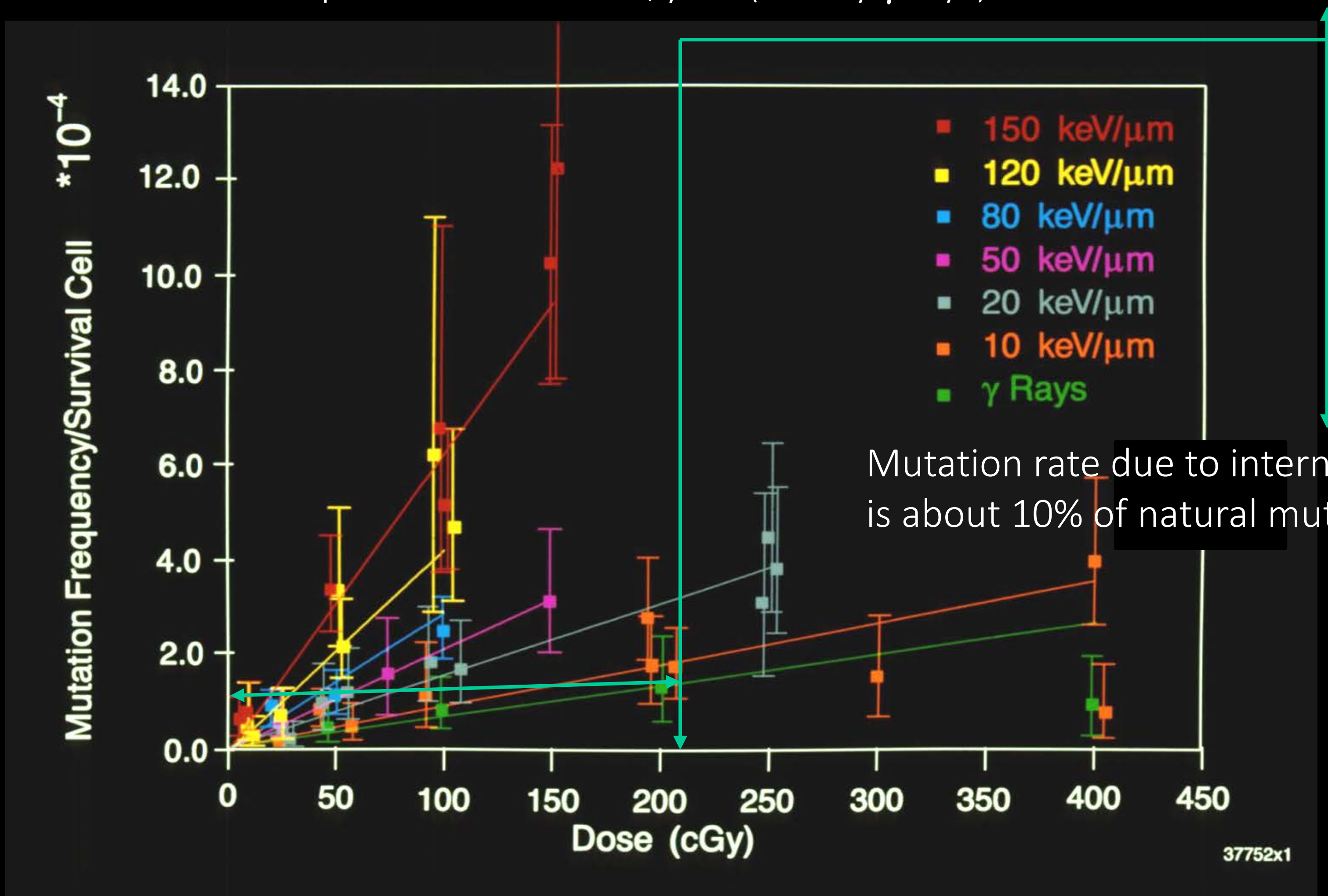




Observed increase with dose indicates long term genetic effects

Is there a natural threshold, e.g. where random mutation mechanisms are exceeded by radiation induced mutation?

Internal radiation exposure is at 30 mSv/year (mainly γ rays). Life time dose is 2.1 Sv (Gy)



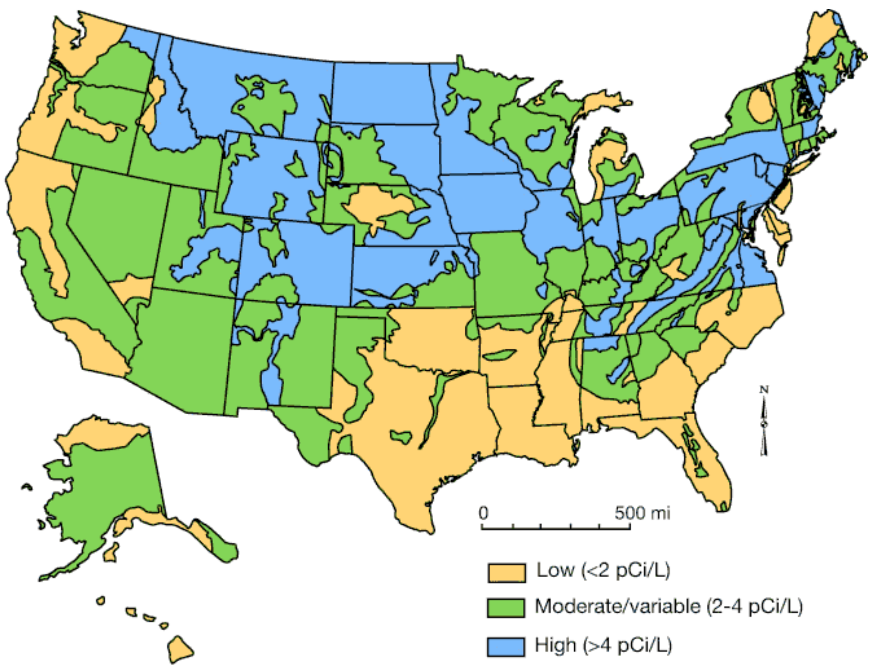
Mutation rate due to internal radiation is about 10% of natural mutation rate!

Radiation-induced Mutagenesis

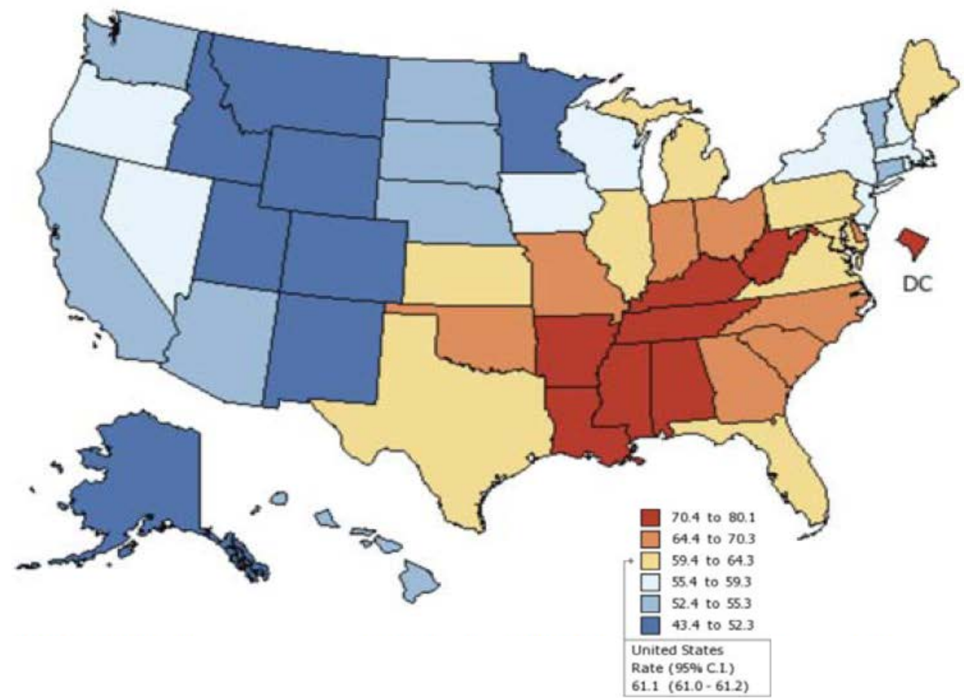
- Radiation *DOES NOT* produce new, unique mutations, but increases the incidence of the same mutations that occur spontaneously.
- Mutation incidence in humans is *DOSE* and *DOSE-RATE* dependent.
- A dose of 1 rem (10 mSv) per generation increases background mutation rate by 1%.
- Information on the genetic effects of radiation comes almost entirely from animal and *IN VITRO* studies.
- Children of A-bomb survivors from Hiroshima and Nagasaki fail to show any significant genetic effects of radiation.
- Other radiation exposed workers (miners, air personnel, radiation workers) also don’t show any statistical significant radiation induced health effects (cancer rate).

Epidemiological studies on large population groups

Impact of Radon level on cancer



Distribution of radon emission in the US (http://www.kgs.ku.edu/Publications/PIC/pic25.html).



Cancer rate in US per 100,000 people according to National Cancer Institute (http://statecancerprofiles.cancer.gov/)

Not a particular convincing correlation, despite corrections for smoker effect.

Cancer risk of Uranium miners

Working Level Month (WLM) reflects the monthly dose for miners due to exposure to radioactive materials. It corresponds to 5 mSv for 2000 working hours underground.

58987 miners recorded from 1946-1990. By 2003 36% had died (20920):

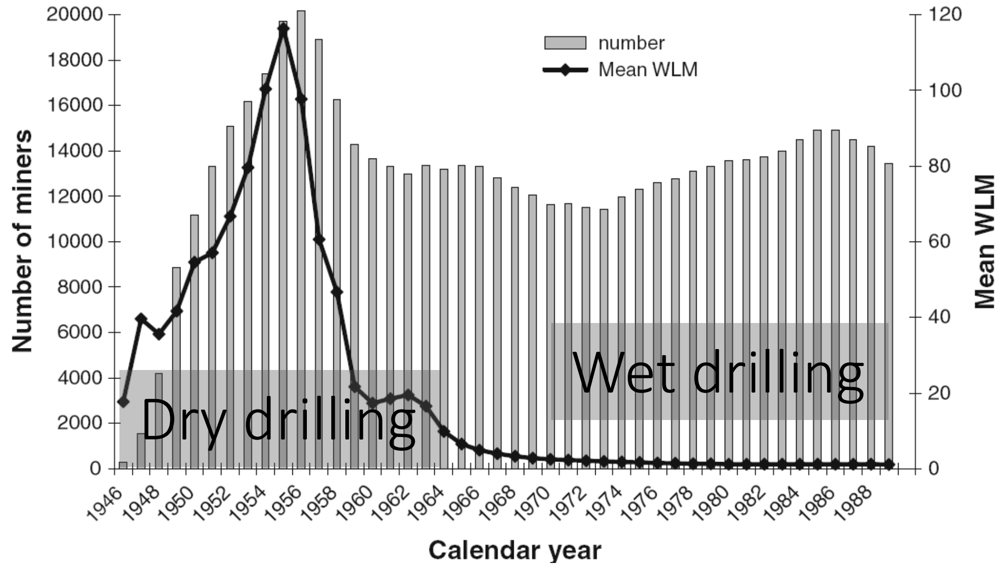
3016 lung cancer,

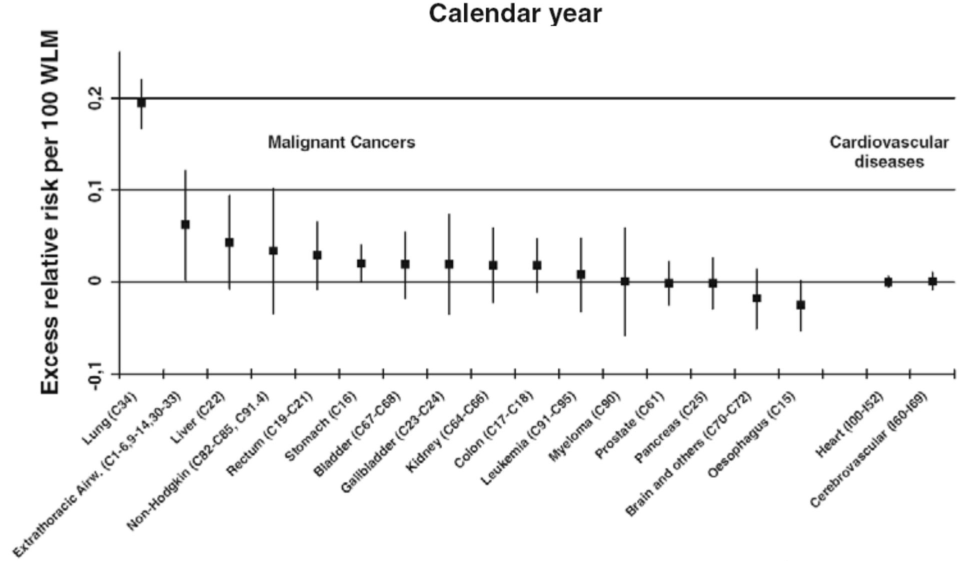
3355 other cancer,

5141 heart problems

1742 stroke.

In comparison with death cause distribution in normal population a risk assessment was made.





The excess relative risk per 100 WLM for miners

Stay away from intense radiation sources