

# Health Effects of Ionizing Radiation

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# Health effects of radiation

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- Ionization radiation is known to produce significant health effects, including cancer and non-cancer diseases and even death, depending on the dose and dose rate.
- The cancer incidence and mortality data are mainly derived from the Japanese atomic bomb survivors in Life Span Study cohort; others include personal exposure occupationally, therapeutically or diagnostically.

# Epidemiological Studies on health effects

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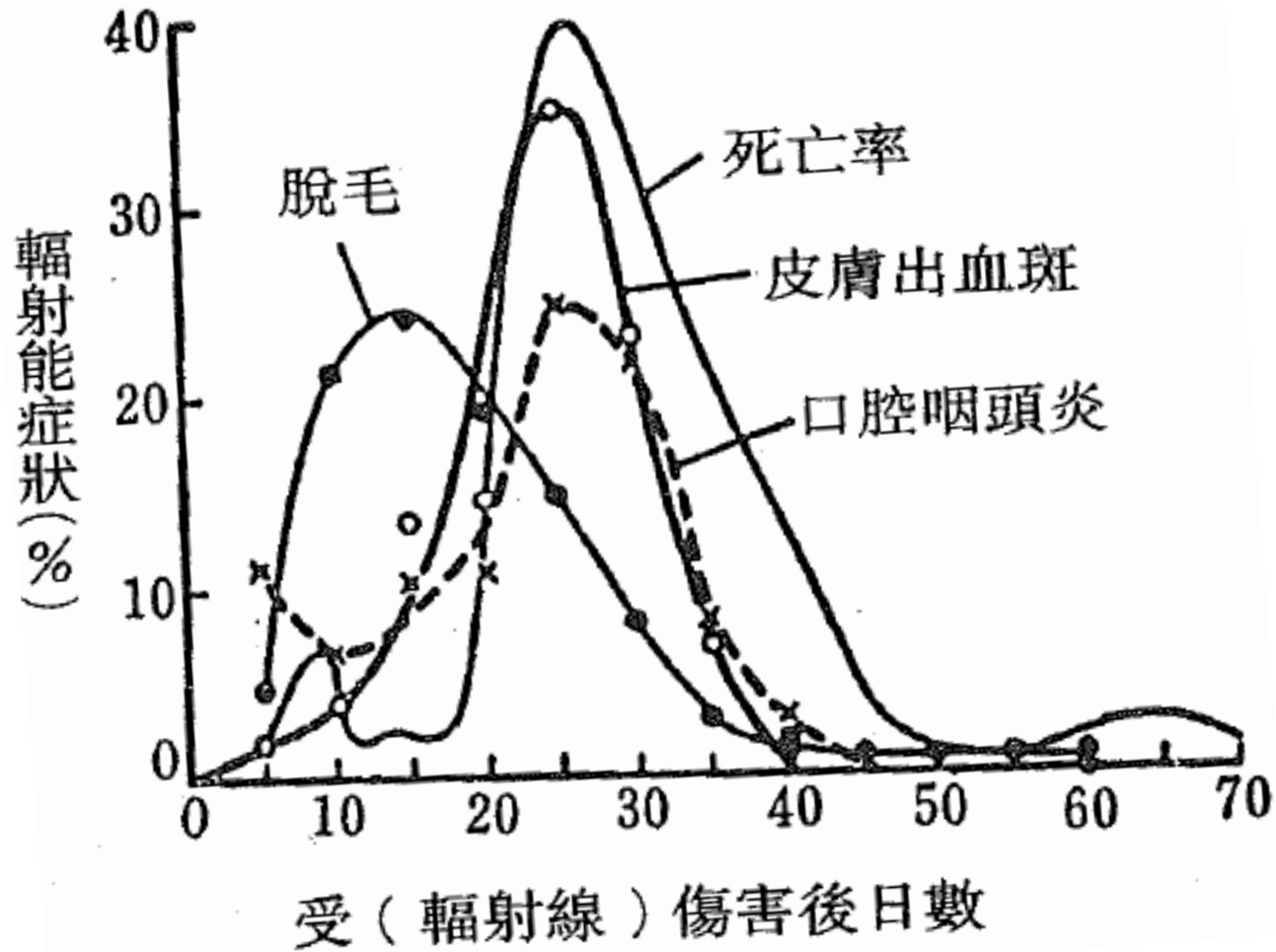
- Extensive epidemiological studies by UN Scientific Committee on Effects of Atomic Radiation and US National Academy of Sciences and various radiobiological studies in the last 15 years or so have improved our understanding of the health effects; excess lifetime risks from cancer and non-cancer risks, i.e. risks over unexposed in a lifetime, determined and reported, e.g. UNSCEAR 2006, 2000, BEIR VII 2006
- According to UNSCEAR Report 2006, excess lifetime risk from all solid cancers of all ages following an acute dose of 1 Sv is estimated to be about 4.3-7.2 % and for leukemia is 0.6-1.0%, depending on the population and the model used.

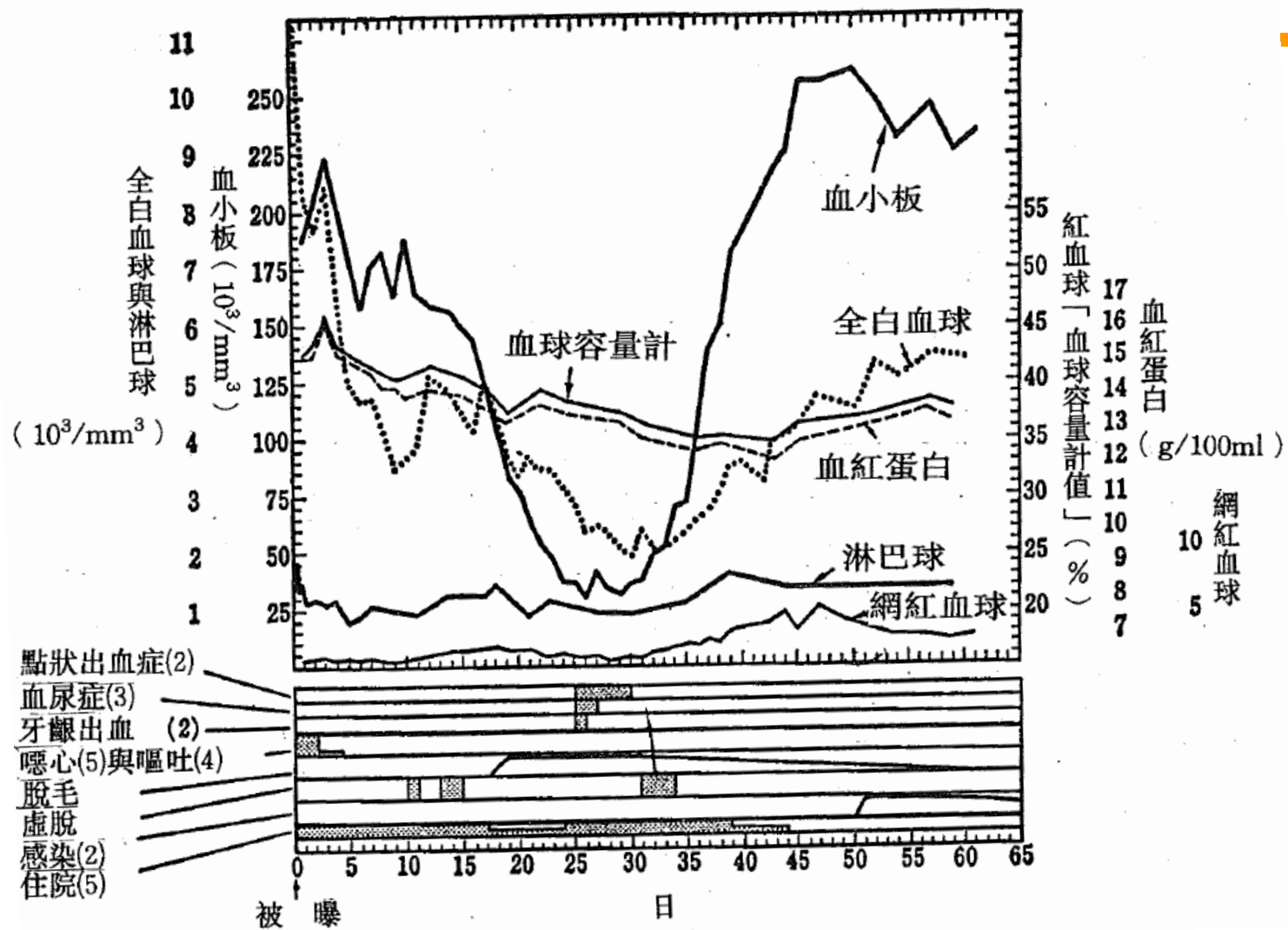
# Sources of Human Data on Health Risk

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- Life Span Study (LSS) cohort of survivors of the A-bombs at Hiroshima and Nagasaki in Japan, involving about 120,000 persons identified in the 1950 census and a core group of survivors within 2 km of ground zero and those non-exposed individuals
- Populations exposed to therapeutic and diagnostic radiation
- Radium-dial painters, involving about 1,000 ind.
- Uranium miners, involving over 60,000 ind.
- Accidents, e.g. Chernobyl power reactor in Ukraine, fallout from BRAVO nuclear weapon test
- Others

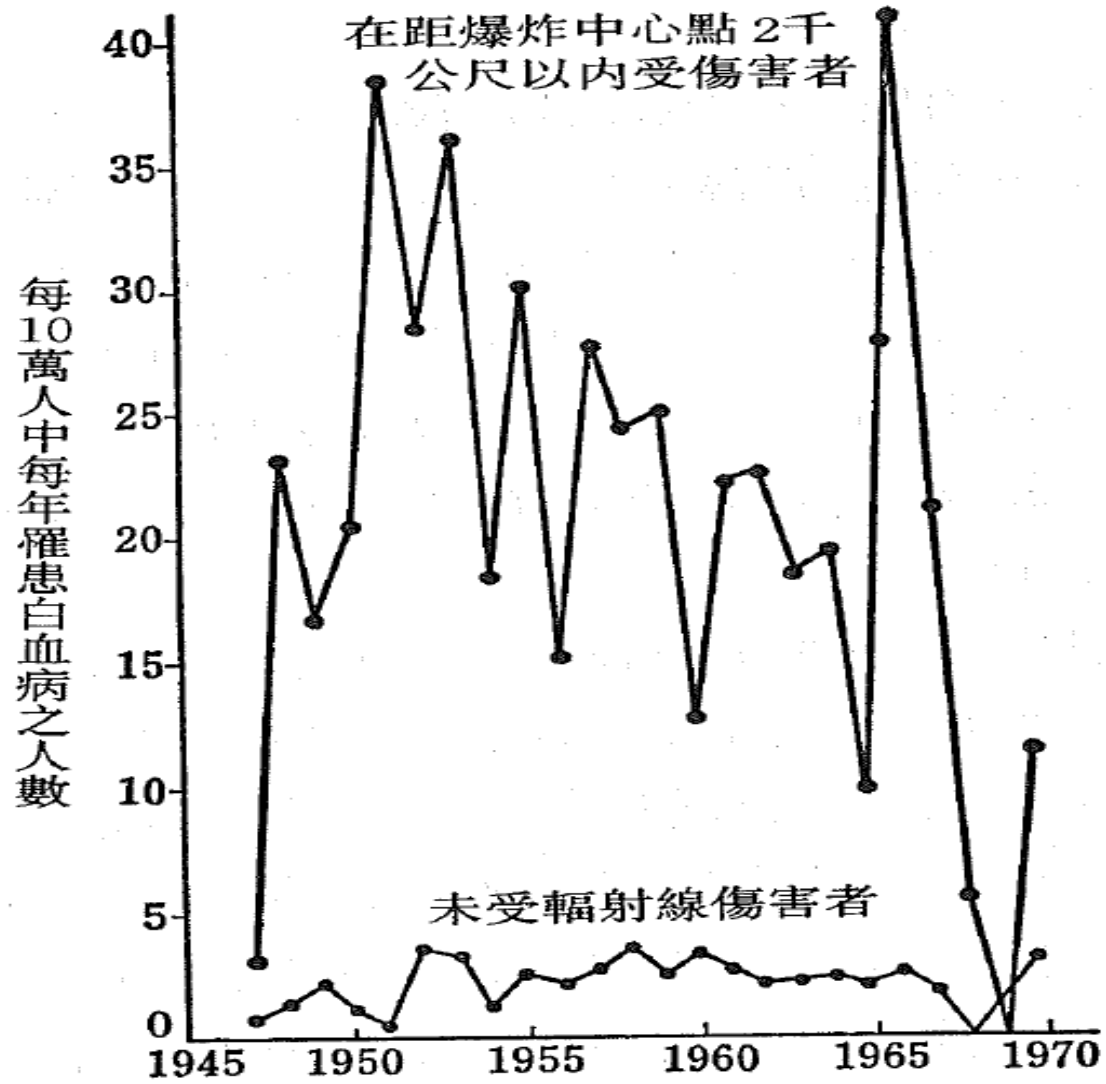
# Incidence of various radiation induced symptoms in A-bomb survivors





**Incidence of various diseases after the accident causing whole-body exposure to radiation at Uranium refinery factory in Tennessee, USA (small sample size)**

## Incidence of Leukemia in A-bomb survivors



# Effects of High Level Ionizing Radiation

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- Single, large short-term, whole body dose of radiation can cause a number of vital tissues and organ to fail simultaneously.
- Syndrome is characterized by 4 sequential stages:
  - Initial stage, lasting until 48 hrs after exposure: tired and nauseous with loss of appetite and sweating
  - Latent stage, lasting from 48 hrs to 2~3 weeks after exposure, feeling of well-being
  - Manifest illness stage: lasting until 6~8 wks after exposure, symptoms develop, e.g. hemorrhaging (内出血) and infection, loss of hair, gastrointestinal symptoms, fever, lethargy (昏睡), etc.
  - Recovery stage (if individual survives), lasting for several additional weeks or months

# Symptoms of acute radiation exposure

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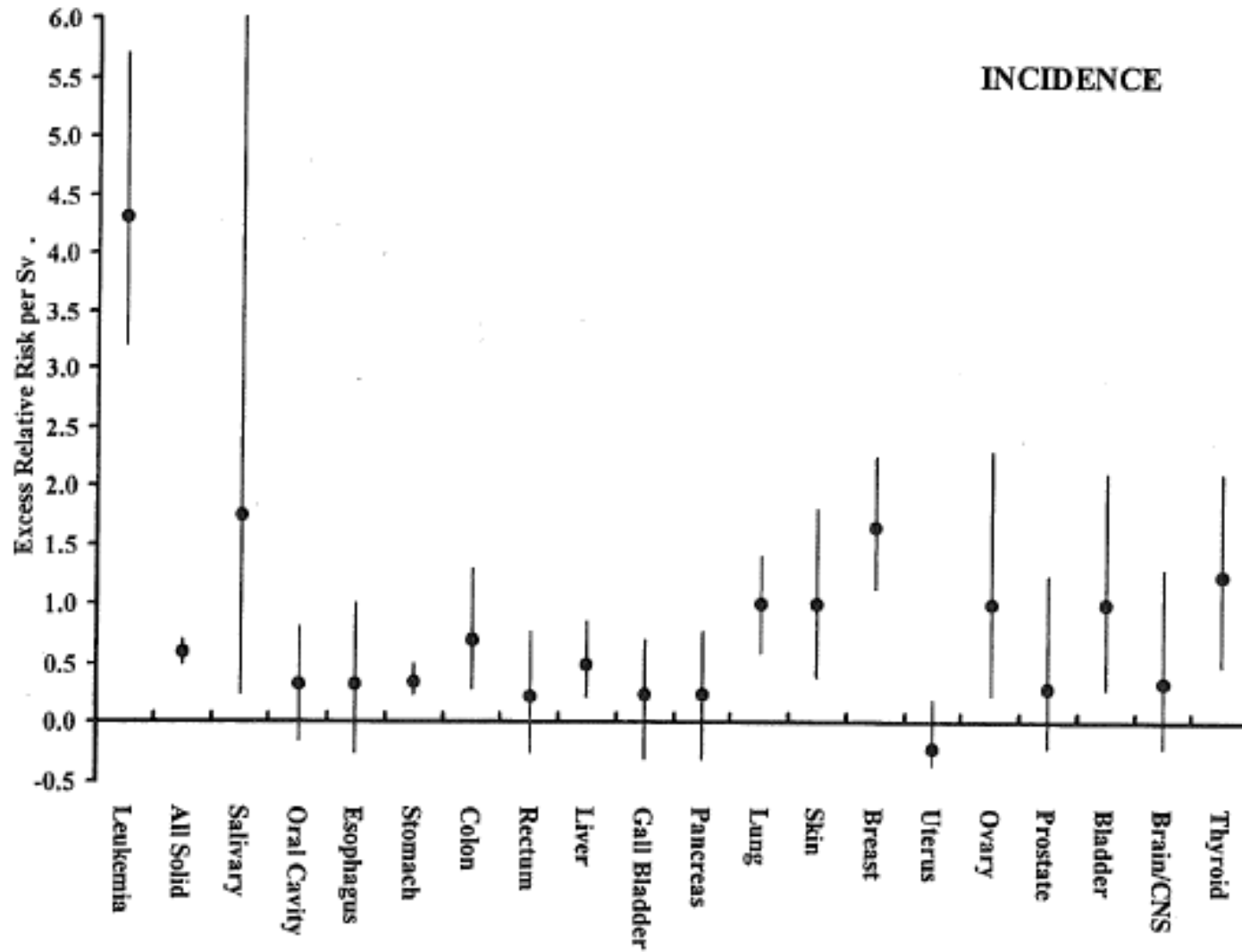
Exposure level (mSv)	Symptoms and Effects
50 - 100	Changes in blood chemistry
500	Nausea within hours
700	Vomiting
750	Hair loss within 2-3 weeks
900	Diarrhea
1,000	Hemorrhage
4,000	Possible death within two months if no treatment
10,000	Destruction of intestinal lining, internal bleeding and death within 1-2 weeks
20,000	Damage to the central nervous system and loss of consciousness within minutes and deaths within hours or days

# Effects of Non-lethal Dosage

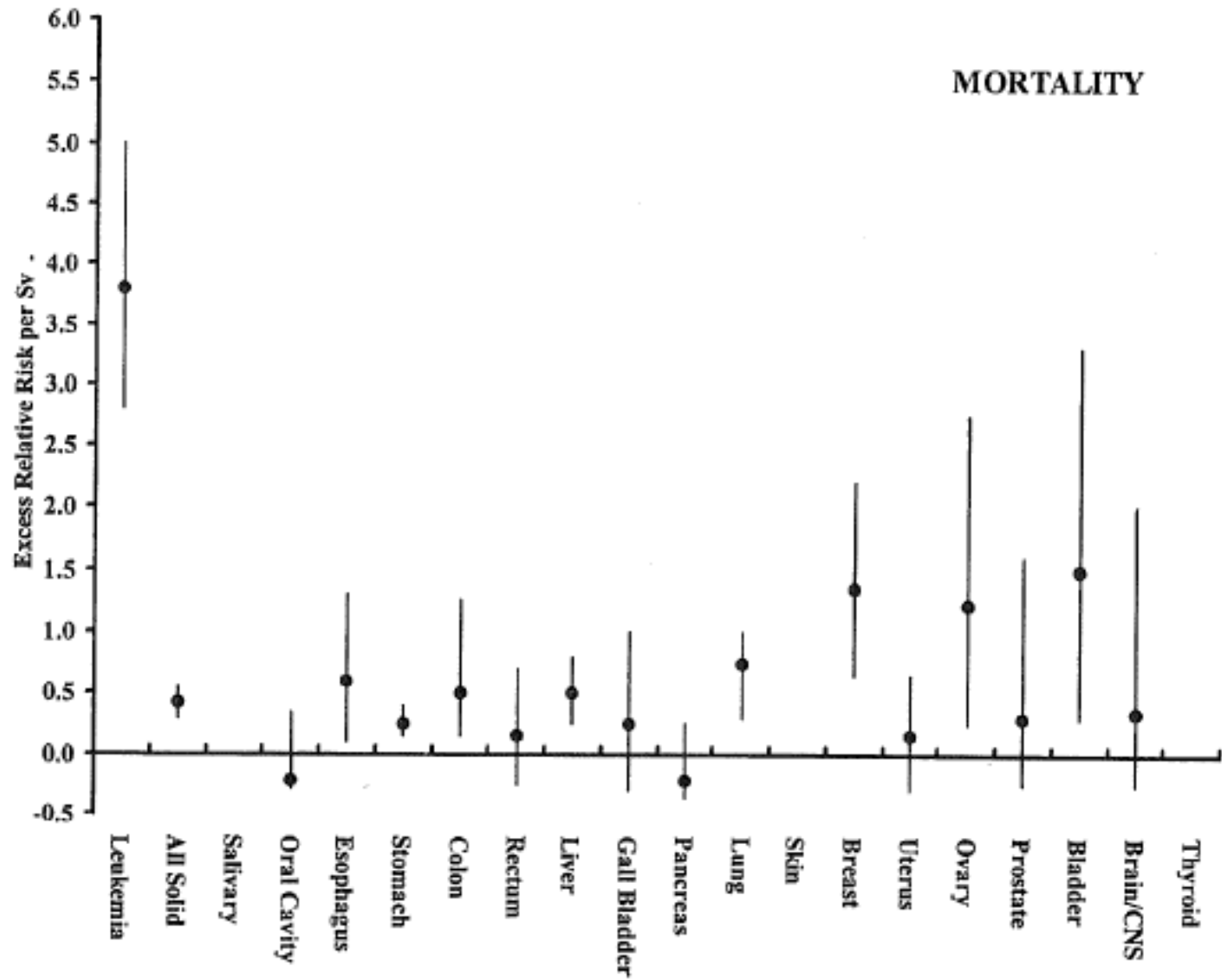
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- LSS data demonstrated a statistically significant association between radiation dose and some diseases other than cancer.
- Excess non-cancer disease mortality risks in the LSS data evident at levels below 4-5 Gy
- Non-cancer effects include infection, stroke, heart disease, and diseases of the respiratory and digestive systems, which are of a non-neoplastic (瘤) nature

## A bomb survivor excess risk in incidence for various cancers (source: UNSCEAR 2006)

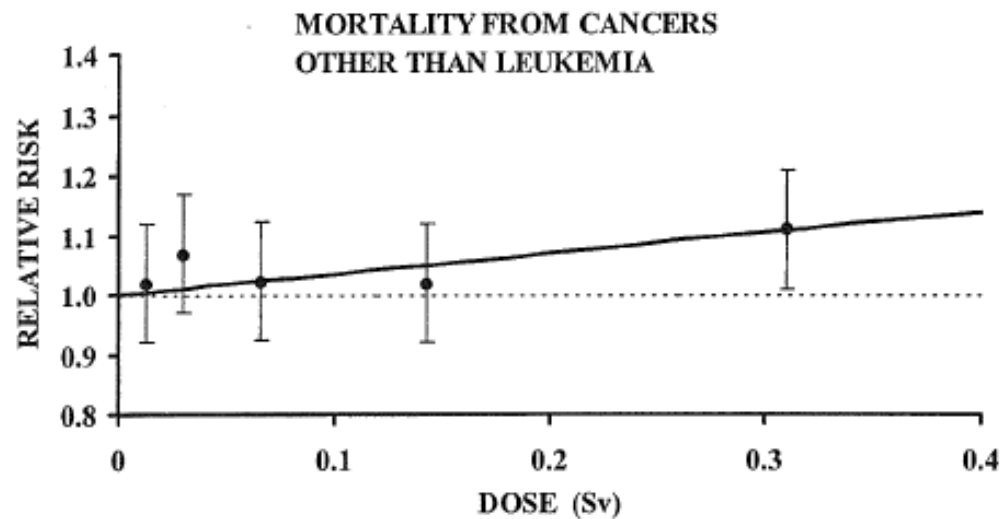
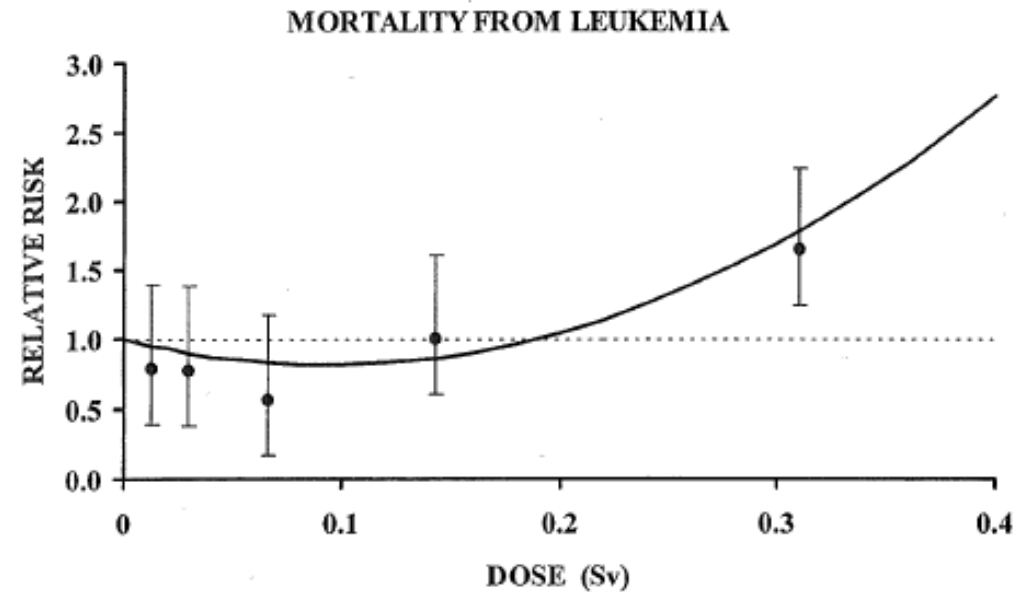


## A bomb survivor excess risk in mortality for various cancers (source: UNSCEAR 2006)



# A-bomb survivor mortality from leukemia and other solid cancers (Source: UNSCEAR2006)

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# Summary of Acute radiation syndrome for $\gamma$ Radiation

Dose (Gy)	Symptoms	Remarks
0 – 0.25	None	No clinically significant effects
0.25 - 1	Mostly none ; a few may exhibit mild prodromal symptoms, e.g. nausea (悪心)	Bone marrow damaged; decrease in red and white blood cell counts and platelet (血小板) count; lymph node and spleen injured; lymphocyte (淋巴細胞) count decreases
1 – 3	Mild to severe nausea, malaise (不適), anorexia (厭食), infection	Hematologic (血液) system damaged
3 - 6	As above, plus hemorrhaging, infection, diarrhea, epilation (脫毛), temporary sterility	Fatalities will probably occur without treatment; LD50/30 is 4 Gy without treatment
More than 6	As above plus impairment of central nervous system	Death expected

Source: “Atoms, radiation and radiation protection”, J. Turner

# Lethal Dosage of ionizing radiation

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- The whole body lethal dose is about 5 Gy which is 5 J/kg. For a 70 kg person receiving 5 Gy of radiation absorbs 350 J of energy, which is approximately 80 calories. If this is eventually converted to heat, the temperature of the body would rise only 0.001 °C.
- A comparatively small amount of energy in the form of ionizing radiation can cause significant biological damage because of the manner in which ionizing radiation interacts with matters.

# Deterministic vs Stochastic Effects

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- Biological effects are either Deterministic or Stochastic
- Deterministic effects – expressed as diseases other than cancers - arise from exposure to high levels of radiation, and become more severe as the exposure increases. A threshold dose (tissues and biological endpoint dependent) usually exists. Acute health effects include burns, radiation sickness, e.g. nausea, vomiting, weakness, hair loss, cataract or even death. For example, death results within hours or days if exposed to over 20 Sv.

# Deterministic vs Stochastic Effects

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- Stochastic effects – expressed as cancers, leukemia, genetic mutation, chromosome alteration, circulatory diseases, etc – arise from long-term, low-level (chronic) exposure to radiation. Increased levels of exposure make these health effects more likely to occur, but do not influence the type or severity of the effect.
- No evidence of cancer induction was found for acute dose below 100 mSv.

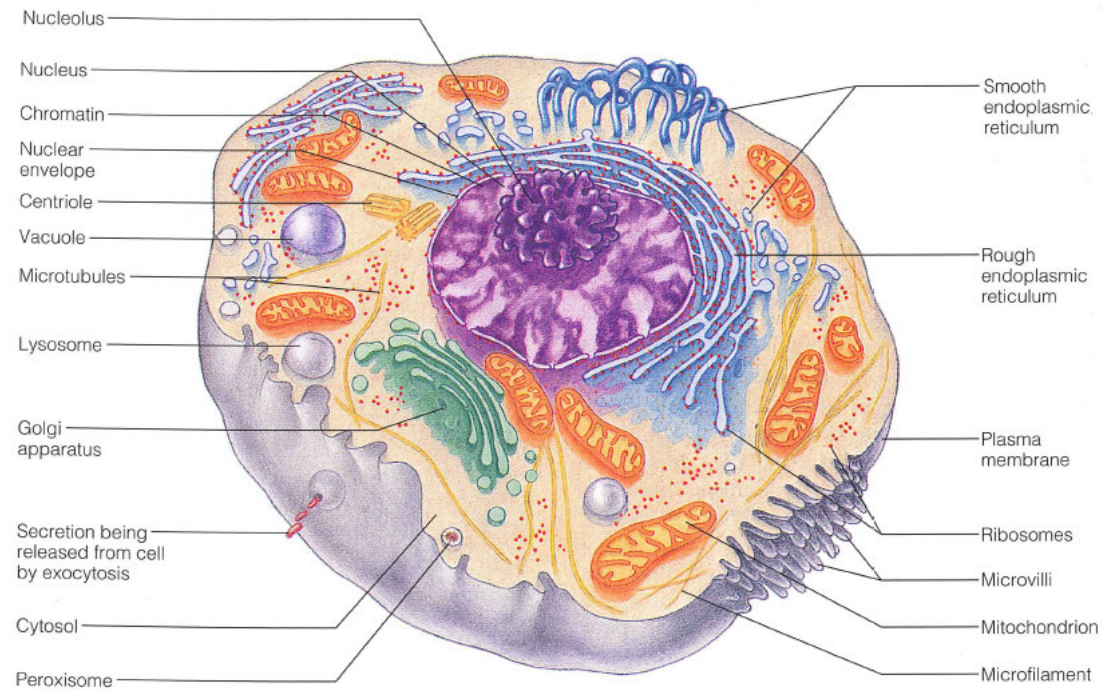
# Mechanism for the Observed Effects

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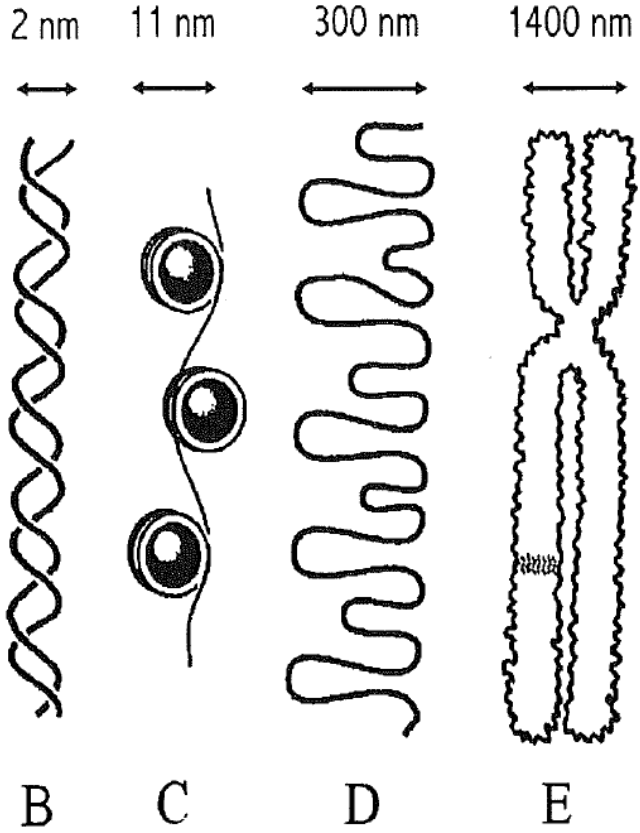
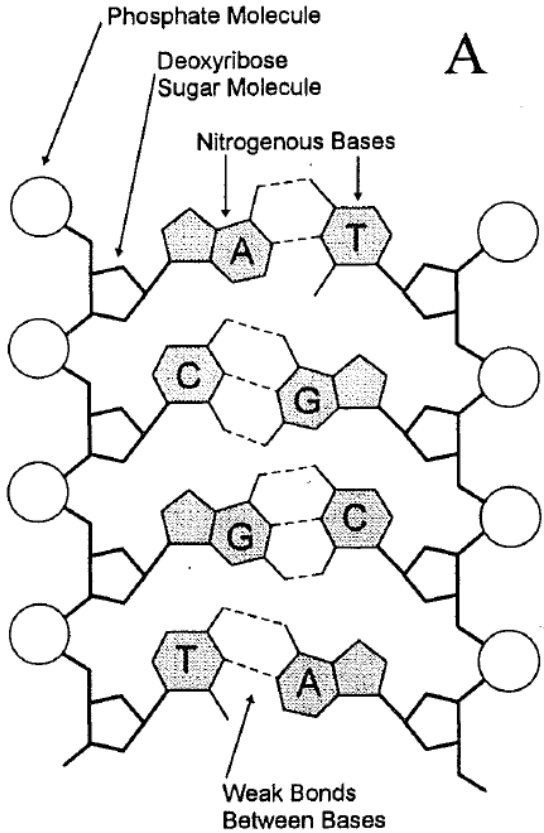
- Ionizing radiation interacts with atoms/molecules in the medium through direct or indirect ionization.
- Direct ionization involves charge separation by coulomb force of incident charged particles, e.g.  $\alpha$  particles, and effect is proportional to the charge and mass of the incident particles.
- Indirect ionization involves mainly inelastic compton scattering whereby kinetic energy from incident photons or neutrons is transferred to the outer-most atomic electrons with which they collide. Photoelectric absorption of photon energy is another pathway.

# Interaction of ionizing radiation with cells

$\gamma$  ray



# Structure of DNA, Nucleosomes and Chromosomes



# Biological Effects of Ionizing Radiation

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- Irradiation of macromolecules, e.g. proteins, including enzymes, DNA can result in partial or full disturbance of their biological functions or inactivation.
- The effects are due to deposition of energy to the cell and its organelles through direct or indirect action

# Linear Energy Transfer (LET)

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- The rate of energy transfer per unit distance along the radiation track is described by its Linear Energy Transfer (LET).
- Low LET ( $< 1$  keV per micron) radiation includes X-ray,  $\gamma$  ray, and  $\beta$  ray. These have radiation weight factor of  $\sim 1$
- High LET ( $> 10$  keV per micron) radiation includes  $\alpha$  particles and neutron particles. The radiation weighting factor of 2-20.

# Consequences of energy transfer

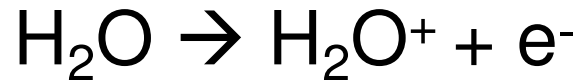
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- Two consequences of the local deposition of energy that can lead to biological damage:
  - (a) the chemical bonds of an essential biomolecule, e.g. DNA can be broken as a direct result of ionization – direct action.
  - (b) reactive chemical species can be produced that subsequently react with essential biomolecules to produce molecular damage – indirect effect.

# Physical and Chemical Effects

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- Typical chemical reactions at cell level (composing of over 70% water) due to the passage of ionizing radiation are:



- The free radicals OH with unpaired electrons are chemically reactive and may diffuse in the cell nucleus to attack a DNA molecule

# Mechanism for the Cell Damage

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- The hydroxyl group OH has been estimated to cause 70% of the damage.
- Molecular oxygen interacts with radiation hydrolysis products to form superoxyl radical and hydrogen peroxide, both of which are chemically reactive. It also acts to “fix” the otherwise repairable damage caused by the free radicals. Hence the presence of oxygen acts to enhance the biological effects of ionizing radiation.

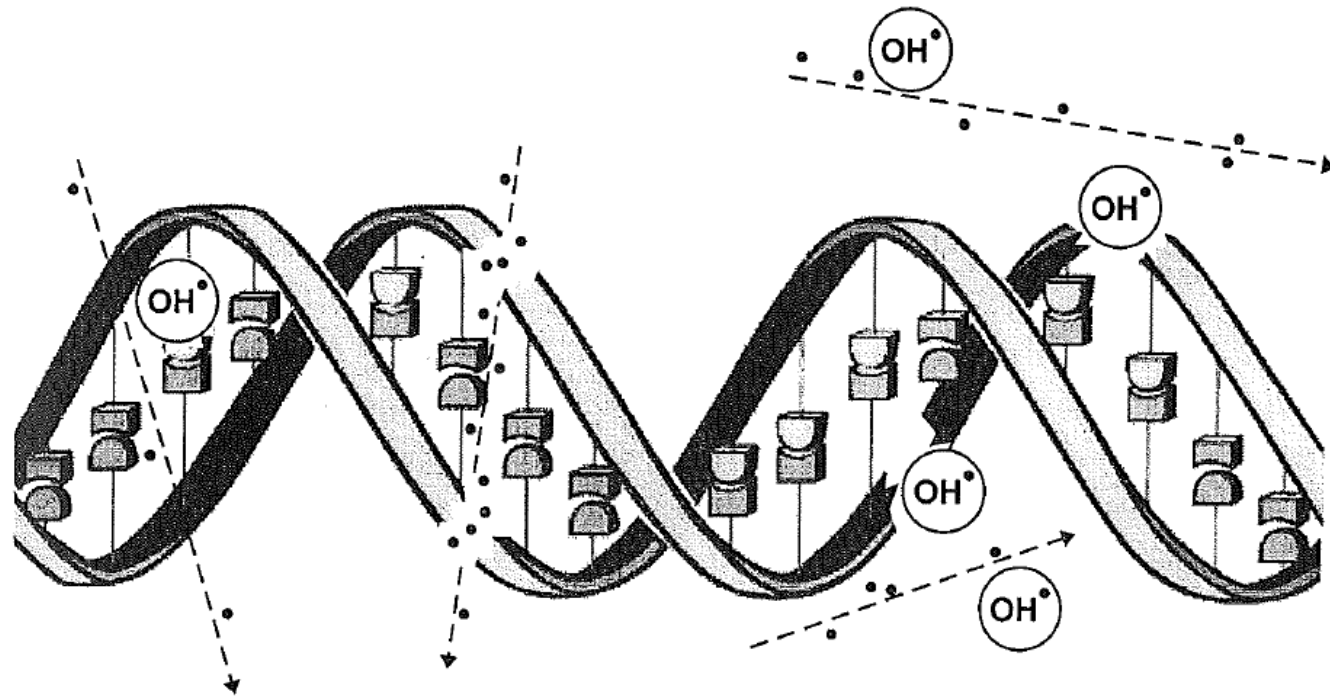
# Damages to DNA by Ionizing Radiation

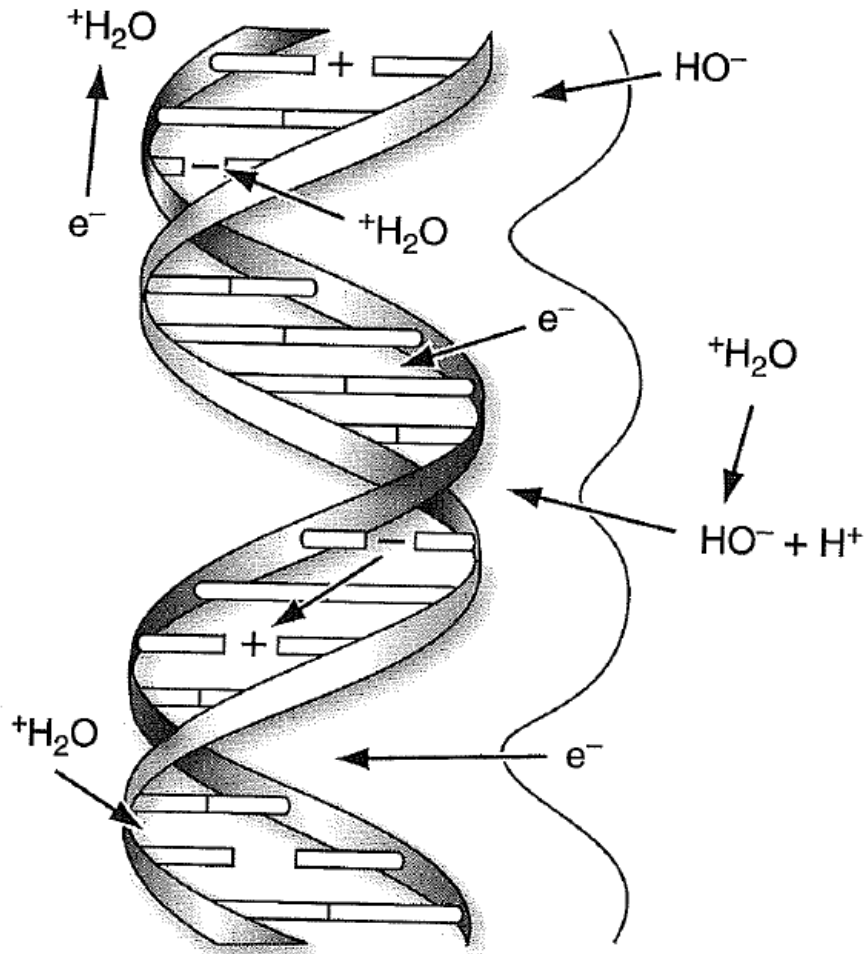
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- DNA is the only significant macromolecule for biological damage, based on studies of selective irradiation of cell components.
- Because a chromosome is highly compact, a single ionization track could interact the DNA molecules multiple times.
- Damage to DNA includes (a) damage to the sugar molecules resulting in single and double strand breakage, (b) damage or deletion of a base, (c) chemical cross linking of two strands and (d) combinations of damage to a local area, termed “locally multiply damaged sites”.

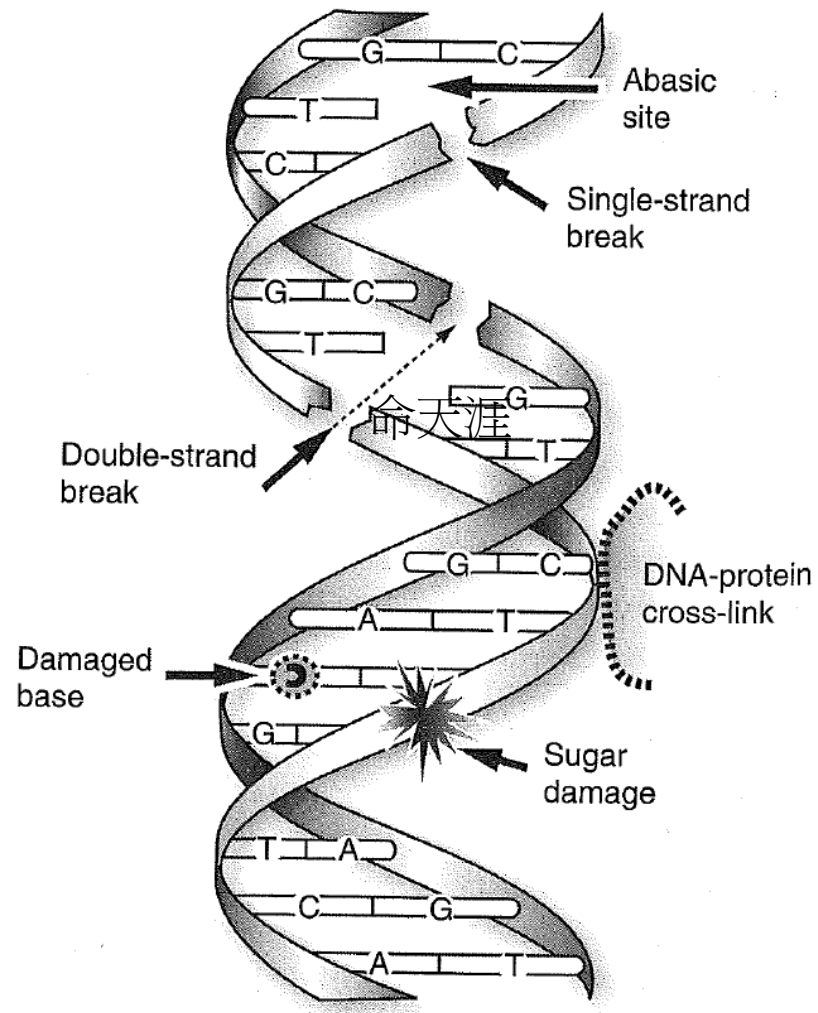
## Schematic illustration of mechanism leading to DNA damage

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**Illustration of indirect effects due to free radicals produced by ionizing radiation**

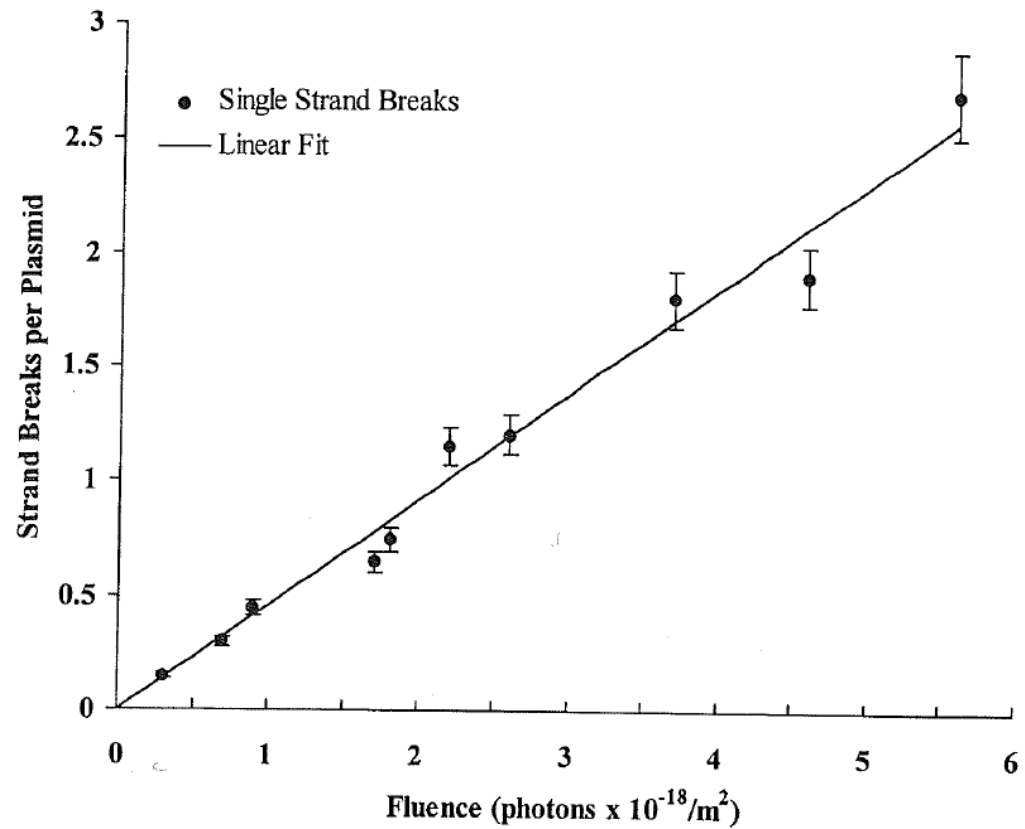


## DNA Lesions exposed to ionizing radiation

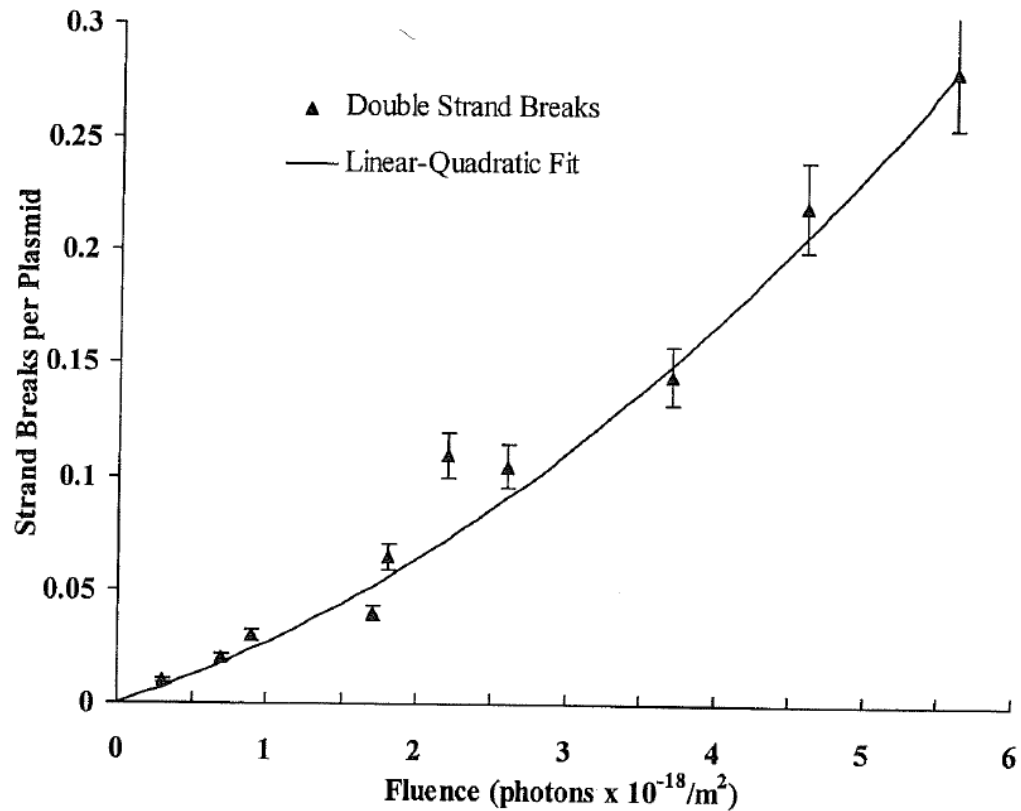
# **Damages to DNA by Ionizing Radiation**

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- The initial damage of most consequences to cell survival is double strand breaks. For cell death to occur, fairly severe DNA damage, probably involving two or more DSB or several local multiply damaged sites, must be produced.
- Such damage may be impossible for the DNA to repair or the repair process may result in the loss or inactivation of important genes.



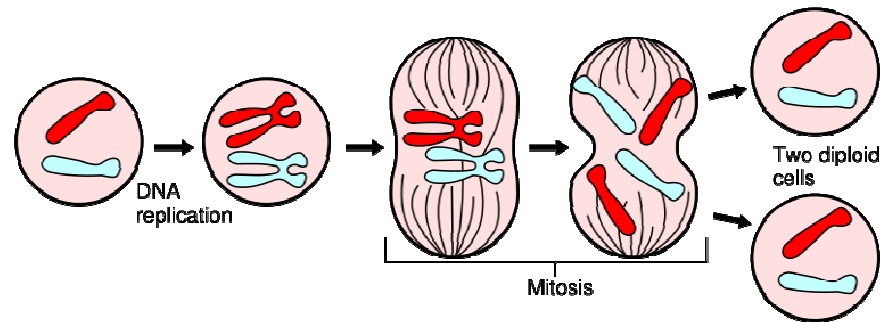
**Dose dependence of single-strand breaks observed in plasmid DNA irradiated with mono-energetic low LET radiation**



**Dose dependence of double-strand breaks observed in plasmid DNA irradiated with mono-energetic low LET radiation**

# Damages to DNA by Ionizing Radiation

- A cell is said to be severely damaged if its DNA are unable to undergo a single successful mitosis (有絲分裂, a process in which the cell separates the chromosomes in its cell nucleus) after irradiation, or they may continue to divide for a few generations but ultimately be unable to sustain a colony of cells.



- Two mechanisms of cell death are caused by ionizing radiation: necrosis (壞死) and apoptosis (細胞自然死亡).

# **Damages to DNA by Ionizing Radiation**

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- Necrosis is a form of traumatic cell death that results from acute cellular injury
- Apoptosis is a process of normal programmed cell death
- In general cell types that divide at higher rates and have less differentiation are most sensitive to cell killing.
- Germ cells, epidermal stem cells, gastrointestinal stem cells are more radiosensitive while nerve and muscle cells are less.

# Effects of low-level low-LET radiation

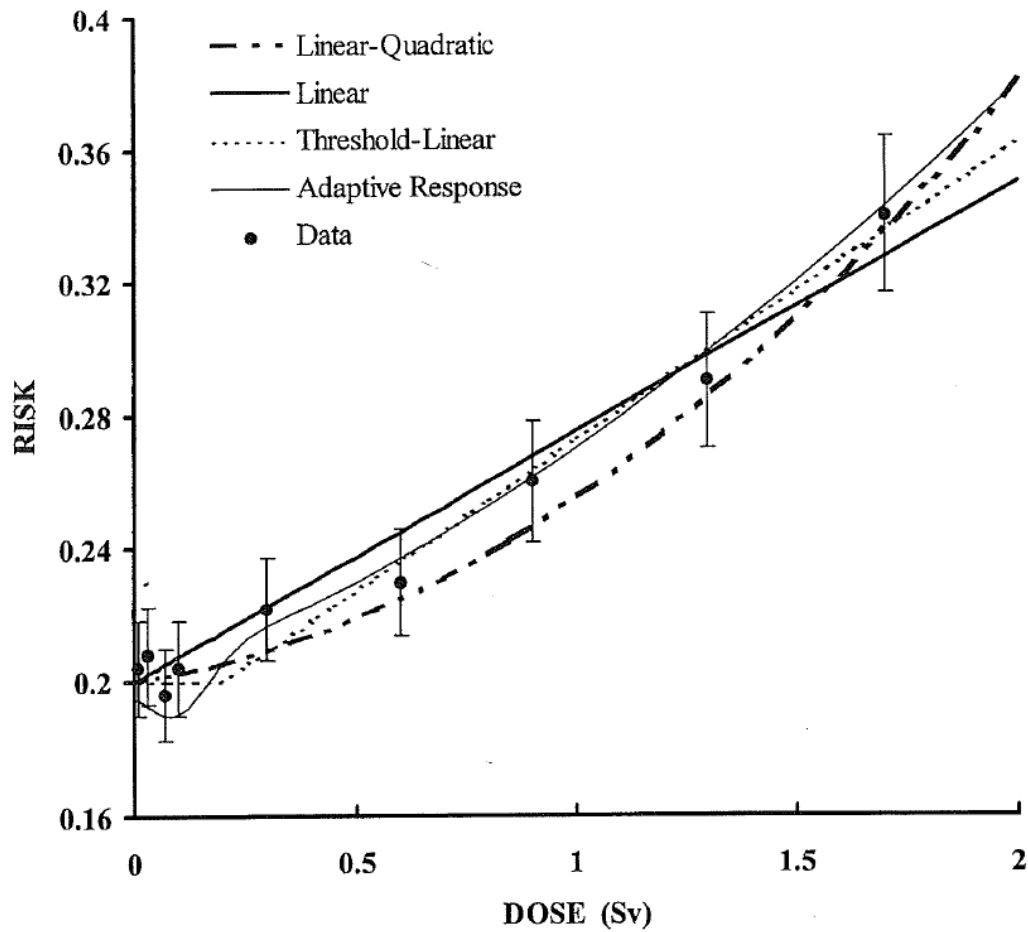
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- BEIR VII Report defines low-level LET radiation as doses in the range of near zero up to about 100 mSv (0.1 Sv) of low-LET radiation. This is the radiation that people are normally exposed to during medical examination and from natural background sources.
- The assessment of the risks at low doses (< 100 mSv) is based on extrapolation from carcinogenic effects observed between 0.2 and 3 Sv, due to epidemiological limitations.

# Effects of low-level low-LET radiation

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- There is no agreement among experts regarding how risk varies as a function of dose at low doses.
- The US National Academy of Sciences BEIR VII Committee conducted a critical review of the epidemiologic and experimental evidence concerning low doses of low LET radiation and concluded that the risk is linear at lower doses without a threshold and the smallest dose has the potential to cause a small increase in risk to humans



**Dose-response models used to fit the observed A-bomb survivor data**

# Biological Defense System in Human

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- First level: Production of anti-oxidants in cells to fight reactive oxygen species generated by ionizing radiation and by any oxidative stress,
- Second level: Elimination of injured cells (mutated or unstable) through two mechanisms (i) apoptosis (細胞自然死亡) which can be initiated by doses as low as a few mSv, thus eliminating cells from the genome of which has been damaged or misrepaired, (ii) death of cells during mitosis (細胞有絲分裂) when lesions have not been repaired.

# Biological Defense System in human

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- Third level: Stimulation or activation of DNA repair systems following slightly higher doses of about ten mSv.
- Fourth level: Activation of the immune system to kill cells that are not sensed to be 'one of ours', possibly formed by the double strand breaks.
- Others: ??
- Cancer risks are generally higher at old ages partially due to impairment of immune system with age to eliminate the mutated cells.

# Conclusion

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- Ionizing radiation is carcinogenic with known adverse health effects
- Man has built in a defense system to repair the damages caused by natural exposure and limited doses and dose rates from diagnostic and therapeutic uses of ionizing radiation
- Any decision that alters the radiation exposure situation should do more good than harm
- All radiation exposures should be kept As Low As Reasonably Achievable, (ALARA)

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**Thank you**