Basic Nuclear Engineering 4
(原子核工学基礎第四)
(4) Effects of radiation (1)

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Possible radiation injuries and effects

1）Death (Acute radiation syndrome)

2）Cancer

3）Infertility

4）Effects on fetus
(malformation, growth retardation)

5）Effects on offspring (hereditary effects)

6）Skin (epilation, ulcer)

7）Vitreous clouding, cataract

Categorization

Deterministic effects

Can be seen only after exposure to the radiation dose above the threshold.

Effects other than carcinogenesis and hereditary effects.

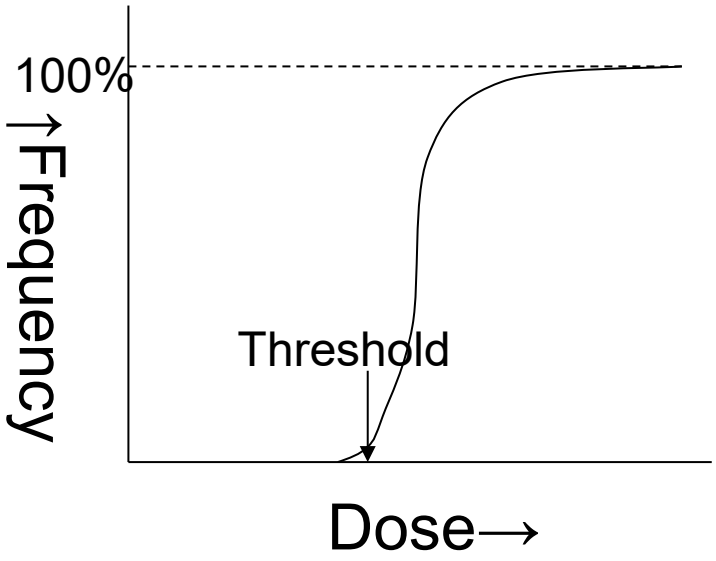
Stochastic effects

Carcinogenesis and hereditary effects.

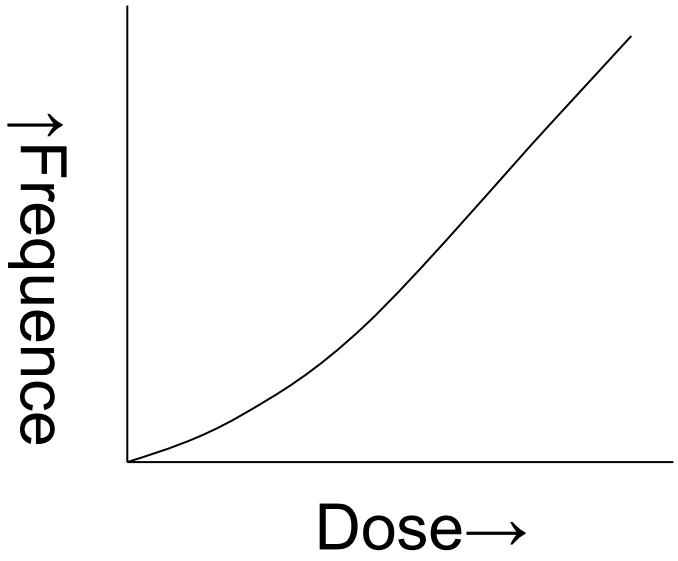
Thought to occur after exposure to even small dose of radiation, i.e., no threshold is assumed.

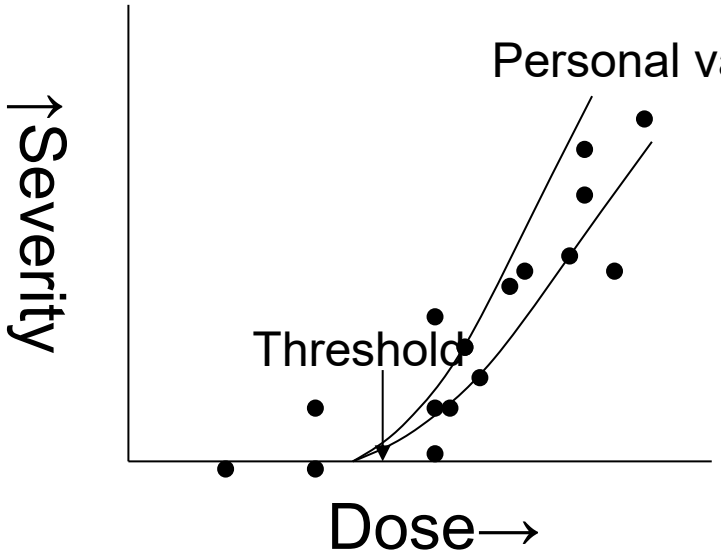
The incidence is thought to increase with radiation dose.

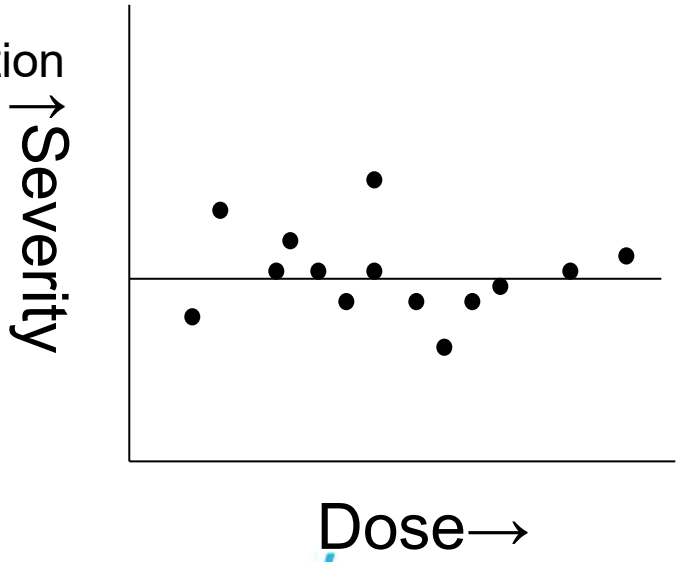
Deterministic Effects



Stochastic Effects





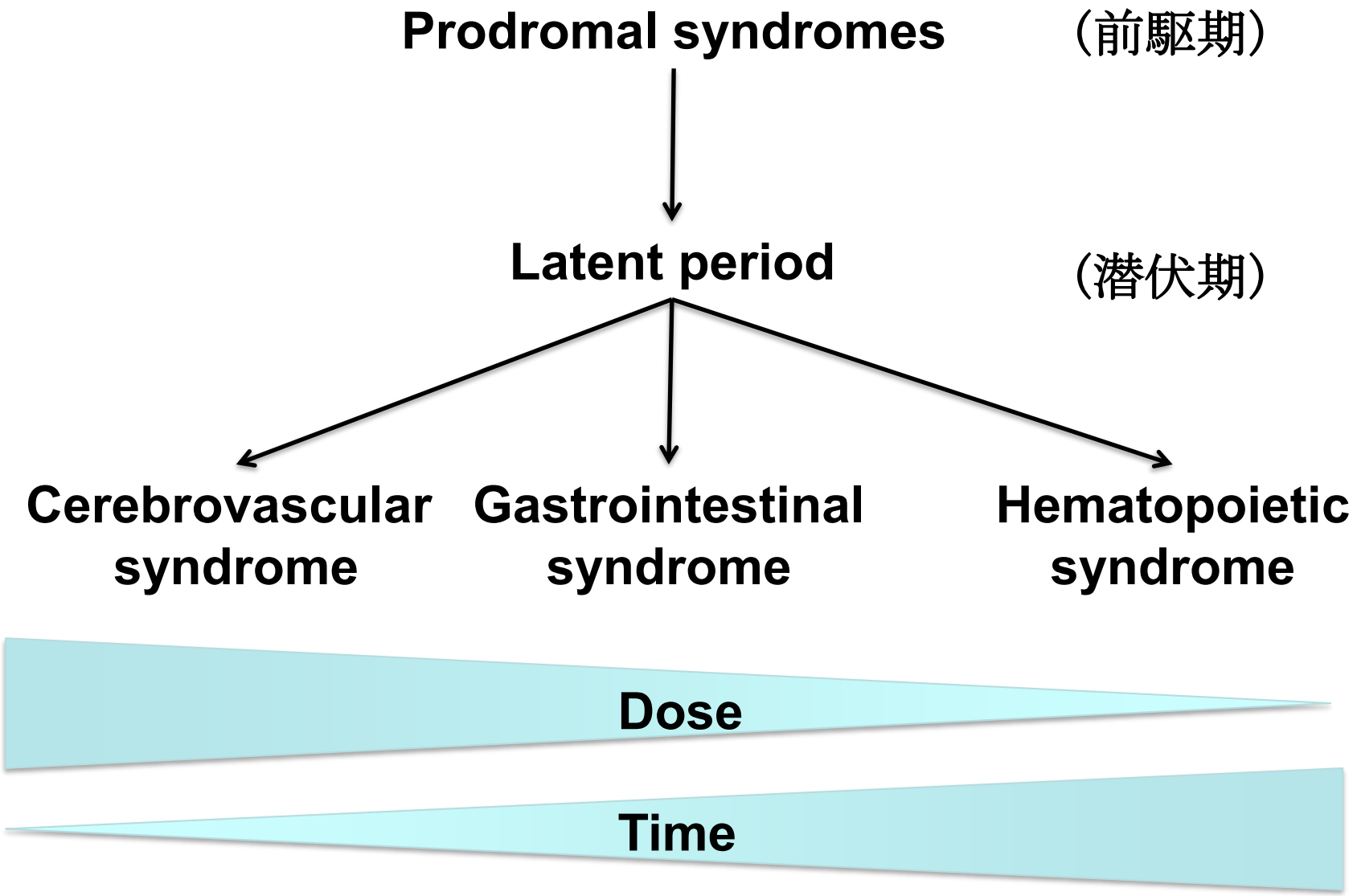


Acute Radiation Syndrome

Dose	Symptom
<0.25Gy	None observed
~0.5Gy	Lymphocyte decrease
~1.5Gy	Sickly feeling (nausea, vomiting, weakness,…)
~4Gy	50% of people die within 1~2 months*(Bone marrow death / Hemtopoietic death) <Half lethal dose>
~7Gy	100% of people die*
~15Gy	Death within 2 weeks (Gastro-intestinal death)
>50Gy	Death in 1~2 days (Cereberovascular death)

***Without bone marrow transplantation or aseptic treatment**

Acute Radiation Syndrome



Bone Marrow (Hematopoietic) Syndrome

Dose：Several to 10 Grays

Timing of death：10 to 60 days after exposure

Mechanism of death：

Bone marrow stem cells cease to proliferate

→Failure of hematopoietic system

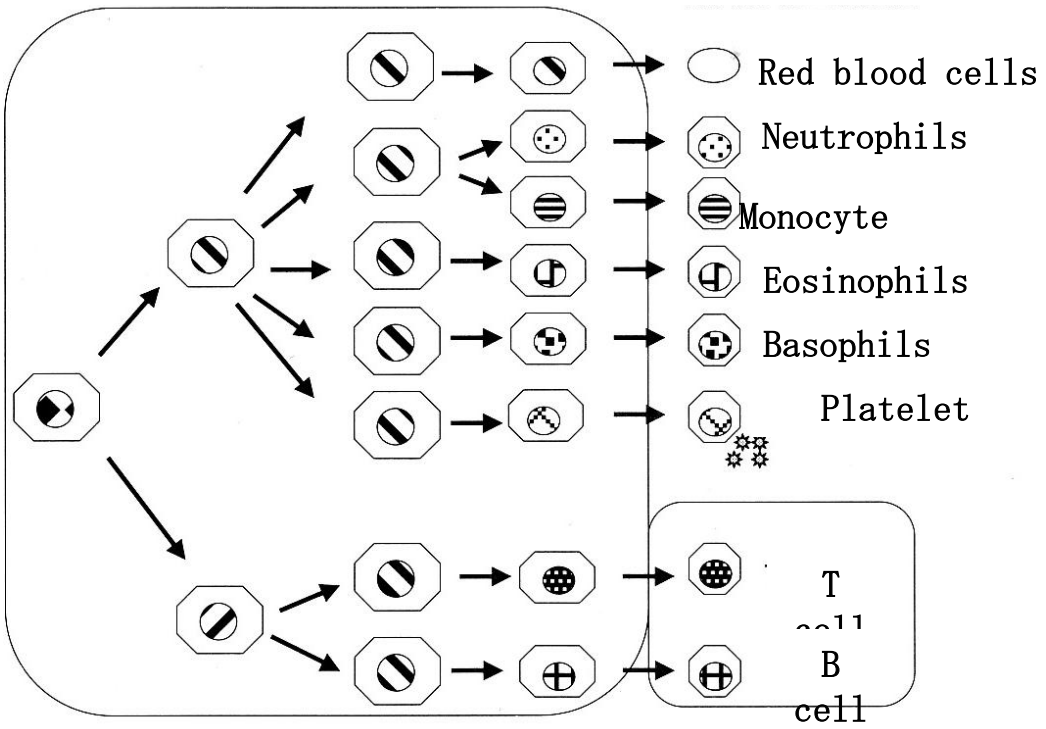
→Infection, loss of blood → Death

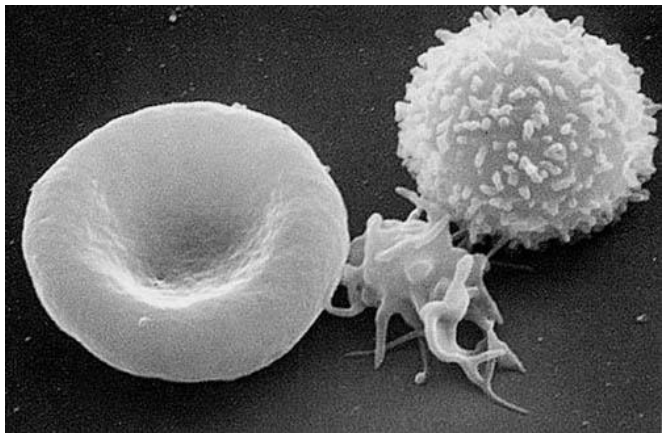
(Sometimes rescued by aseptic treatment or bone marrow transplantation)

Blood cells and function

	Function	Number	Life time
Red Blood Cell	Oxygen transport	450-500million/mm3	~120days
White Blood Cell		4000-10000/mm3	
Lymphocyte	Immunity	~25% of WBC	100-300days
T lymphocyte	Cellular Immunity		
B lymphocyte	Humoral Immunity (Antibody production)		
Natural Killer cells	Removal of cancerous or infected cells		
Granulocyte	Inflammatory response	~60% of WBC	4-8hours
Neutrophil			
Eosinophil			
Basophil			
Monocyte	Phagocytosis	3~8% of WBC	10-20hours
Platelet	Hemostasis (clotting)	10-40million/mm3	3-10days

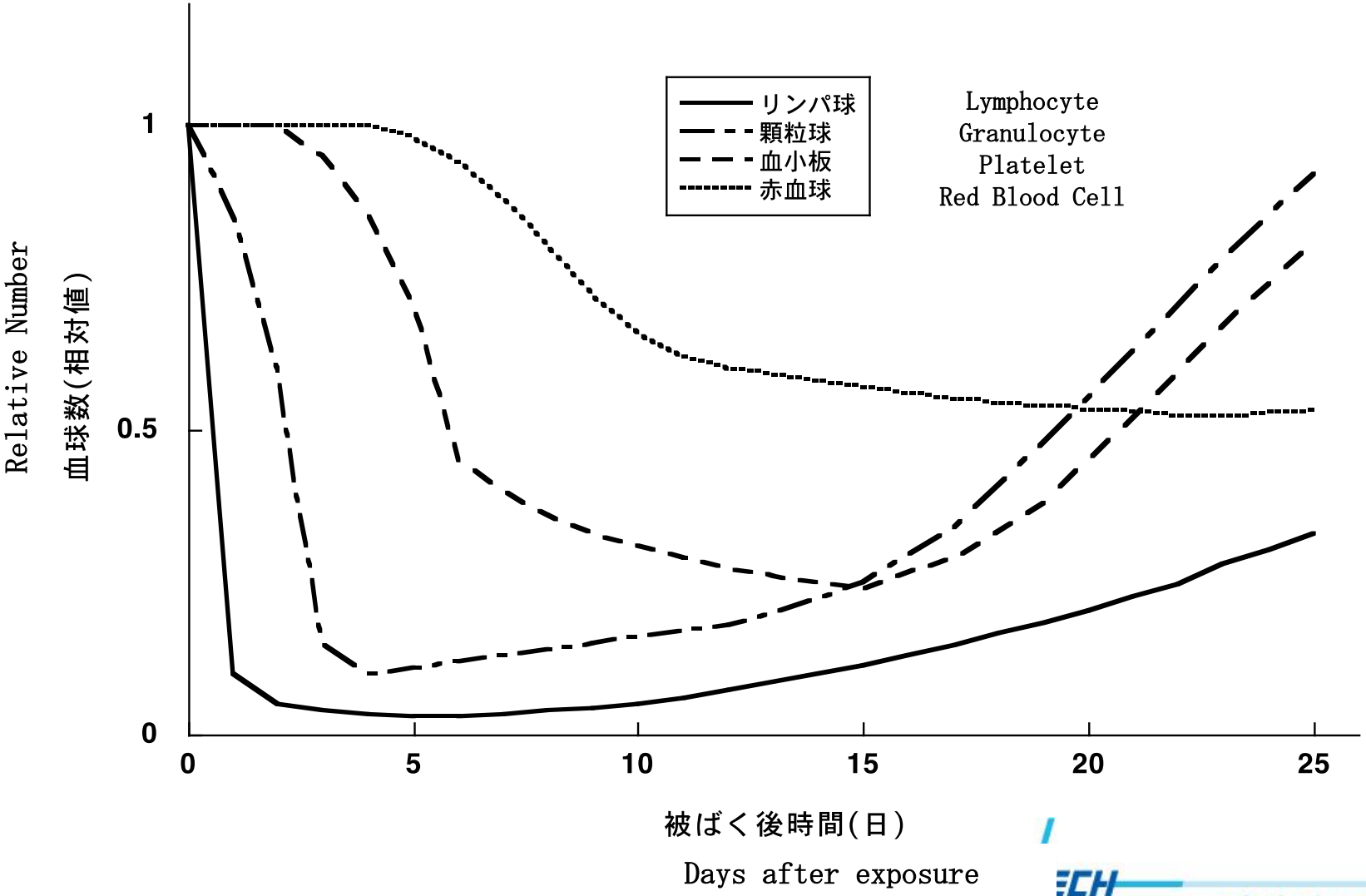
Lineage of blood cells





RBC, Platelet and WBC

Changes in the number of blood cells after radiation exposure



Gastrointestinal Syndrome

Dose：10～50Gy

Timing of death：2～3 days after exposure

Mechanism of death：

Stem cells in crypt cease proliferation

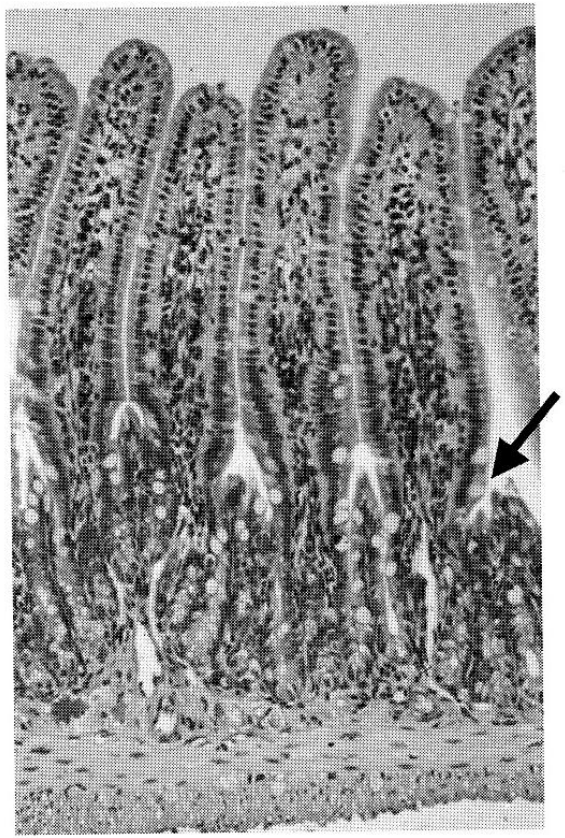
→Failure in the renewal of epithelial cells

→Loss of villi

→Leakage of water and electrolyte,
Loss of blood, Infection

→Death

Gastrointestinal Syndrome



Cross-section of mouse small intestine
「放射線医科学」(大西武雄監修、学会出版センター) より

- The small intestine has many protruding micro villi. This increases the surface area and merits the ingestion of water, mineral and nutrition.
- Stem cells reside in the crypt at the bottom of the villi (arrow) and migrates toward the tip of the villi upon proliferation and differentiation.
- Cells reached the tip eventually drop off. This turnover takes several days.

Gastrointestinal Syndrome

「放射線医科学」(大西武雄監修、学会出版センター)より

・Stem cells are highly radiosensitive.

・The reproductivity of the stem cells is lost upon receiving several Grays. Then there is no longer supply of new cells.

・Micro villi are lost and ingestion of water, mineral and nutrition is severely compromised. Moreover, these substances leak out from the damaged villi.

・Blooding and infection occur.

・Leads to lethality in several days.

・If there are a few surviving stem cells remaining, the villi are regained.

Cerebrovascular Syndrome

Dose : >50Gy

Timing of Death : Within 1～2 days after exposure

Mechanism of Death :

Lesion on vascular system or cell membrane(?)

→Failure in central nervous system function

→Heart muscle stop(convulsion, shock)

Summary of Acute Radiation Syndromes

	Dose	Time of death	Mechanisms	Cause of death
Bone marrow (Hematopoietic)	3–10Gy	2,3 weeks –2 months	Apoptosis of lymphocytes Loss of proliferative capacity of stem cells	Infection, loss of blood
Gastrointestinal	10–50Gy	~1 week	Loss of proliferative capacity of stem cells in crypt	Failure in absorption and leakage of electrolyte, infection, loss of blood
Cereberovascular	>50Gy	Within 1–2 days	Damage on blood vessels and cellular	Shock, convulsion

Infertility

Male	**0.1Gy**	**Temporary**
	2.5～6Gy	**Permanent**
	Fractionated 15Gy	**Permanent**
Female	**0.65～1.5Gy**	**Temporary**
	2.5～6Gy	**Permanent**
	Fractionated 15Gy	**Permanent**

Skin (dermal)

Dose	Symptom
> 3Gy	Epilation
3～6Gy	Erythema (reddening), pigmentation (small colored dots)
7～8Gy	Blister (small liquid-filled vesicle)
> 10Gy	Ulcer, shrink of skin (later)
> 20Gy	Refractory (difficult to cure) ulcer, increased skin cancer probability

Effects of in utero exposure

Time of exposure	Major effects	Threshold
Preimplantation (-8d post fertiliz.)	Embryonic death	0.1Gy
Organogenesis (8d～8w)	Malformation (Congenital anomalies)	0.1Gy
Fetus (8w～birth)	Growth delay	0.5～1Gy
Esp. 8-25w	Mental development delay	0.2～0.4Gy

＊ Possibilities of cancer and hereditary effects are considered throughout the period. No threshold assumed for cancer and hereditary effects

Sensitivity of Various Organs to Radiation

High (sensitive)	Bone marrow
	Lymphoid organs (Spleen, Thymus, Lymph node)
	Reproductive organ (Testis, Ovary)
	Gastro-intestinal tract
	Skin, Hair, Lens
	Lung, Liver, Kidney, Pancreas, Thyroid grand
Low (Refractory)	Muscle, Bone, Connective tissue, Fat
	Nervous system

Bergonie-Tribondeau's Rule

(1) Organs or tissues, in which cells are vigorously proliferating, tend to be radiosensitive
E.g., Bone marrow, Epithelium of gastro-intestinal tract, Lymphoid organ, Testis

Exception: Ovary is radiosensitive, despite that ovary cells have ceased proliferation.

(2) Organs or issues, in which cells are not proliferating any more, tend to be refractory to radiation

E.g., Neuron, Muscle, Bone, Connective tissue, Fat

Bergonie-Tribondeau's Rule

(3) Tissues, in which cells are expected to undergo large number of cell division, tend to be radiosensitive

Radiosensitivity is higher in embryo than in child and adult.

Bone is radiosensitive during embryo and childhood.

(4) Functionally or morphologically undifferentiated cells tend to be radiosensitive

Cancer Example 1: Uranium miners

Increased risk of lung cancer of uranium miner is reported in the survey in USA and Canada. It is thought to be caused by high concentration of Radon (Rn) and its decay product such as Polonium (Po). Nevertheless, possible contribution of other factors, like chemical toxicity, inhalation of dust and confounding factors such as smoking are also considered.

Cancer Example 2: Dial painters

If the figures in the dial of watch are written with fluorescent paint including radium, it glows even in dark. Dial painters, who wrote letters on dial with fluorescent paint, usually dipped their brushes into the tank of radium (Ra) paint and then used their tongue to sharpen usually sharpen points to paint. As the result, radium migrated to the bones and and developed bone tumors, especially in the lower jaw.

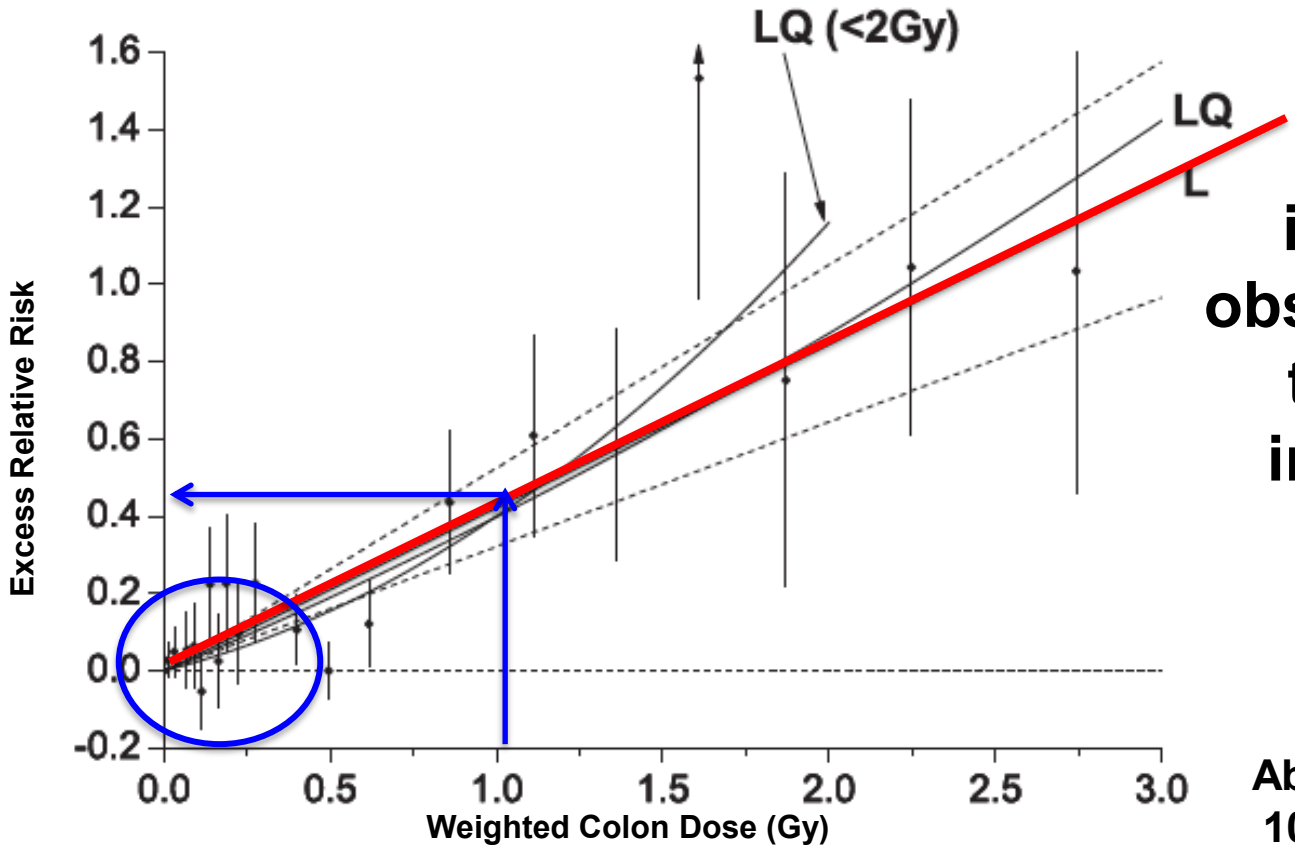
Cancer Example 3: Thorotrast

Thorotrast was used for enhanced contrast in vascular radiography. As the radioactive thorium (mainly 232) accumulated in liver, increase in liver cancer incidence was observed. In addition, radium (mainly 224), which is a descendent radionuclide of thorium, accumulated in bone marrow, the incidence of leukemia was also increased.

Cancer Example 4: Chernobyl accident

Increased incidence of thyroid cancer was observed in children after Chernobyl accident. It is thought to be caused by radioactive iodine (mainly iodine 131), through radiocontaminated cow milk.

Solid cancer in atomic bomb survivors



Ozasa et al., Radiat. Res. , 177, 229-243 (2012)

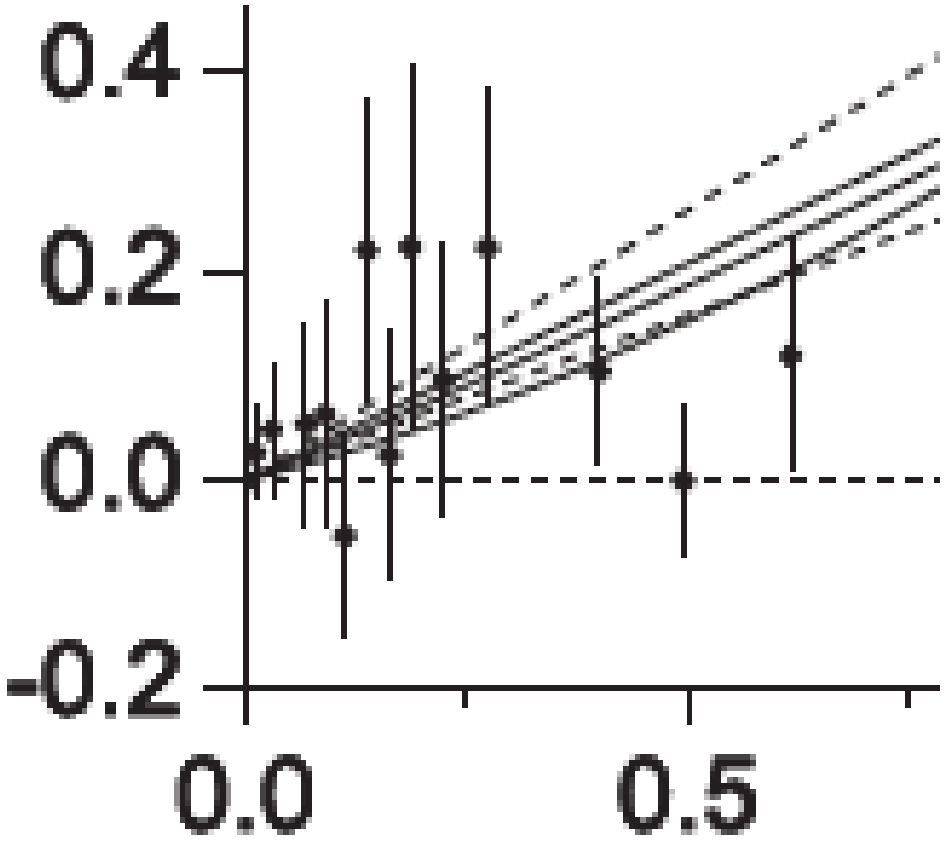
The symbol indicates the observed risk and the error bar indicates 95% confidence interval.

Absorbed dose of γ + 10 X Absorbed dose of n

Mostly linear increase above 100 mSv.

Slope: 0.42/Gy (in EAR about 10% increase at 1 Gy, as the risk in the control population is about 20%).

Solid cancer in atomic bomb survivors



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In low dose region (up to 100-200mSv) the error bar intersects 0.0 line.
“Statistically significant” increase is not observed.

Why we can't see increase below 100 mSv

1) Limitation of epidemiology and statistics: requirement for huge number of subjects

2) Personal difference in life style and genetic factors

→*It's not seen although there is*

3) Biological defense mechanisms

→*It's not seen because there isn't*

Models of low dose radiation effect