Early Effects from Internal Radiation: An Overview

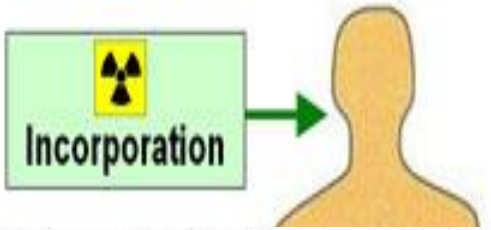
F. Ménétrier
CEA/DSV/Prositon

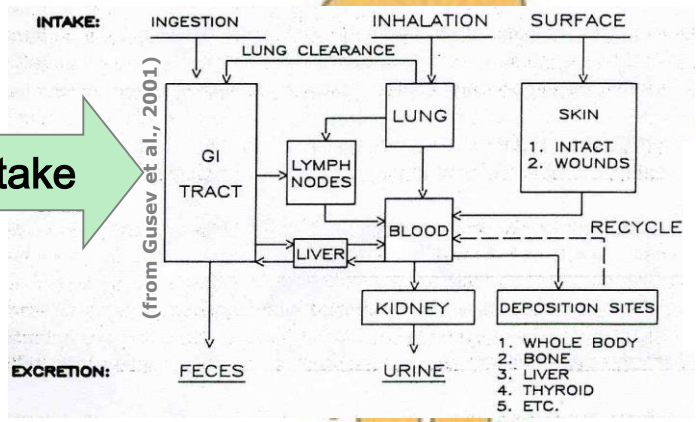
Internal Contamination

- Nature of radionuclide
- Quantity-dose
- Speciation
- Route of entry
- Age

Uptake

Biokinetics

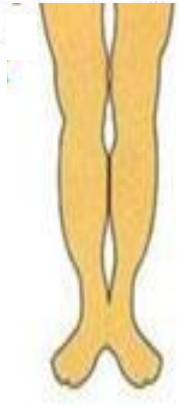




ICRP Models

Resulting internal dose ?

Health effects ?



Excretion

From biokinetics to health effects

- Target organs or uniform distribution: link with toxicity?
- Speciation and route of entry
- Radioactive properties of radionuclide: 238-Pu / 239-Pu

Soluble part
Systemic transfer

^{131}I
Thyroid

^{239}Pu
Skeleton, liver

^{241}Am
Skeleton, liver

^{137}Cs
Uniform repartition

^{3}H
Uniform repartition

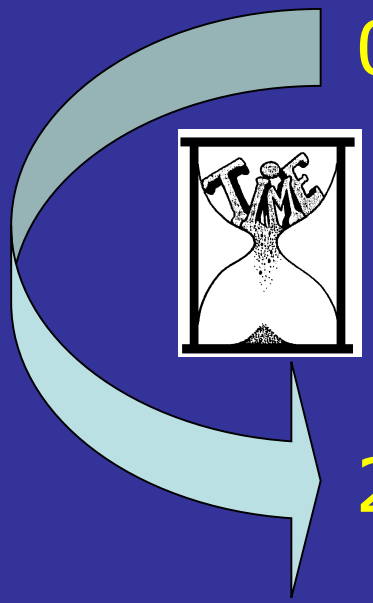
^{210}Po
Red bone marrow, Liver, kidneys, blood vessels, spleen

^{235}U
Skeleton, kidneys

Insoluble part → **firstly Local Target: lung, skin…**

Adverse health effects

Deterministic effects	Stochastic effects
• A threshold known at which effects appear • Increase of gravity with dose	• No threshold known • Probability of effects may increase as the exposure level increases



Here focuse on early deterministic effects

Radiological toxicity or Chemical toxicity

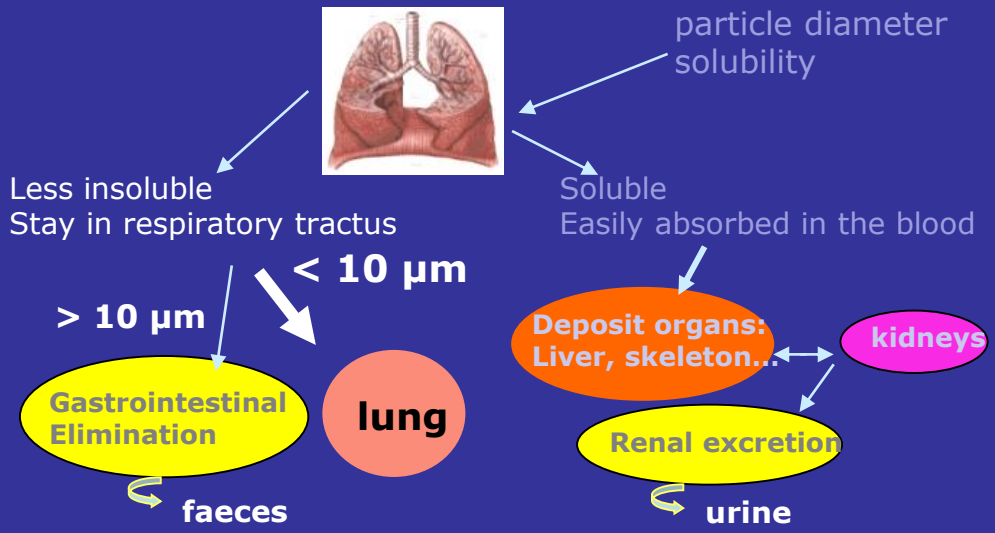
Experimental studies ? Human Cases in the past ?

Examples

1. Experimental studies with Plutonium

Life-span studies in animals to help predict risks associated with accidental intake by inhalation in workers - Pacific Northwest National Laboratory and Lovelace Respiratory Research Institute

- Inhalation of 239-Pu dioxide insoluble, alpha particles
- particles ≤ 3 µm AMAD
- Exposure of beagle dogs
- Calculation of absorbed lung dose from initial lung deposition and final lung deposition at time of death and lung mass, assuming a long-term retention function



1. Experimental studies with Plutonium

With 239-Pu

- **Lymphopenia**: first observed in the peripheral blood from 60 d after exposure, significant at 112 d for Initial Lung Burden 29 kBq/kg, 180 d for 14 kBq/kg
- **Lymphoid atrophy and Fibrosis of lung-associated lymph nodes** – accumulation of Pu particles.
- **Radiation pneumonitis + pulmonary fibrosis**: from 105 days for ILB 4kBq/kg – inflammatory process
- But Pulm. fibrosis could occur more than 10 years after exposure at lower exposure levels
- pulmonary fibrosis appears with absorbed lung dose from 5.9 Gy (on beagle dogs) – Otherwise retrospective studies on Plutonium workers concluded that lung fibrosis in human may appear from absorbed lung dose 0.5 Gy - Higher sensitivity of human?
- A more uniform distribution of dose over the lung would be correlated with a higher occurrence of radiation pneumonitis (size of particles)

(Muggenburg, Guilmette et al, 2008)

Radiological effects as a function of dose and time

Early deterministic radiological effects

1. Experimental studies with Plutonium

Difference of pattern between 238-Pu and 239-Pu

Particles of 238-Pu more soluble than those of 239-Pu due to increased fragmentation produced by higher specific activity compared to 239-Pu

Translocation of significant amount 238-Pu TO bone and bone marrow

Both lymphopenia AND neutropenia

More rapid clearance from lung

Pulmonary fibrosis appeared for 8 kBq/kg for 238-Pu instead of 4 kBq/kg for 239-Pu and disease less protracted

Early deterministic radiological effects

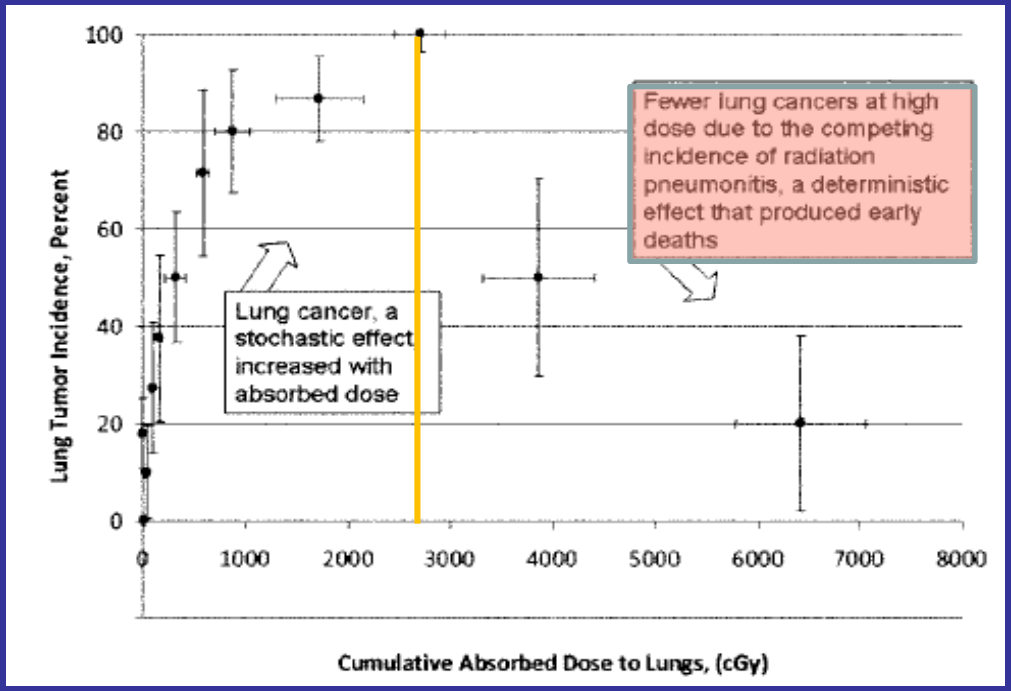
1. Experimental studies with Plutonium

- Lung cancer: Increase from ≈0 incidence between 0 and 200 cGy to 100% incidence at ≈ 2,800 cGy
- Lung tumors incidence decreased at the highest 239-Pu dioxide exposure level

Because of increasing incidence of radiation pneumonitis with lung doses > 2,000 cGy

Early deaths before lung cancers could develop

After inhalation of 239-PuO_2 AMAD 2.3 µm



(Fisher at al, 2010)

Early deterministic radiological effects

2. Human Cases and experimental studies with Polonium

- Case of Litvinenko - ingestion → Ingestion of 1-3 GBq, assuming 10% absorption to blood, 0.1-0.3 GBq would be likely fatal within 1 month

- Case of a Russian worker
Death in 13 days – inhalation
estimated at 530 MBq with limited data
Possibly: 20 Gy to the lung on first day + high dose to kidney
< 2 Gy to the bone marrow at the time of death
Ilyin (2001)

Time after intake (days)	Cumulative absorbed dose, Gy GBq^{-1} ingested						
	RBM	Gut	Liver	Kidneys	Spleen	Skin	Testes
1	0.2	0.04	1.1	1.9	0.7	0.1	0.2
2	0.4	0.09	2.5	4.1	1.5	0.3	0.4
3	0.6	0.1	3.8	6.2	2.2	0.5	0.7
4	0.8	0.2	5.1	8.2	3.0	0.6	0.9
5	1.0	0.2	6.3	10	3.7	0.8	1.2
10	2.0	0.5	12	18	7.1	1.8	2.6
15	2.8	0.6	16	25	10	2.9	4.2
20	3.6	0.8	20	30	13	4.0	5.9
25	4.2	0.9	23	35	15	5.2	7.7
30	4.8	1.0	25	39	16	6.4	9.4

(Harrison et al, 2007)

Cumulative doses to organs/tissues of a reference adult male after ingestion of 210-Po (assuming 10% absorption to blood)

Polonium considered toxic only if taken internally (breathing, eating, through an open wound).

Early deterministic radiological effects

2. Human Cases and experimental studies with Polonium

Experimental and human data consistent with theoretical risk estimated:

- target organs: bone marrow, liver, kidneys, spleen, intestine, lymph nodes, skin, gut and lung after inhalation
- even if bone marrow failure could be prevented, damage to other organs could be fatal

(Scott; 2007)

- Time distribution of deaths depends on level of activity administered:

- Death after < 1 month: systemic burden > 1 MBq/kg body-mass
- Death after >1 month: systemic burden 0.1 – 1 MBq/ /kg body-mass

- < 0.02 MBq/kg body-mass: more risk of cancer than deterministic effects

- Ingestion of 1 µg may be lethal for radiosensitive people and a few tens mg lethal for all people

Early deterministic chemical toxicological effects

3. Human cases with Uranium

Case	Early Symptoms (< 4 weeks)	Late symptoms (≥ 4 weeks)
deliberate ingestion 15g U acetate Peak U conc: 100 µg U /g kidney (Pavlakis et al., 1996)	Acute renal failure (dialysis for 2 weeks) Refractory anemia Effects in muscles, heart, liver and intestines	6 months: still biochemical signs of kidney dysfunction Other signs resolved
Industrial accident, burn with U nitrate and oxide Peak U conc: 35 µg U /g kidney (Zhao and Zhao, 1990)	Skin burns and renal dysfunction (at 1d, critical state at 7d) U absorbed through burned skin	Renal function: normal at 1 month
Accidental inhalation, UF_4 powder Peak U conc : 10 µg U /g kidney	7d abdominal pain and diarrhea	From 78d to 590d: renal dysfunction Increase of U in urine: peak at 2mo, background level 3y after exposure

Early deterministic chemical toxicological effects

3. Human cases with Uranium

Kidney U conc (µg U/g kidney)	Acute renal effects	Predicted outcome
high	Possible severe clinical symptoms	likely to become ill
	Possible protracted indicators	may become ill
	Possible transient indicators	not likely to become ill
low	No detectable effects	no clinical effect

Roszell, 2009

- Distinguish biological effects from clinical effects
- It would be useful to have biomarkers of renal dysfunction: Retinol-Binding Protein, osteopontin but not significant
- Recovery

Conclusion

Internal contamination could provoke early deterministic effects with a high toxicity or even death

Conditions

- Nature of RN (alpha-emitters), isotope, route of intake and speciation, high dose and high-dose rate to body organs

Consequences

Damage or Cell killing, **Organ dysfunction, Organ failure, inflammatory reaction:** bone marrow, also in liver and kidney (with Po), lymphopenia, fibrosis in lymph nodes, lung fibrosis, (with Pu), renal tubular cells in the kidney (with U)

Fatal failure after short (days to several weeks) or long delay (months)
For 210-Po for example, bone marrow failure prevented, multiple organs damages could be fatal

Time distribution of effects depends on level of activity administered

Need

Biomarkers for early diagnosing biological effects to prevent health effects and predict potential recovery

Thank you for your attention