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# Medical Management and Treatment of Contaminated Patients

## Strategy for Individuals vs Mass Casualties

4<sup>th</sup> EURADOS Winter School

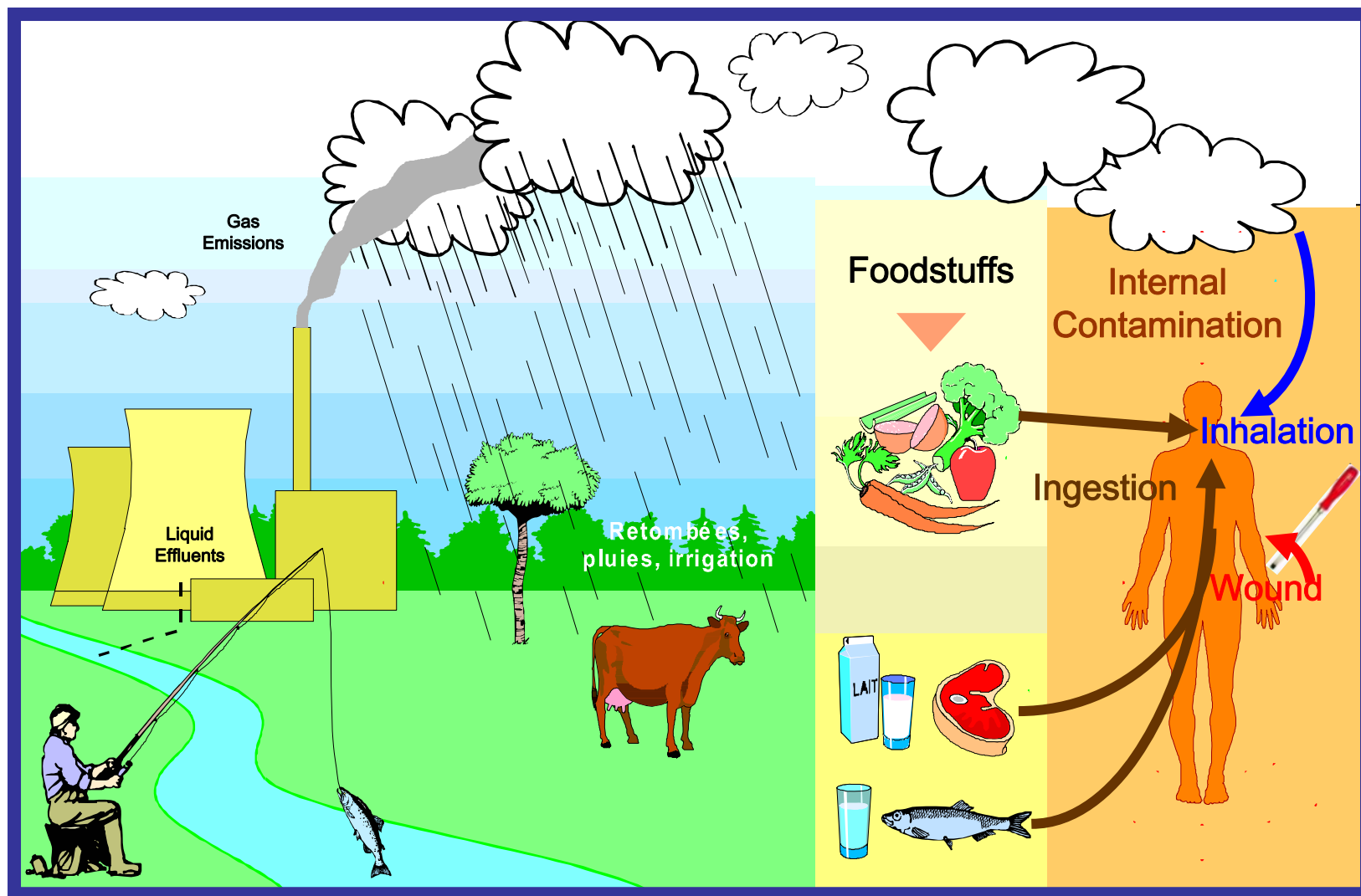
Radiological Emergencies – Internal Exposures

Rome, 3 February 2010

# Treatment of Contaminated Patients: Challenges

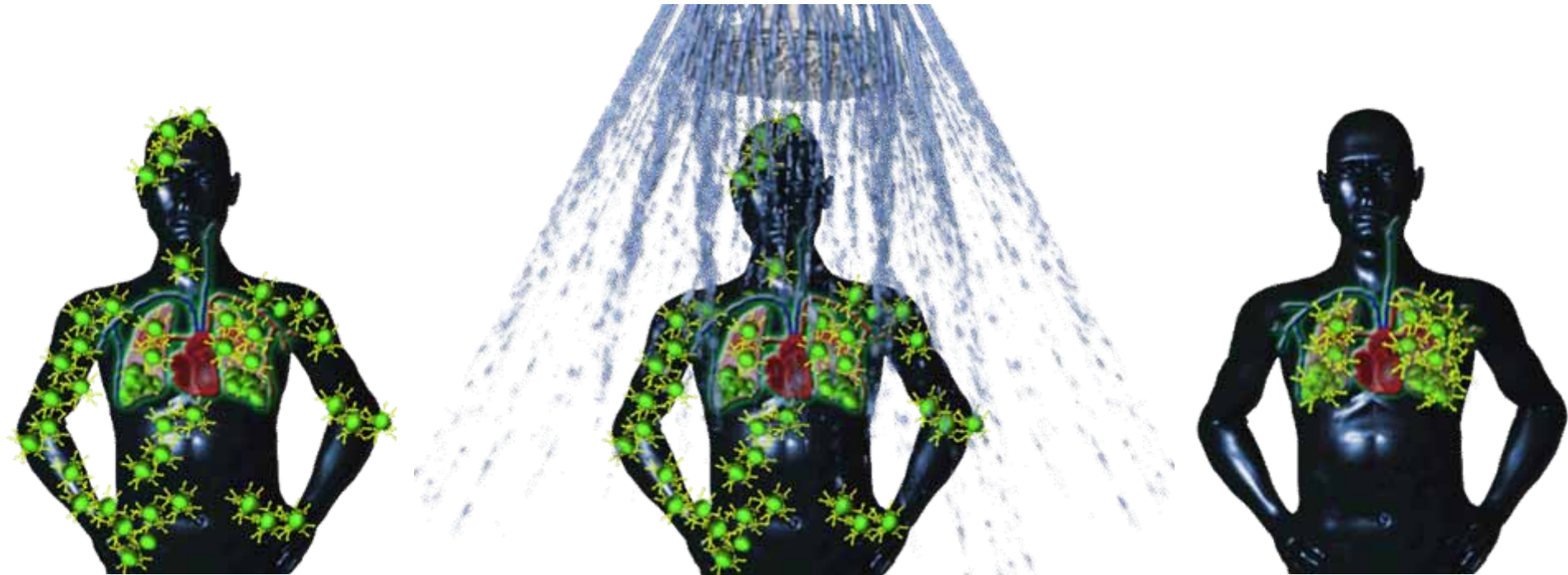
- Accidental radiation exposures are rare (hopefully)
- While some cases of irradiation have been extensively described, **very few cases of internal contamination are well-documented**
- Internal contamination **doesn't cause clinical symptoms**
- Incorporation is **time-dependant**, it can occur in minutes, or it can take days to months
- As long as radioactive materials are on or in a person, the person is being irradiated
- Very **few specific drugs are available**
- Occurrence of a possible internal contamination **may lead to a panic in the population** and stress disorders

# Internal Contamination Pathways



# Management of External Decontamination

- Remove contaminated clothing Efficacy:  $\pm$  80-90%
- Shower the casualties (hair also, but don't shave)
- Avoid aggressive agents that may compromise skin



# Treatment of Internal Contamination: Concepts

Reduce the absorption of the radionuclide

Increase the excretion of the radionuclide

- Decrease or avoid as possible the intestinal absorption
  - Aluminium phosphate limits the absorption of  $^{32}\text{P}$
- Saturate the target organ
  - Stable iodine competes with radioactive iodine
- Dilute the radionuclide
  - Tritium behaves like water
- Displace the radionuclide
  - Ca competes with Sr in binding with bone matrix
  - Sr-gluconate permits isotopic dilution of radioactive Sr
- Chelate or bind the radionuclide

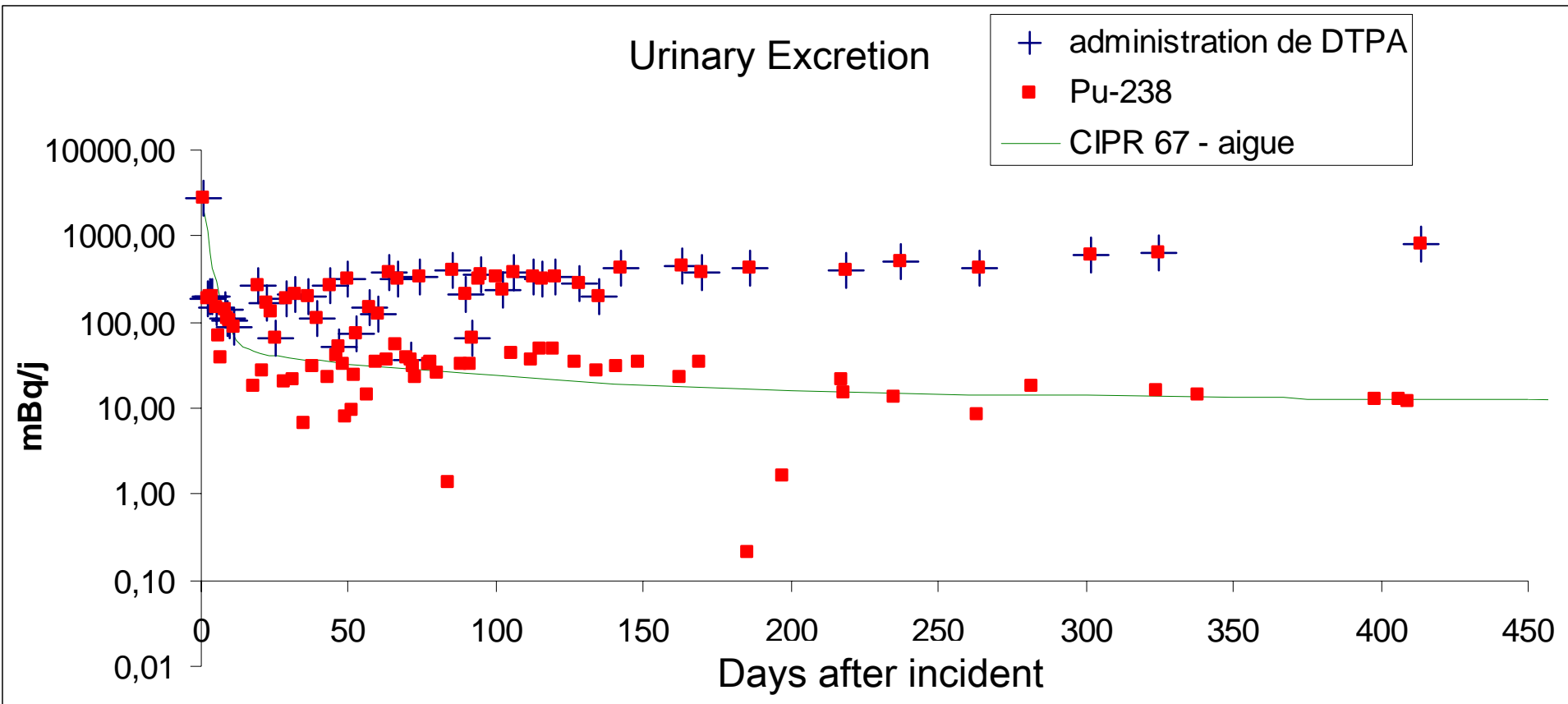
# Treatment of Internal Contamination: Chelation

- The chelating agent will bind or trap the radionuclide within the blood and/or target organs
- Once chelated, the radionuclide will be removed from the tissue/organ and will be urinary and/or fecally excreted
- **Major chelating agents:**
  - DTPA: trisodium diethylenetriamine pentaacetate
  - DMPS: dimercaptopropansulphonate
  - Succimer/DMSA: dimercapto succinic acid
  - EDTA: ethylenediaminetetraacetic acid
  - Penicillamine
  - BAL: dimercaprol

# Chelating Agents: DTPA

- Radionuclides: Pu, Transplutonics (e.g.,  $^{241}\text{Am}$ ), Np, Th, Ru, Ni, Rare Earths (e.g. Eu, Er, Gd), Y, Zr
- **DTPA should not be used for uranium decorporation**
- Therapeutic Scheme:
  - **IV administration**:
    - 1g in 250ml fluid (e.g., G5, NaCl) injected in 30min
    - 1g as undiluted DTPA 25% solution in slow IV push over 3-4min
    - Use Ca-DTPA the first day and alternate daily with Zn-DTPA to avoid calcium depletion
    - Use Zn-DTPA in pregnant women
  - **Inhalation**: nebulize with 4ml Ca-DTPA 25% solution diluted 1:1 with sterile water or normal saline solution

# Chelating Agents: DTPA



Urinary excretion of  $^{238}\text{Pu}$  (assessment made using IMBA software)

*From E. Blanchardon et al.*

# Other Chelating Agents (more: TMT Handbook)

Agent	Radionuclide	Therapeutic Scheme
DMPS	As, Bi, Au, Hg, Po	300mg 4 to 8 times a day (oral administration)
BAL	As, Bi, Au, Hg, Po DMPS should be preferred because of the BAL toxicity	2mg/kg deep IM 4 times/d for 2 days, then 2 times the 3rd day, then once a day for 5-10 days
DMSA	$^{210}\text{Pb}$ , $^{51}\text{Cr}$  (FDA approved pediatric dosing for lead poisoning)	10mg/kg every 8 hours for 5 days, then one dose every 12 hours the two following weeks (oral administration)

# Treatment of Internal Contamination: Others Agents

- **Water Diuresis for Tritium contamination**
  - Isotopic dilution, enhancement of excretion
  - 3-4 (up to 6-10) liters of liquid/day (orally, beer accepted!)
  - Alternative: up to 3 liters/day IV of G5 in water or saline solution (only if oral intake impossible)
  - **Duration: 5 days**
- **Prussian Blue for Cs/Tl/Rb contamination**
  - Inhibition of enterohepatic cycle, increase fecal excretion
  - Oral administration (Radiogardase)
  - Adults & adolescents: 3g/d in 3 doses (up to 10-12g/d)
  - Children: 1-1.5g/d in 3 doses
  - **Divides by a factor of 3 the half-life of Cs**
  - Successfully used in the Goiania accident
  - **Duration of treatment will depend of bioassay results**

# Treatment of Contaminated Wound

- Patients with wounds are of highest priority
- Objective: Avoid the entry of radionuclide and reduce the resorption rate
- Wash the wound with water or Ca-DTPA 25% solution for wounds contaminated with actinides (Pu)
- Spread 1g rodhizonate powder for wounds contaminated with strontium
- Surgical excision around wounds to remove contamination could be performed in extreme cases
- Avoid aggressive decontamination

# Stable Iodine Prophylaxis: Rationale

- In case of accident occurring in a NPP or detonation of a nuclear weapon, large amounts of radioactive iodines will be released to the atmosphere ( $^{131}\text{I}$  and shorter-lived isotopes)
- Iodine concentrates in the thyroid gland
- Thyroid cannot distinguish between radioactive and non-radioactive iodine
- Inhalation or ingestion of radioactive iodine can lead to radiation injury to the thyroid (e.g., thyroid cancer)
- Thyroid cancer risk is strongly age-related: fetuses, infants and children are at highest risk

# Stable Iodine Prophylaxis

- **Prophylaxis** is a measure designed to **preserve health and prevent the spread of a disease**
  - Stable iodine competes with radioactive iodines
  - Stable iodine prophylaxis will be used to limit the binding of radioactive iodine in the thyroid
  - **Stable iodine must be used rapidly (but not too fast!)**
- **Need for predistribution and local stockpiles**
- Stable iodine prophylaxis is being used also (mainly) to fight against dietary iodine deficiency (e.g., through salt iodization)

# Stable Iodine Prophylaxis: Dosage

Single dosage of stable iodine for different age groups  
(WHO recommendations, 1999 update)

Age Group	Mass of Iodine (mg)	Mass of KI (mg)	Mass of $\text{KIO}_3$ (mg)	Fraction of 100-mg tablet	Fraction of 50-mg tablet
Adults & adolescents (over 12 years old)	100	130	170	1	2
Children (3-12 years old)	50	65	85	$\frac{1}{2}$	1
Infants (1 month to 3 years old)	25	32	42	$\frac{1}{4}$	$\frac{1}{2}$
Neonates (birth to 1 month old)	12.5	16	21	$\frac{1}{8}$	$\frac{1}{4}$

# Stable Iodine Prophylaxis: Formulation

- **Tablet of 65-mg KI (50-mg I)** is the most frequently formulation met in the EU
- Some differences should be noted:
  - **2 countries use potassium iodate**
    - United Kingdom: 85-mg  $\text{KIO}_3$  (50-mg I)
    - The Netherlands: 170-mg  $\text{KIO}_3$  (100-mg I)
  - **4 countries use other formulations of KI tablet**
    - Finland, Spain, (France): 130-mg KI (100-mg I)
    - Poland: 32-mg KI (25-mg I)

→ **Need for a European harmonization**

# Stable Iodine Prophylaxis: WHO vs FDA

	Reference Level: Avertable Dose to the Thyroid (mGy)		Mass of KI (mg)		Mass of Iodine (mg)	
	WHO	FDA	WHO	FDA	WHO	FDA
Adults over 40 yrs	5,000	5,000	130	130	100	100
Adults over 18 through 40 yrs	100	100	130	130	100	100
Pregnant or lactating women*	10	50	130	130	100	100
Adolescents over 12 through 18 yrs	10	50	130	65	100	50
Children over 3 through 12 yrs	10	50	65	65	50	50
Infants 1 month through 3 yrs	10	50	32	32	25	25
Newborns from birth through 1 month**	10	50	16	16	12.5	12.5

# Major Adverse Effects Observed

- Molecules used for internal contamination treatment are safe and lead very rarely to side effects
- BAL and penicillamine are the more toxic drugs currently in use
- Hyper- or hypothyroidism (stable iodine)
- Allergy (stable iodine, DMPS, DMSA, penicillamine)
- Renal disorders (DMPS, penicillamine)
- Blood pressure disorders (DTPA, DFOA, Co-EDTA, Ca-gluconate)
- Modification of electrolyte balance (Prussian Blue,  $\text{NaHCO}_3$ , water diuresis)
- Constipation (Aluminium phosphate, Prussian Blue)

# Conclusion: Challenges for the Future

- Despite the fact that few drugs are commercially available, the principles for treating contamination with radioactive material are well known
- Pharmaceutical industry should engage in funding and performing research for the development of new drugs
- International arrangements should be defined to provide countries with stockpiles where/when needed
- Policy makers should think about specific procedures enabling healthcare providers to use nationally-non-approved drugs

→ More research and efficient international cooperation

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