

# Lovelace Respiratory Research Institute

## Medical Countermeasures for Treating Internal Deposits of Radionuclides

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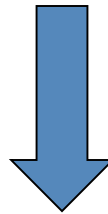
[www.LRRI.org](http://www.LRRI.org)



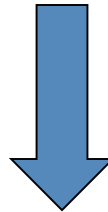
# Goal of Decorporation



**DECORPORATION**

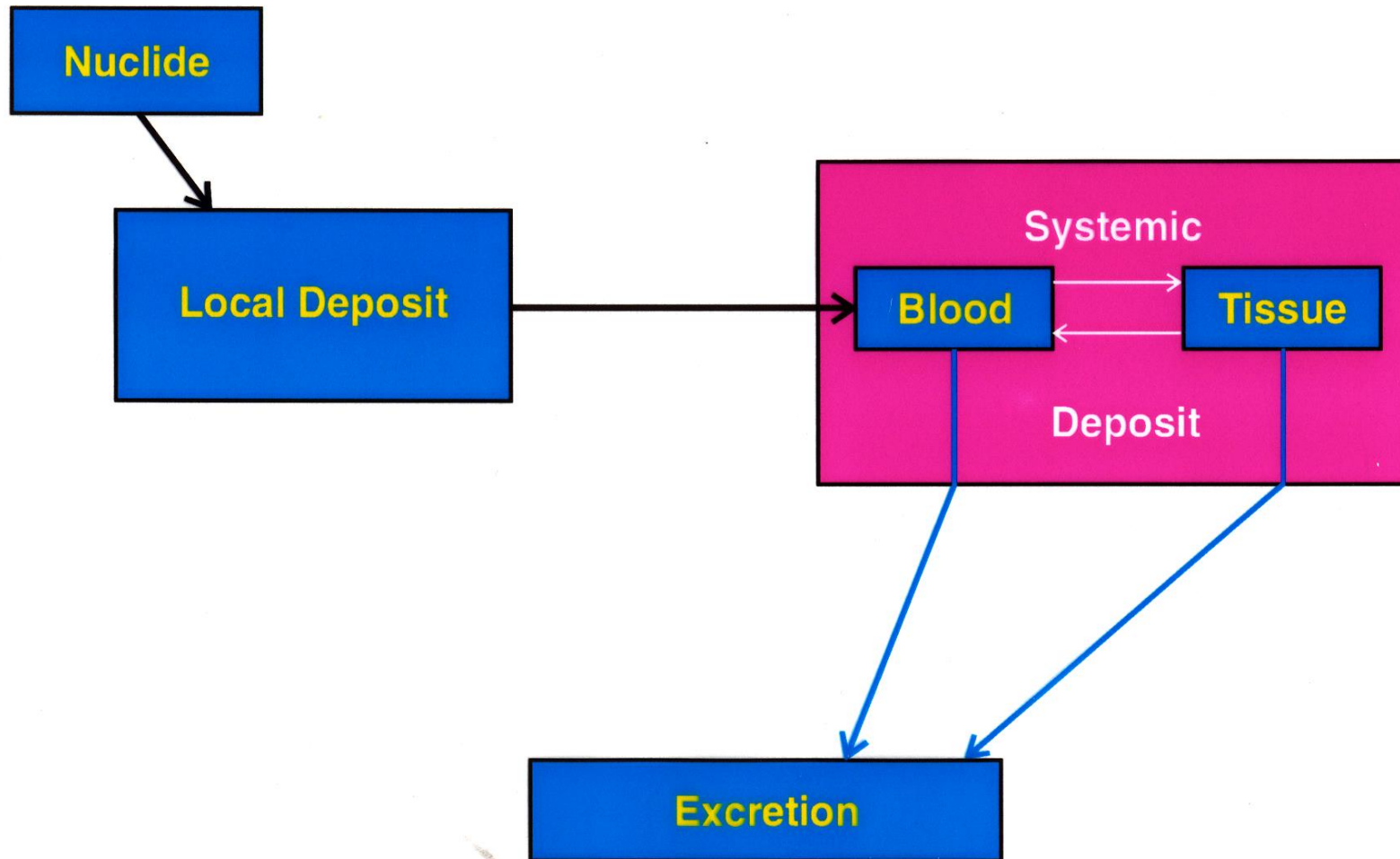


**DOSE REDUCTION**

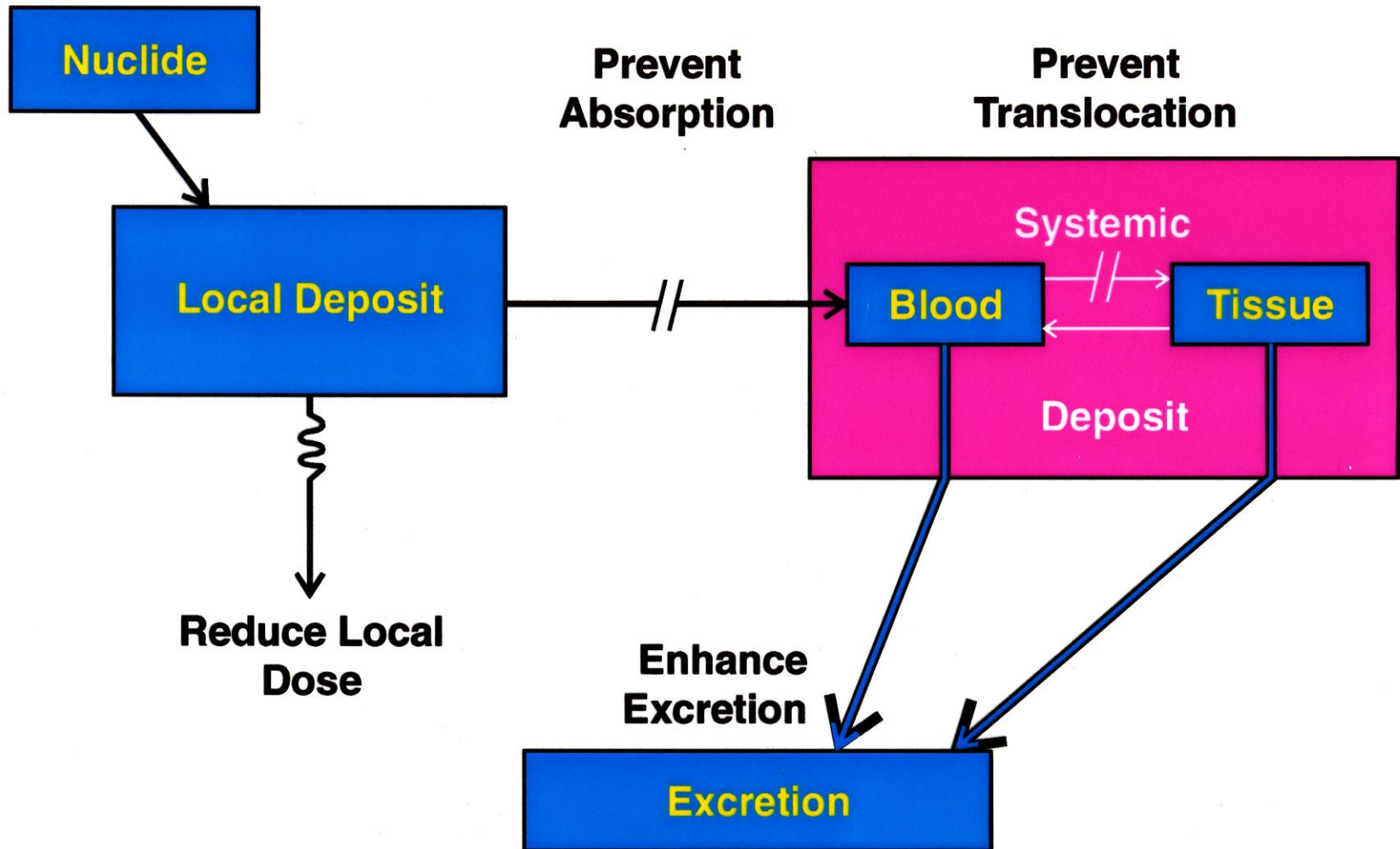


**RISK REDUCTION**

# Decorporation Strategy



# Decorporation Strategy



# Treatment Strategies for Highly Contaminated People



- **Chemical Methods for Soluble Materials**
  - **Blocking agents (KI)**
  - **Isotopic dilution (Ca, Zn, K)**
  - **Ion exchange (Prussian Blue, alginates)**
  - **Chelating agents**
    - **EDTA (Pb, Zn, Cu, Cd, Cr, Mn, Ni)**
    - **DTPA (Pu, Am, Cm, Lanthanides)**
    - **DMSA, DMPS, BAL (Hg, Pb, Cd, As, Au, Po)**
- **BARDA stockpile (USA)**

# Some Consensus Guidance



NCRP REPORT No. 65

**MANAGEMENT  
OF PERSONS  
ACCIDENTALLY  
CONTAMINATED WITH  
RADIONUCLIDES**



National Council on Radiation Protection and Measurements

## Radiation Protection Dosimetry

### GUIDEBOOK FOR THE TREATMENT OF ACCIDENTAL INTERNAL RADIONUCLIDE CONTAMINATION OF WORKERS

A Joint Publication for the  
Commission of the European Communities  
Directorate-General for Science, Research and Development  
Radiation Protection Programme  
and the  
US Department of Energy  
Office of Health and Environmental Research

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NCRP REPORT No. 161

**MANAGEMENT OF  
PERSONS  
CONTAMINATED WITH  
RADIONUCLIDES:  
HANDBOOK**



# Features of DTPA (diethylenetriaminepentaacetic acid)



- **Ca and Zn chelates (Ca better on day 1)**
- **Administered dose: 30  $\mu\text{mole kg}^{-1}$  (1 g per 70 kg)**
- **Accepted routes of administration**
  - **Intravenous injection or infusion**
  - **Nebulized DTPA solution**
- **GI absorption: about 3%**
- **Effective for Th, Pu, Am, Cm, Cf**
  - **Not U, Np**
- **Matching drug and actinide biokinetics is key to successful decorporation**

# Example of DTPA Efficacy in Humans



- **1976 Hanford  $^{241}\text{Am}$  accident in which one worker received an intake of about 200 MBq**
- **DTPA treatment begun within 2 h of exposure; multiple treatments daily over first weeks, daily for about 1 y, then more separated.**
  - **583 g administered 1976-1980**
- **Surgery plus daily surface decon during first week**
  - **185 MBq → 14 MBq in 10 d**
- **Total excretion:**
  - **41 MBq (half in first 3 d)**
  - **80% in urine**
  - **98% in 1 y**
- **About 99% dose sparing to systemic organs**



# Issues and Research with Actinide Decorporation



- **Oral forms:**
  - **Need for stockpiling**
- **Targeting intracellular deposits:**
  - **Liposomes**
- **Targeting inhaled deposited radionuclides:**
  - **Aerosols**
- **Need for better chelating agents?**

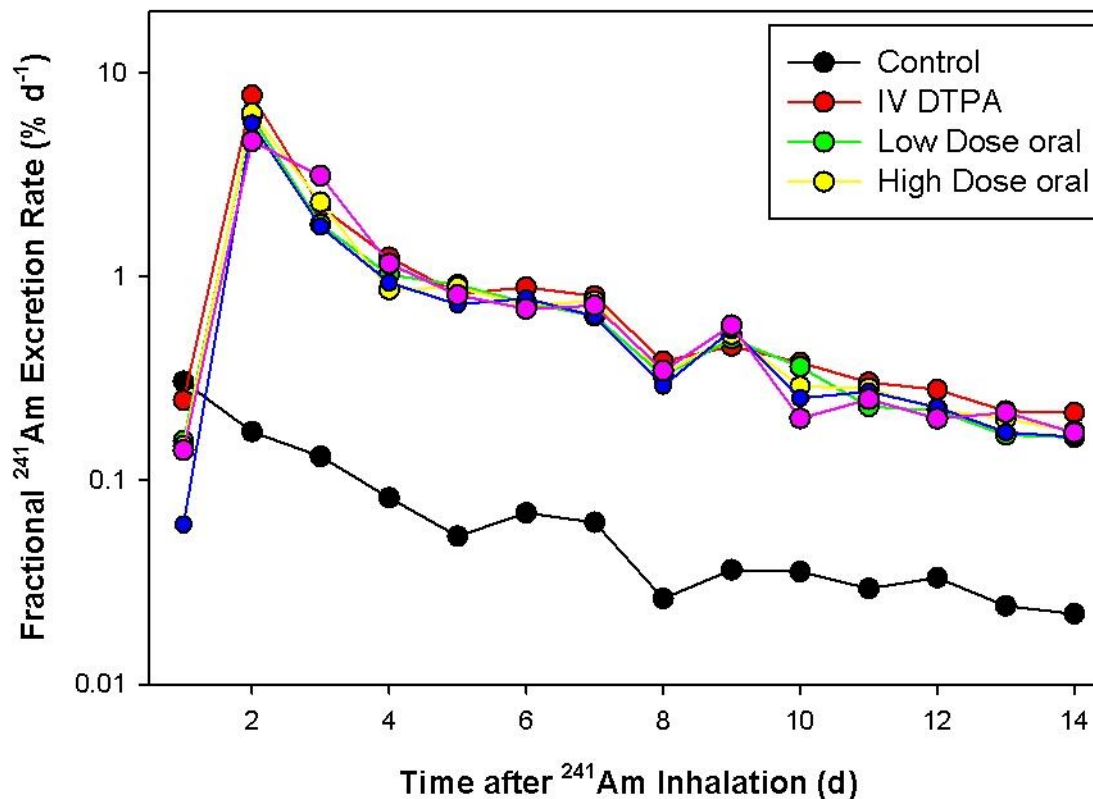
# Efficacy of an Oral Formulation of DTPA



- Rats given single inhaled dose of  $^{241}\text{Am}(\text{NO}_3)_3$
- CaDTPA at 1 d
- Either IV or oral (high and low dose) ZnDTPA daily through 7d
- Sacrifice at 14 d
- Material balance design (>90% recovery)

# Efficacy of Oral Formulation of DTPA for Decorporating Am-241 In Rats

Excretion of  $^{241}\text{Am}$  Excreted in Urine in Rats That Inhaled Am-Nitrate

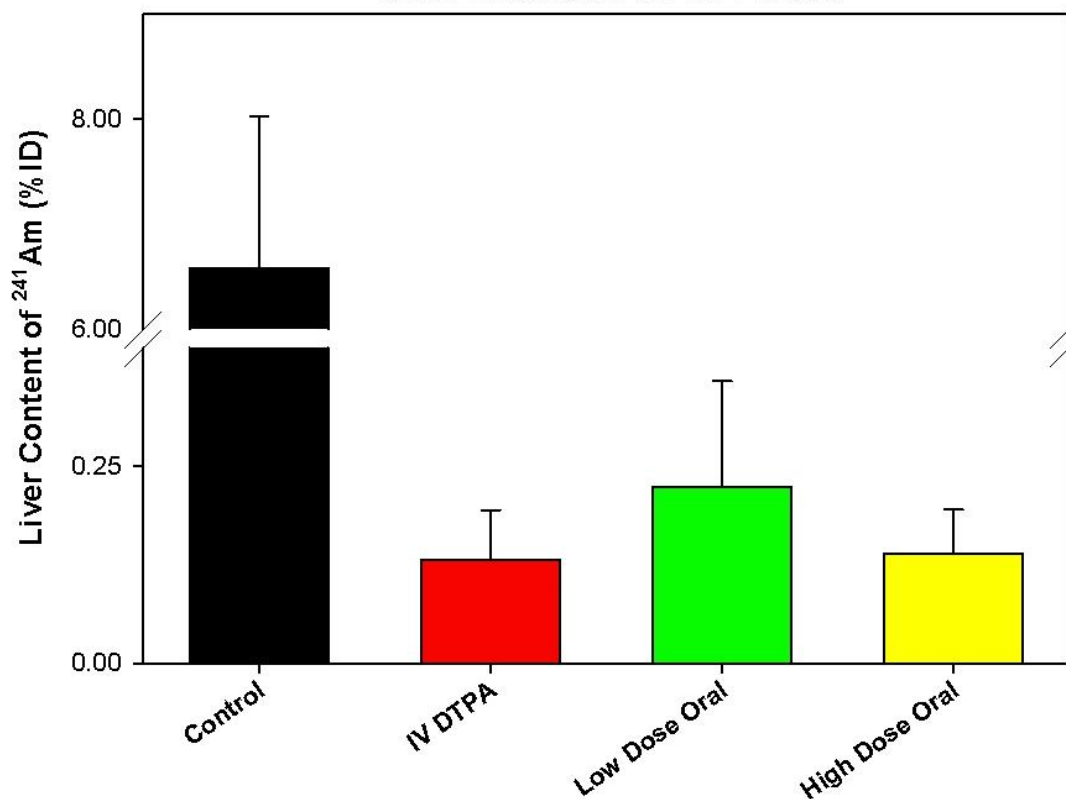


(proprietary data)

# Efficacy of Oral Formulation of DTPA for Decorporating Am-241 In Rats



Liver Retention of  $^{241}\text{Am}$  in Rats 14 Days after Inhalation of Am-Nitrate



Treatments daily on d 1-7; sacrifice on d 14

(proprietary data)

# Enhancing Intracellular Uptake of DTPA for Decorporation



- **$^{238}\text{Pu}$ -citrate injected IV in rats**
- **DTPA (free, or conventional or “stealth” liposome) @ 2 h**
- **At 16 d:**

<b>Sample</b>	<b>Ctrl</b>	<b>Free</b>	<b>Lip(conv)</b>	<b>Lip(stlth)</b>
<b>Liver</b>	<b>4.8</b>	<b>3.6</b>	<b>1.5</b>	<b>2.6</b>
<b>Bone</b>	<b>63</b>	<b>50</b>	<b>45</b>	<b>42</b>
<b>Urine</b>	<b>7</b>	<b>16</b>	<b>25</b>	<b>22</b>

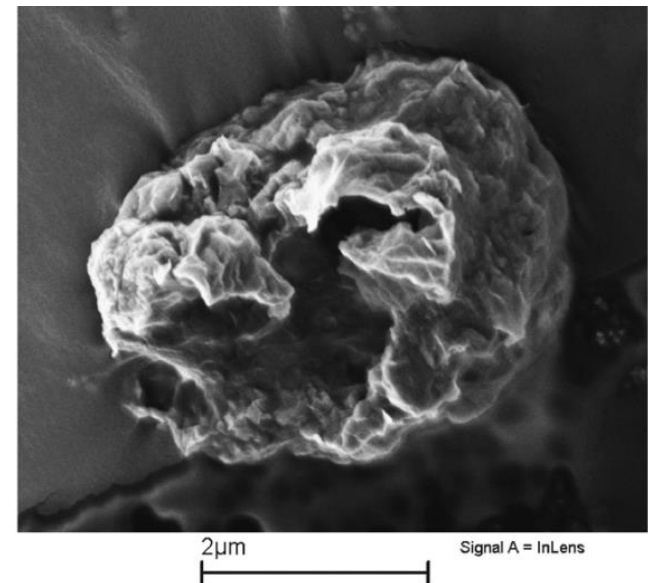
- **Prolonged retention of stealth liposomes; increased intracellular uptake**

Phan et al. 2004

# Targeting Inhaled Actinide in Lung

- Dry powder DTPA powder
- Insufflated into rats exposed to  $^{238}\text{Pu}$ -nitrate 2 h or 7 d previous

	% Initial Lung Dose		
	Lung	Bone	Liver
<b>Control</b>	<b>32</b>	<b>30</b>	<b>2.3</b>
<b>DTPA-iv (1h)</b>	<b>25</b>	<b>24</b>	<b>1.2</b>
<b>DTPA-aer (1h)</b>	<b>8</b>	<b>16</b>	<b>1.0</b>
<b>DTPA-iv (7d)</b>	<b>27</b>	<b>26</b>	<b>1.1</b>
<b>DTPA-aer (7d)</b>	<b>19</b>	<b>30</b>	<b>1.2</b>



# Efficacy of LBNL HOPO Compounds for Decorporating Pu-239 in Dogs

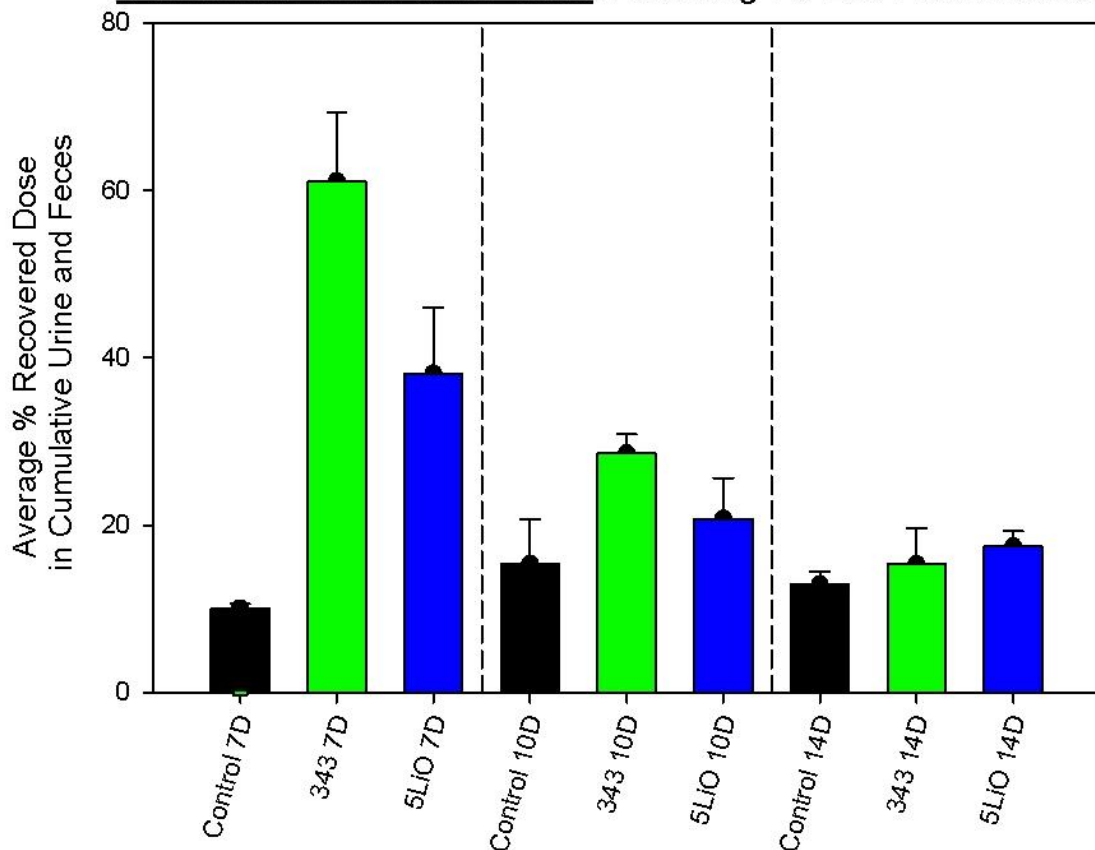


- **Groups of 3 female dogs**
- **Single IV injection of  $^{239}\text{Pu}$ -citrate**
- **3,4,3 Li[1,2 HOPO] (octadentate) or 5-LiO[Me 3,2 HOPO] (tetradentate) ligands**
  - **Single oral administration given at 0.5, 3, 7 days after Pu**
  - **3,4,3 Li[1,2 HOPO] @100  $\mu\text{mole}/\text{kg}$ ; 5-LiO[Me 3,2 HOPO] @300  $\mu\text{mole}/\text{kg}$**
- **Sacrifice 7 days after therapy**
- **Material balance design (about 87% average recovery)**

# Efficacy of LBNL HOP0 Compounds for Decorporating Pu-239 in Dogs



Average % Recovered Dose in Cumulative  
Combined Urine and Feces Following Pu-239 Administration

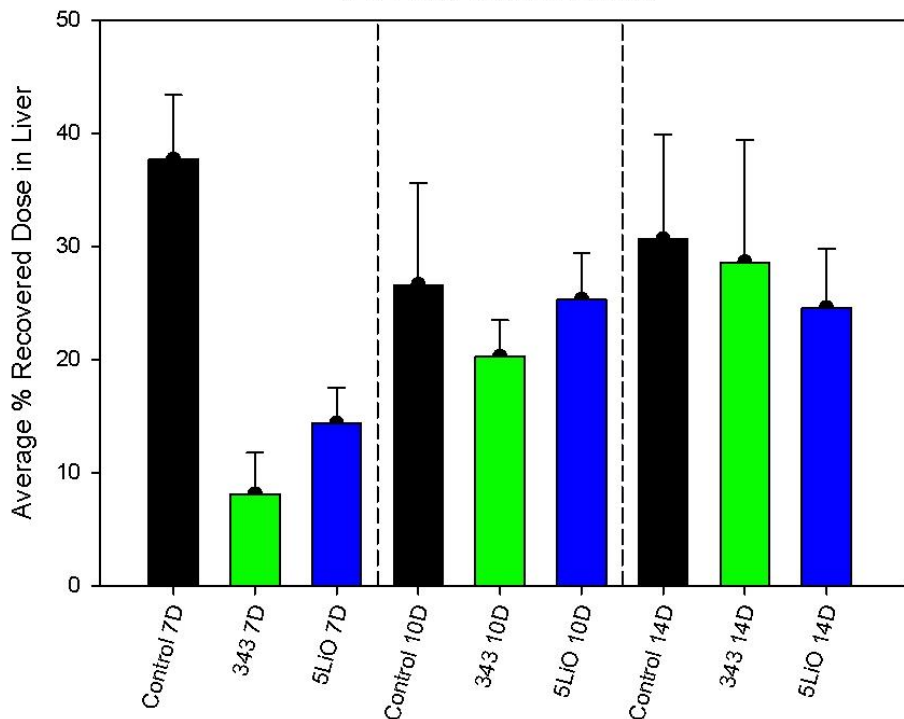




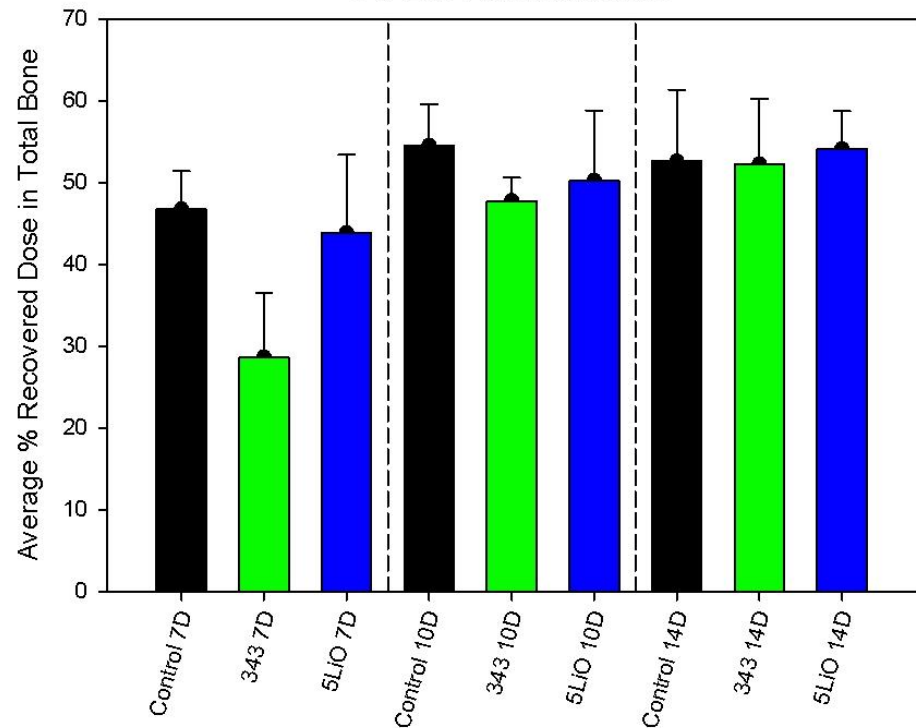
# Efficacy of LBNL HOP0 Compounds for Decorporating Pu-239 in Dogs



Average % Recovered Dose in Liver Following Pu-239 Administration



Average % Recovered Dose in Total Bone Following Pu-239 Administration



- **For trivalent and tetravalent actinides, good treatments exist using DTPA**
- **Recent research seeks to improve efficacy and ease of administration by:**
  - **Oral formulation**
  - **Dry powder aerosols for inhaled radionuclide**
  - **Enhancing intracellular uptake**
  - **Demonstrating new compounds**
- **Chelators for other radionuclides needed:**
  - **For example, Co, Sr, Ir, Po, Ra**
  - **Pediatric formulations needed**

# Sustained Action of DTPA for Decorporating Pu in Humans

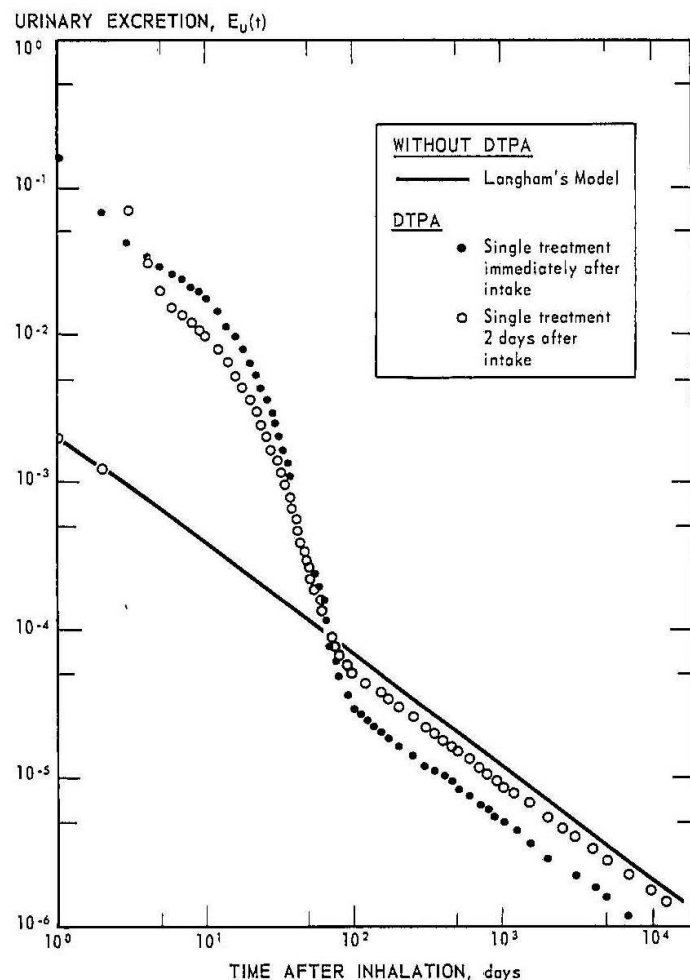


FIG. 3. Comparison of predicted urinary excretion rates after acute intake of transportable plutonium with DTPA administered immediately and 2 days after contamination.

# TREATMENT STRATEGIES FOR HIGHLY CONTAMINATED PEOPLE



## **Reduce the dose to be received by accelerating radionuclide removal**

- **Physical Methods for Insoluble Materials**
  - **Skin decontamination**
  - **Nasal irrigation**
  - **Emetics, gastric lavage, purgatives**
  - **Surgical excision**
  - **Bronchopulmonary lavage**