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The NIAID Radiation Nuclear Countermeasures and Biodosimetry Development Program: An OVerview

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DAIT/NIAID/NIH

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Environmental Chemistry Laboratories, Berkeley

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DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

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- *This material is presented from my own perspective, and should not be taken as representing the viewpoint of the Department, NIH, or NIAID.*

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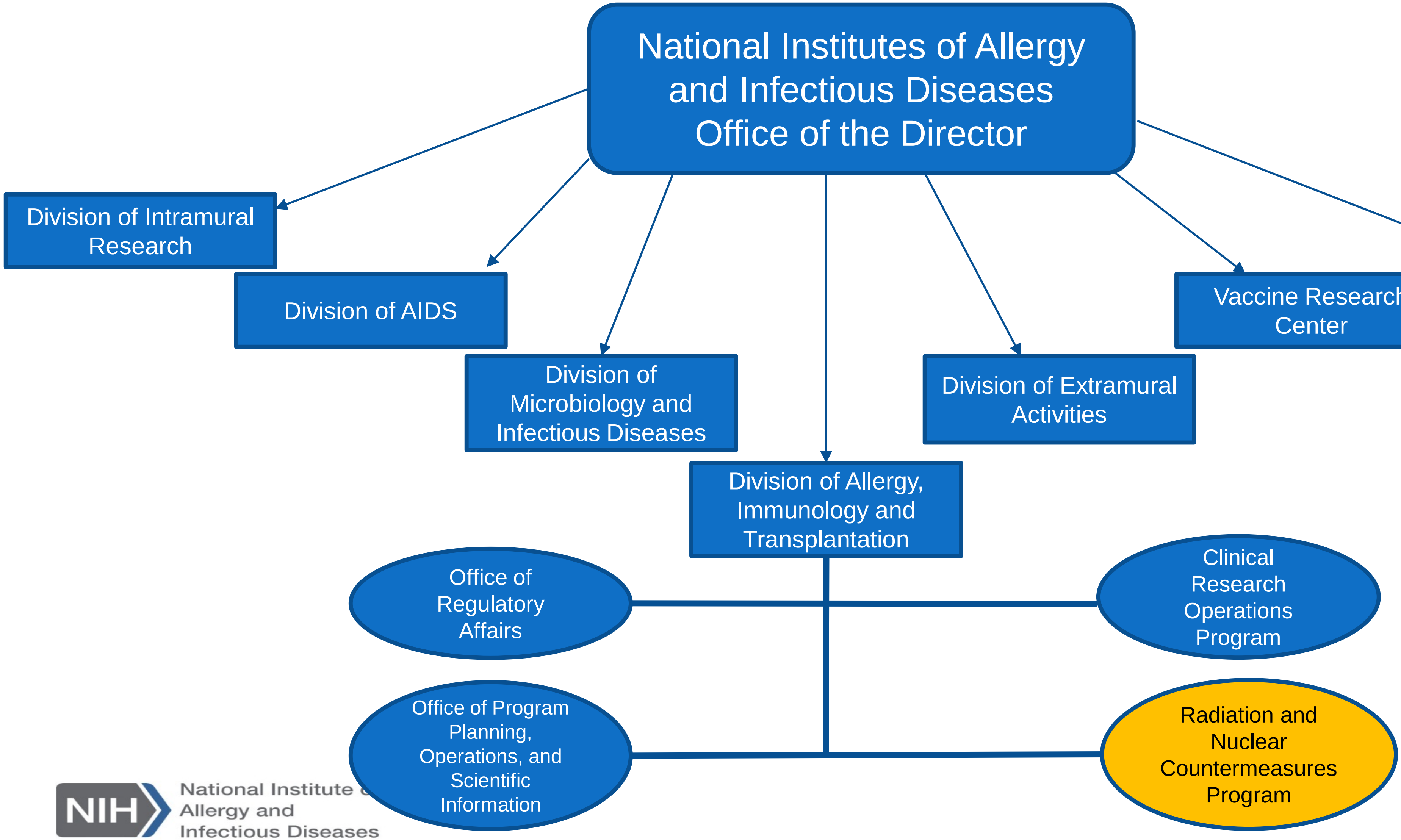
NIAID-RNCP Architecture: Who are we?



NIAID-RNCP: Our Mission

In 2004, NIAID was directed by HHS to foster a research program to accelerate development of radiation/nuclear medical countermeasures (MCMs) for the Strategic National Stockpile.

Mission:

- Support early to mid-stage research to develop radiation/nuclear MCMs and biodosimetry devices
- Provide funding opportunities:
  - Grants, collaborative agreements, contracts, inter- and intra-agency agreements

Sources of Environmental Radiation Contamination

- Natural sources:
  - Cosmic Radiation (Uranium, Thorium)
  - Terrestrial Radiation (Uranium, Actinium, Thorium series)
  - Internal Radiation (Soil, water, vegetation-Uranium, thorium, Radon)
- Man-made sources:
  - Radioactive material in medicine (Diagnostics, therapeutics, research)
  - Industry
  - Nuclear industry
  - Nuclear warfare

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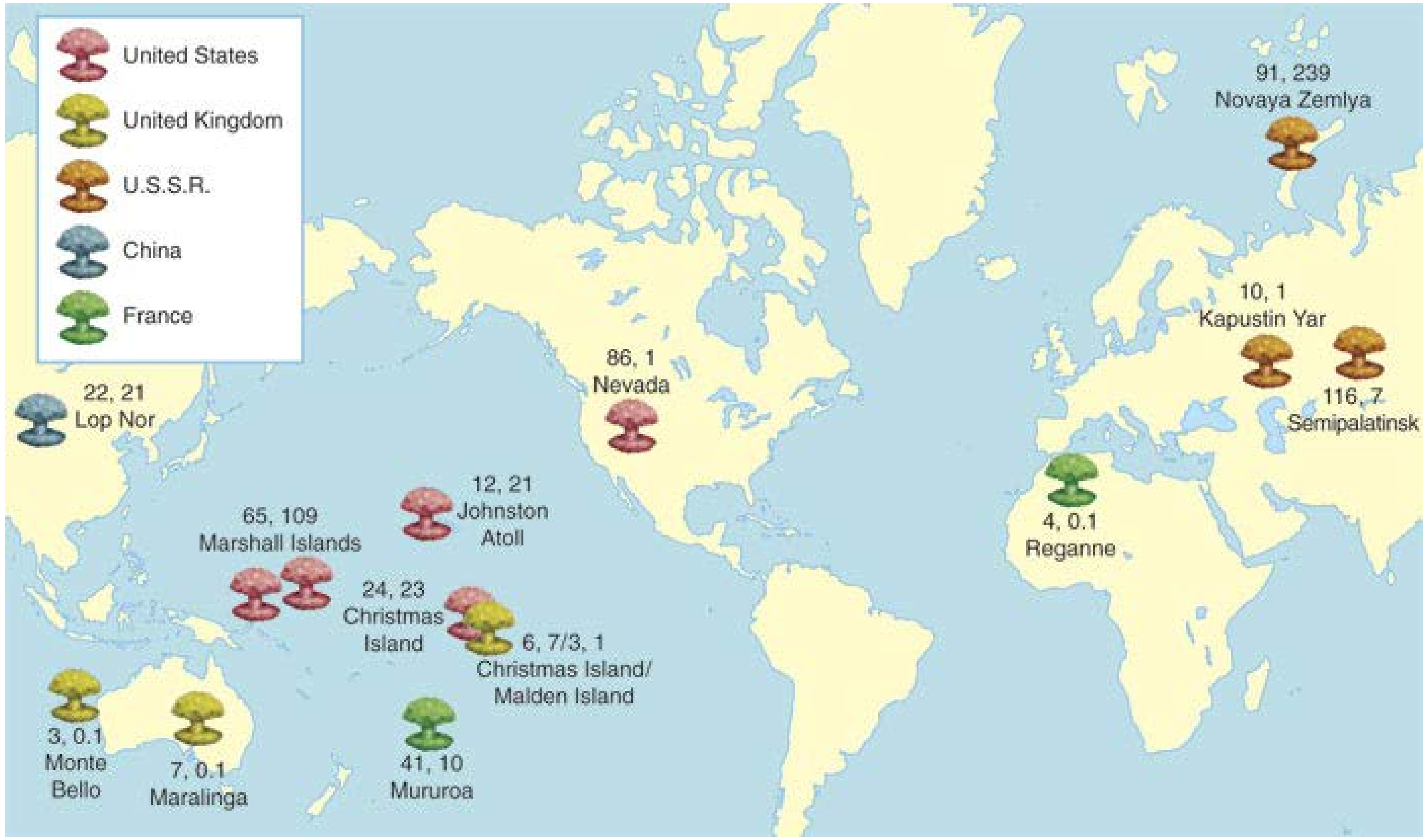
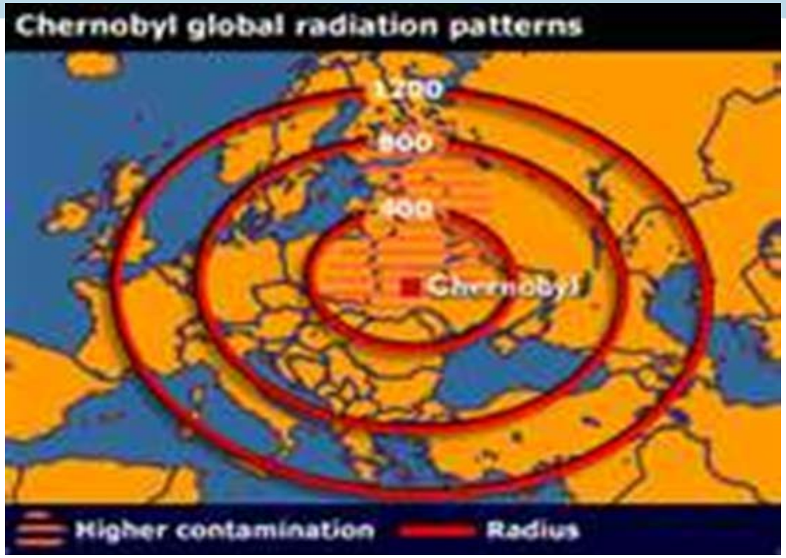
Background radiation

Man-made radiation





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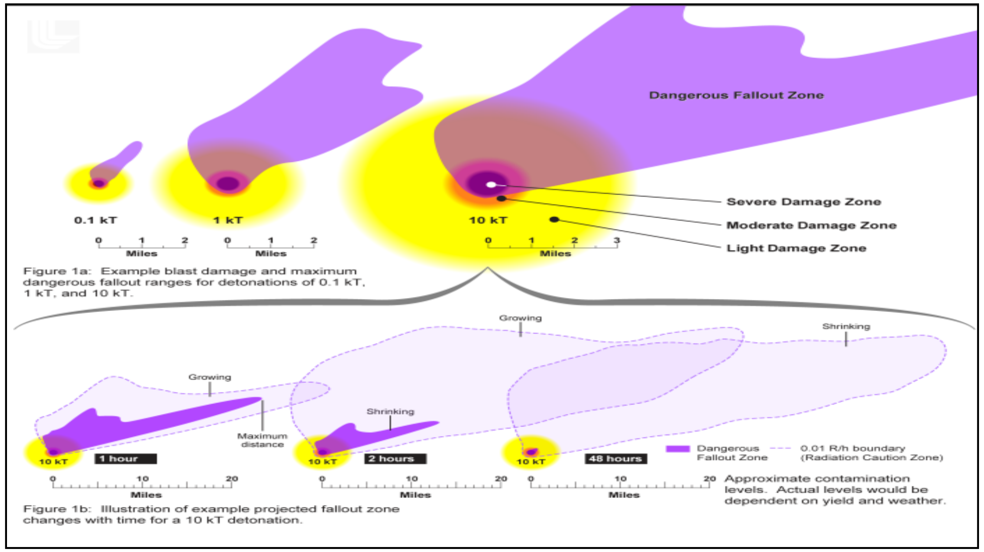
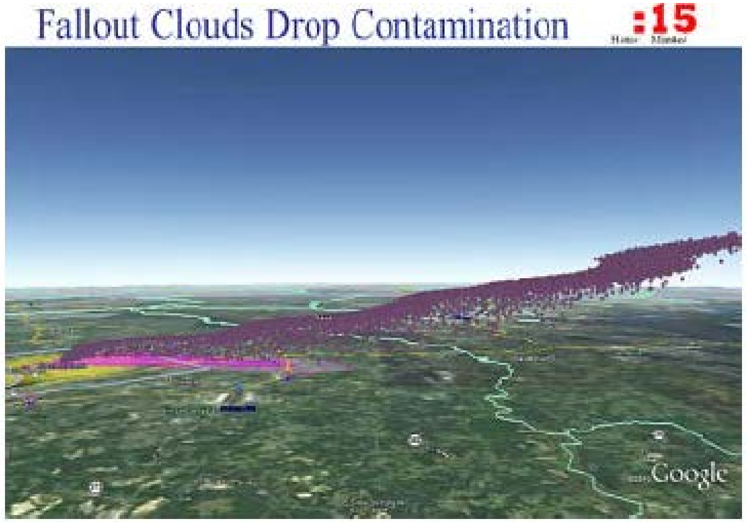
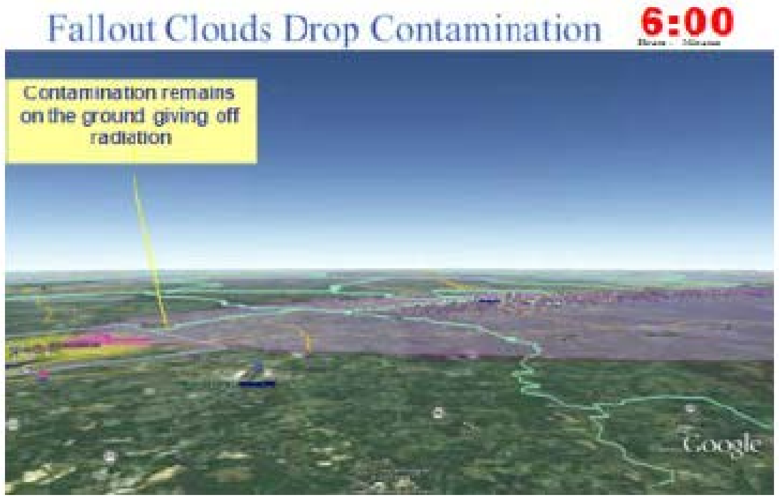
Fallout pattern after a radiological event

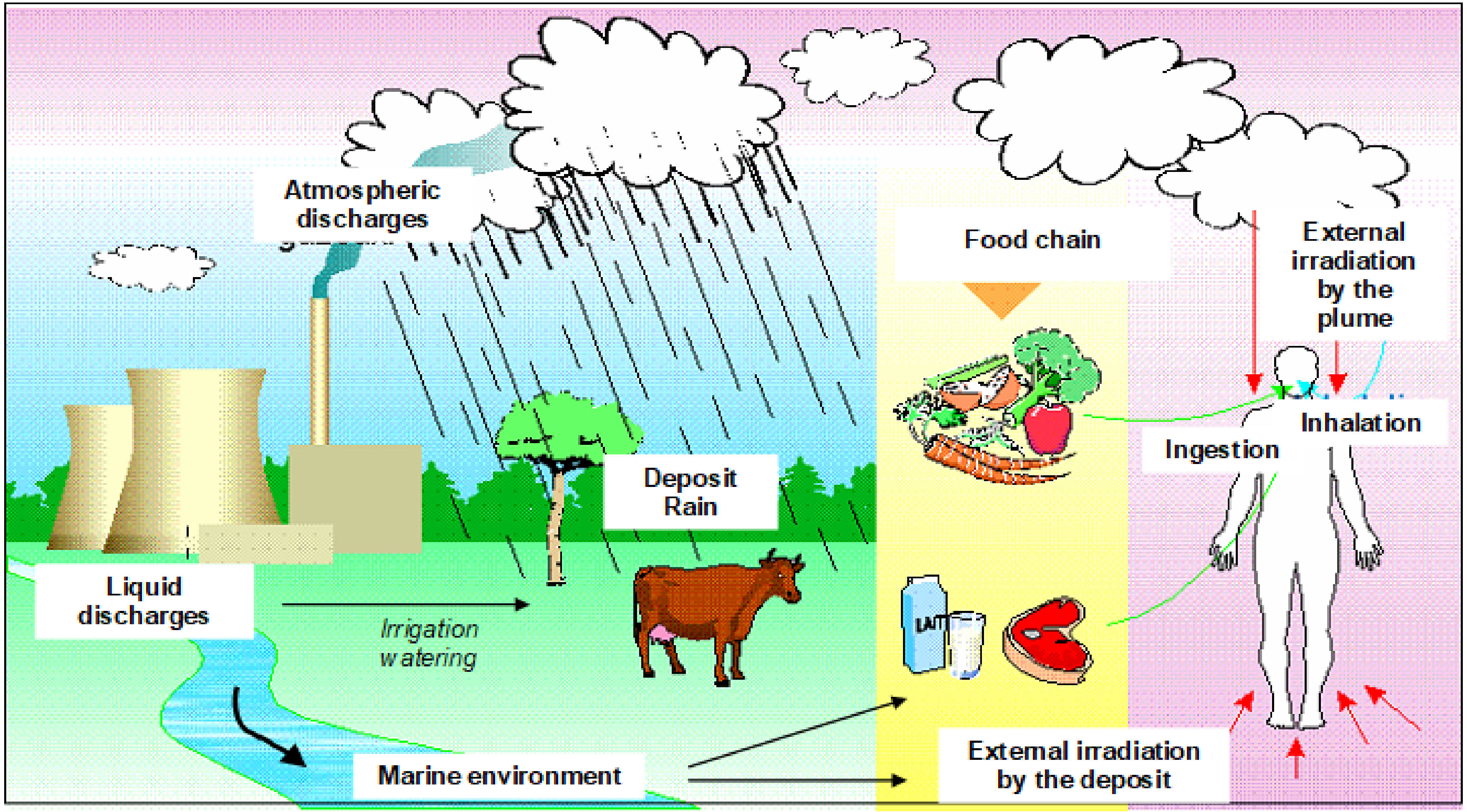




View from the South, 15 minutes after detonation



Impact of a large scale radiological incident



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Medical intervention is a small aspect of the enormous problem…..

Important aspects of fallout

- Fallout decay rapidly- Releasees more than half its energy in the first hour
- Primary hazard is exposure to deeply penetrating particulate radiation
- Fallout is visible- such as salt or sand
- Fallout is not a significant inhalation hazard

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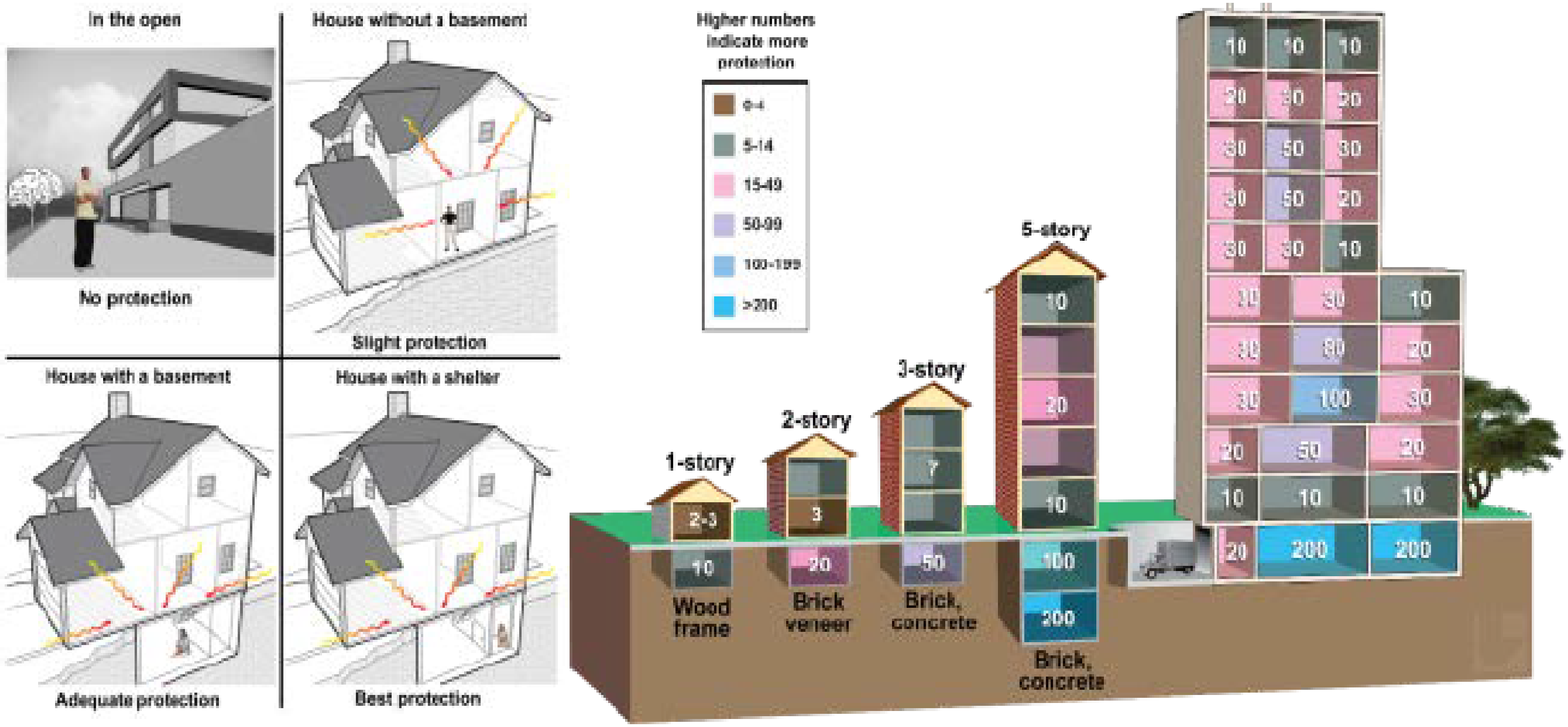
Primary consideration for fallouts: human safety



A protection factor of just 10 or higher is considered adequate protection against fallout radiation. For simple, wood frame houses, just going into a basement is enough to offer adequate protection. For those in large office or apartment buildings, going into the center of the building or deep underground offers very high levels of protection against radiation.

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Fallout results in exposure over long distance…

However fallout comprises of a complex mixture of radioactive isotopes with different half lives

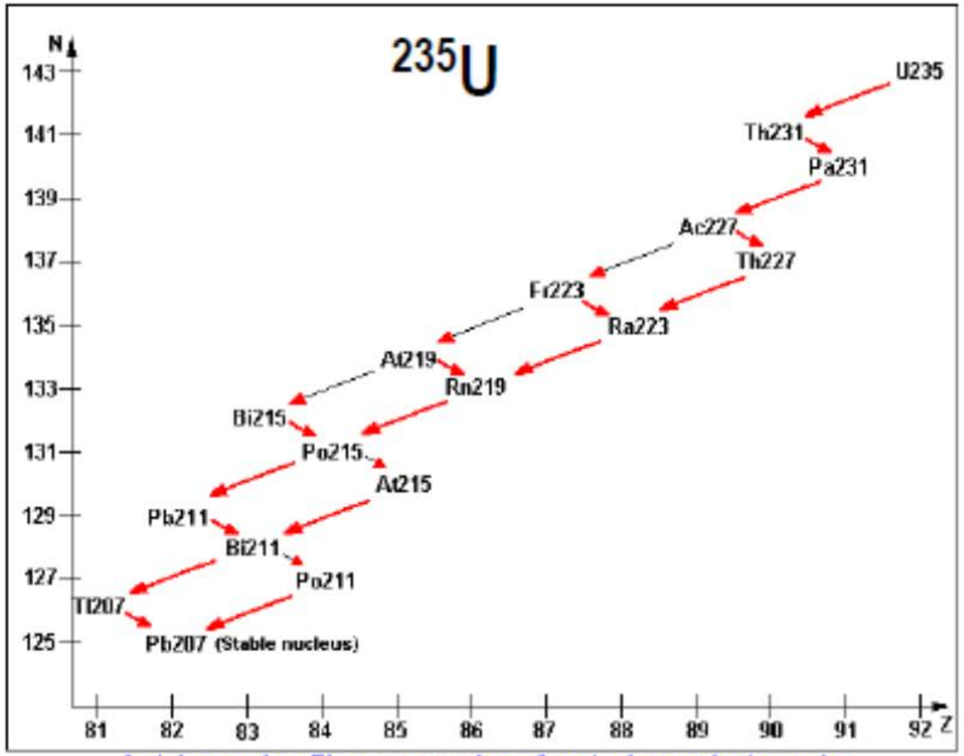
Nuclide	Half-life	Nuclide	Half-life
^{55}Fe[a]	2.7 a	^{127}Sb	3.9 d
^{64}Cu[a]	13 h	^{129}Te	70 min
^{77}As	39 h	^{129}Sb	4.4 h
^{83}Br	2.4 h	^{131m}Te	30 h
^{88}Rb	18 min	^{131}I	8.0 d
^{89}Sr	51 d	^{132}Te	78 h
^{90}Sr	29 a	^{132}I	2.3 h
^{90}Y	64 h	^{133m}Te	55 min
^{91}Sr	9.6 h	^{133}I	21 h
^{91m}Y	50 min	^{135}I	6.6 h
^{92}Sr	2.7 h	^{137}Cs	30 a
^{92}Y	3.5 h	^{139}Ba	83 min
^{93}Y	10 h	^{140}Ba	13 d
^{95}Zr	64 d	^{140}La	1.7 d
^{95}Nb	35 d	^{141}La	3.9 h
^{97}Zr	17 h	^{141}Ce	33 d
^{97m}Nb	53 s	^{142}La	91 min
^{99}Mo	66 h	^{143}Ce	33 h
^{99m}Tc	6.0 h	^{143}Pr	14 d
^{103}Ru	39 d	^{144}Ce	280 d
^{103m}Rh	56 min	^{144}Pr	17 min
^{105}Ru	4.4 h	^{145}Pr	6.0 h
^{105}Rh	35 h	^{147}Nd	11 d
^{106}Ru	370 d	^{149}Pm	53 h
^{109}Pd	14 h	^{149}Nd	1.7 h
^{112}Ag	3.1 h	^{151}Pm	28 h
^{115}Cd	53 h	^{153}Sm	46 h
^{117}Cd	2.5 h	^{237}U[a]	6.8 d
^{117m}In	2.0 h	^{240}U[a]	14 h
^{121}Sn	27 h	^{240m}Np[a]	7.2 min
^{125}Sb	2.8 a	^{239}Np[a]	2.4 d
^{127}Sn	2.1 h	$^{239+240}Pu$[b]	24,000/6,600 a

[a] Activation product.
[b] Fuel material. Only cumulative depositions and intakes over all tests were estimated.

Half-lives of radioactive Fe, Sb, Cs, and Pu are several years

Why does Fallout matter?

RADIOACTIVE DECAY CAN INVOLVE MANY STEPS BEFORE A STABLE SPECIES IS FORMED



Actinium series. The mass number of each element in the series is equal 4n+2. Where n is a positive integer.

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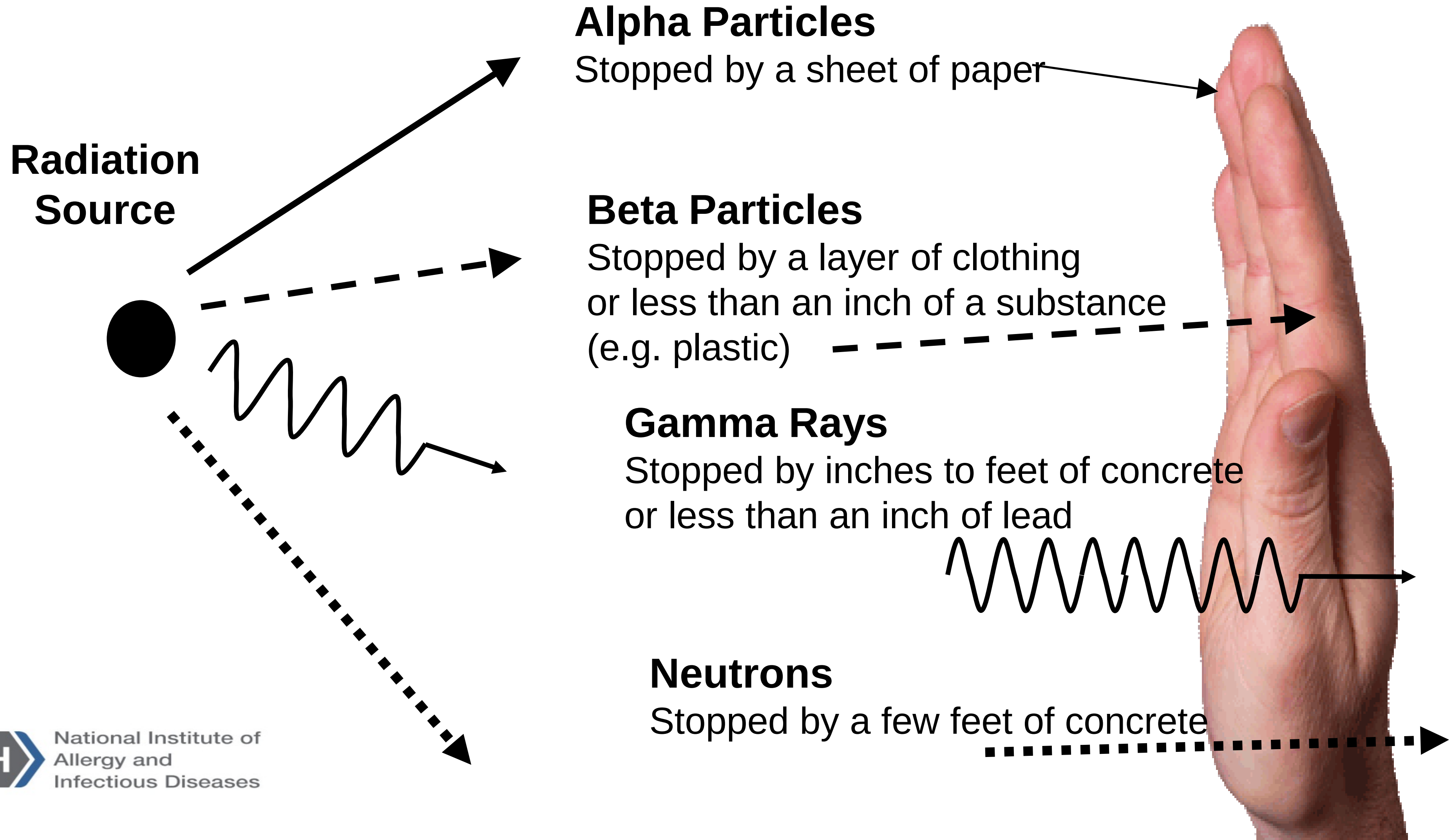
Penetration abilities of different types of radiation



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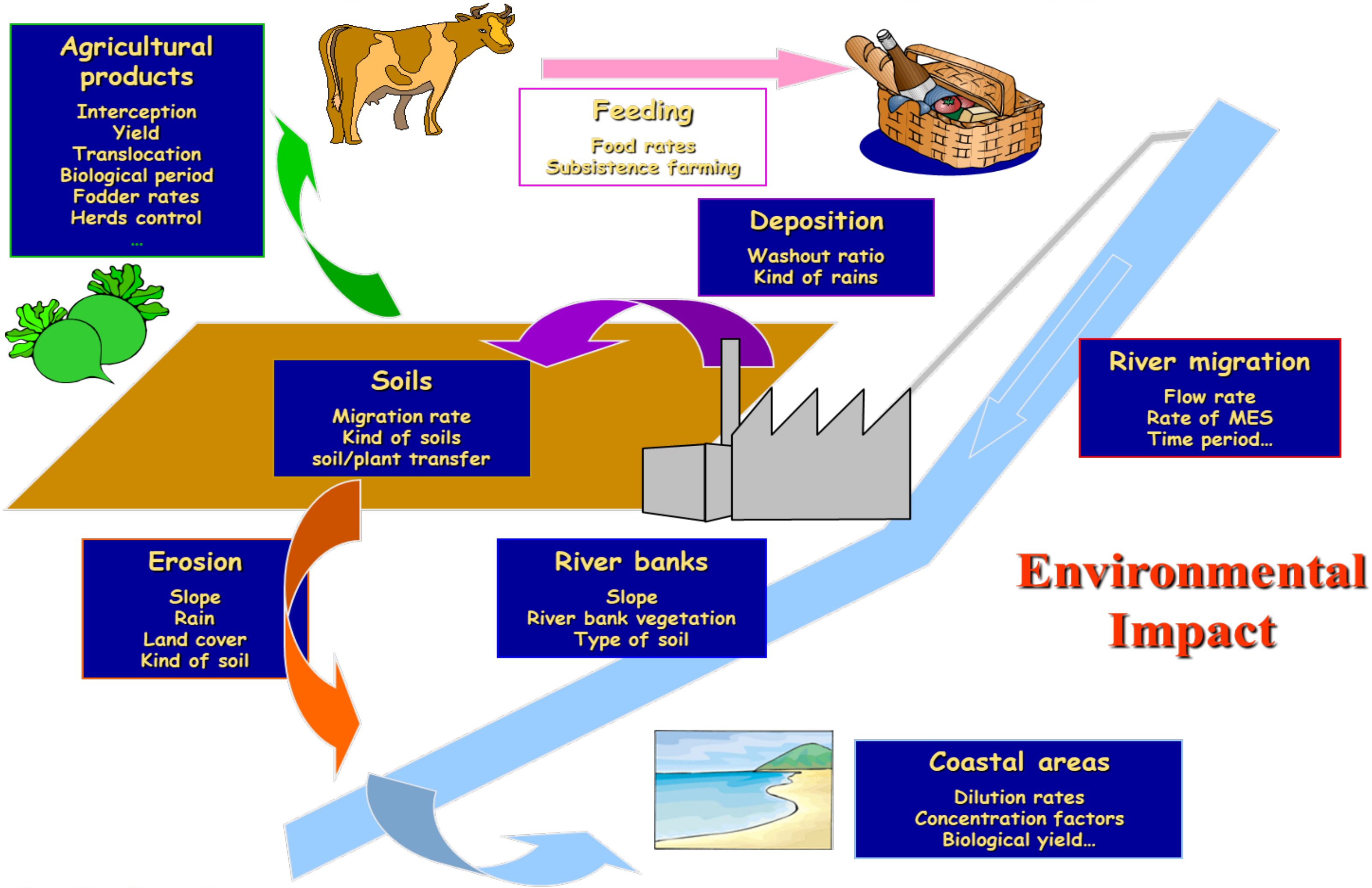
Impact on the environment



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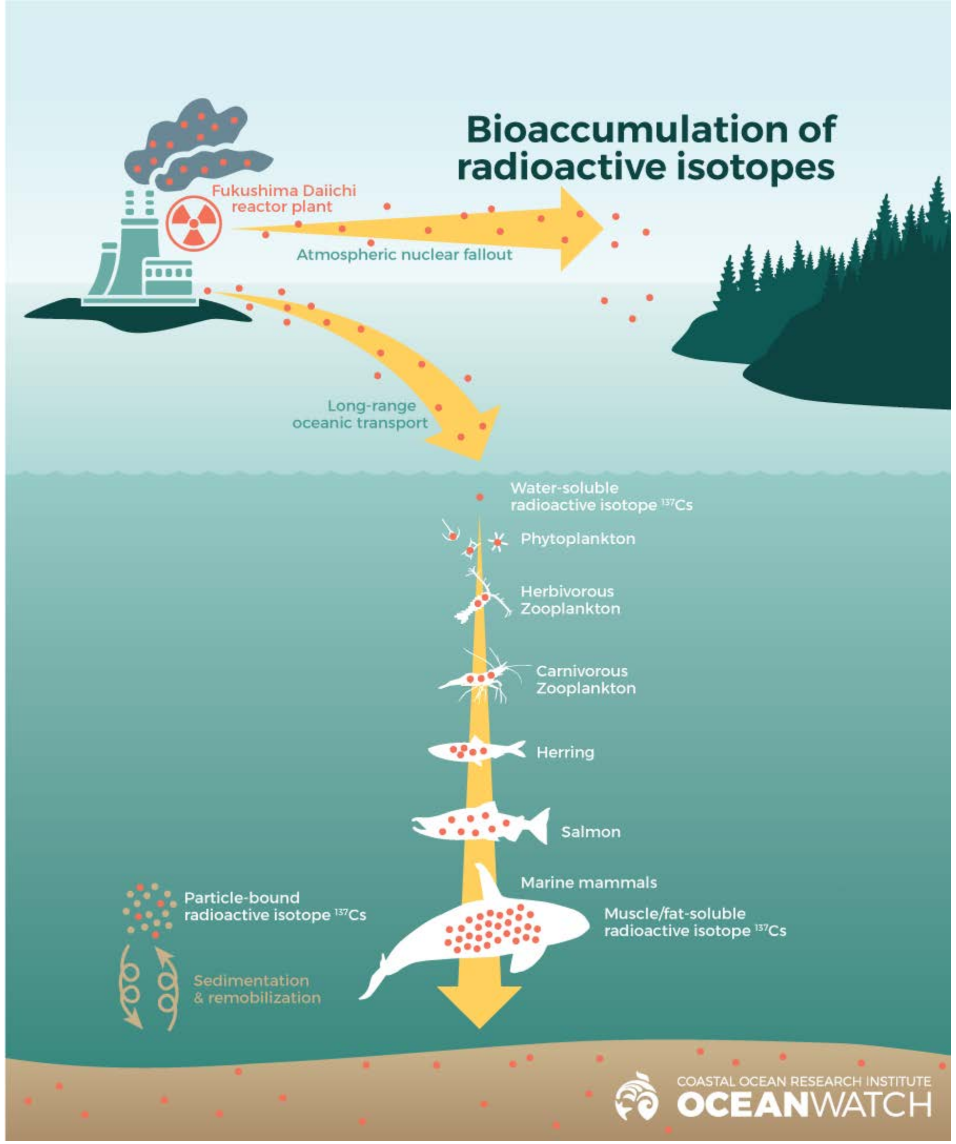
Bioaccumulation: Coming full circle



Radiation & the environment: Assessing effects on plants and animals

An overview of a recent report issued by the United Nations Scientific Committee on the Effects of Atomic Radiation

MINI REVIEW

Consequences of nuclear accidents for biodiversity and ecosystem services

Henrik von Wehrden1,2, Joern Fischer2, Patric Brandt2, Viktoria Wagner3,4, Klaus Kummerer ¨ 5,
Tobias Kuemmerle6,7, Anne Nagel2, Oliver Olsson5, & Patrick Hostert6

Conservation Letts 2012. 1-9

Pathological findings of Japanese Black Cattle living in the restricted area of the Fukushima Daiichi Nuclear Power Plant accident, 2013–2016

Jun SASAKI,1 Kayoko HIRATANI,1 Itaru SATO,2 Hiroshi SATOH,3 Yoshitaka DEGUCHI,4 Hiroyuki CHIDA,5 Masahiro NATSUHORI,6 Takahisa MURATA,7 Kenji OCHIAI,1 Kumiko OTANI,8 Keiji OKADA9 and Nobuhiko ITO6

Animal Science Journal, 2017, 88, 2084-2089

Unit for measuring radiation dose

- Amount of energy absorbed per unit weight of organ or tissue is absorbed dose and expressed a gray (Gy).
- 1 Gy = 1 joule radiation energy per kg organ/tissue
- 1 cGy = 1 rad

- Sievert (Sv) is absorbed dose x weighting factor of radiation (quality factor)
- 1 Sv = Dose (Gy) x rad weighting factor (WR)

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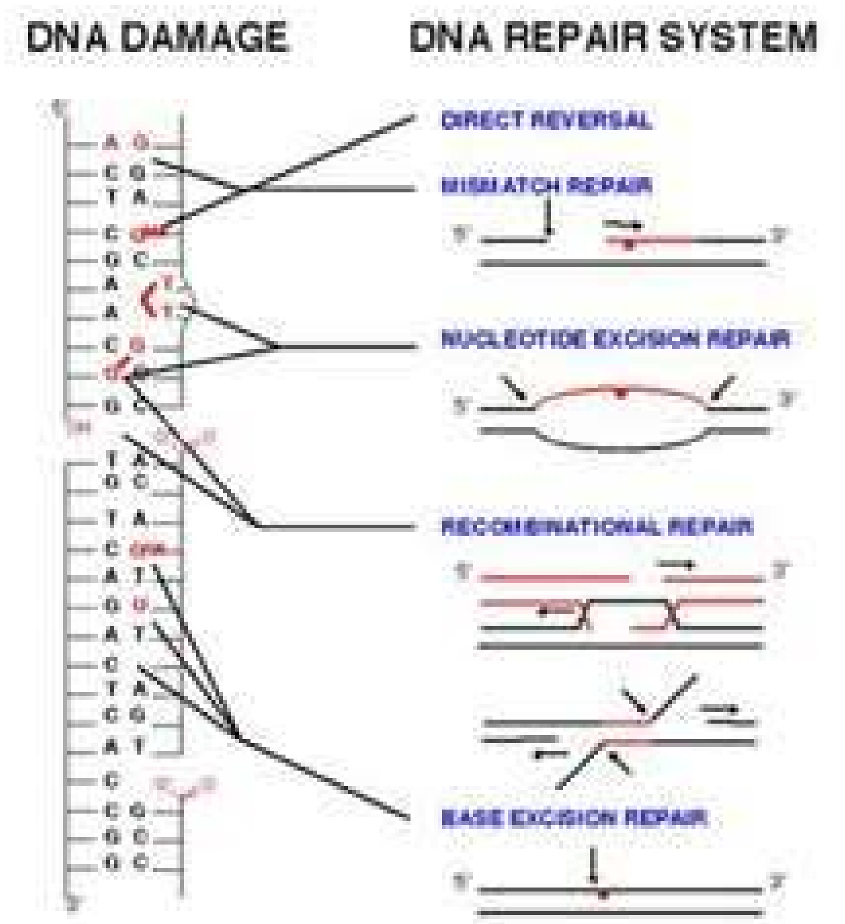
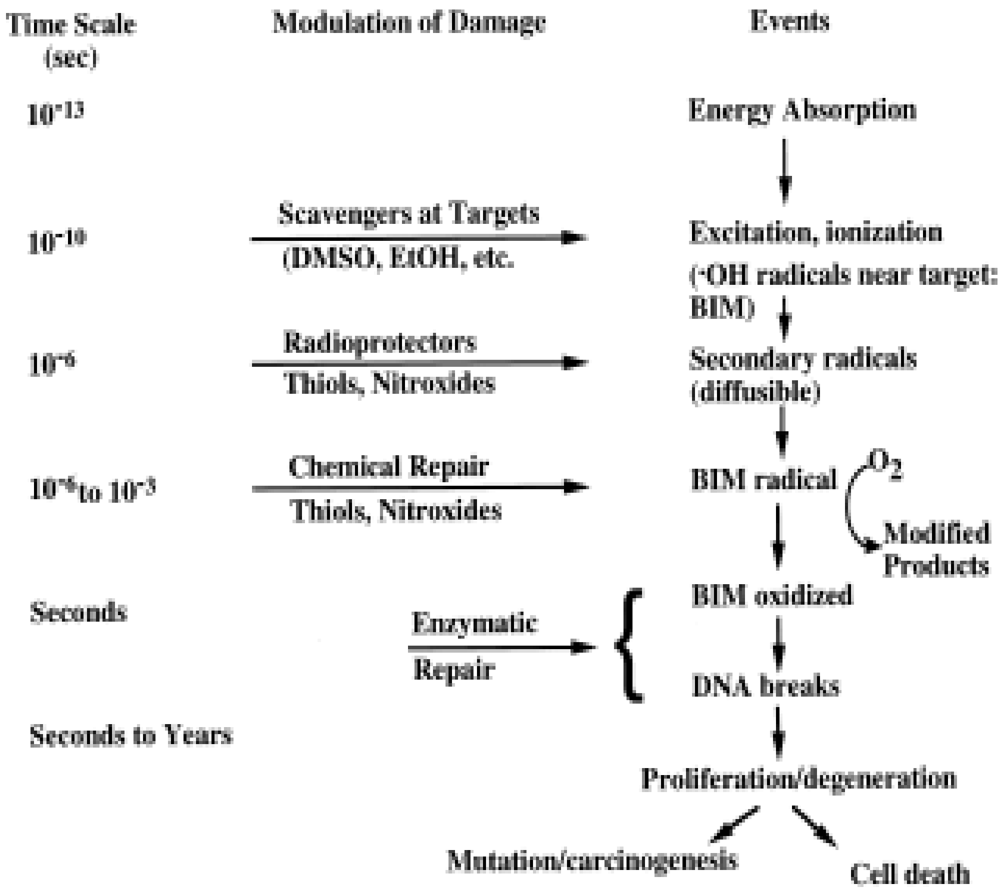
Average annual dose to humans

Annual dose is 0.05 Sv (50 mSv)

- 10 Sv - Risk of death within days or weeks
- 1 Sv - Risk of cancer later in life (5 in 100)
- 100 mSv - Risk of cancer later in life (5 in 1000)
- 50 mSv – TLV annual dose for radiation workers in any one year
- 20 mSv – TLV annual average dose, averaged over five years

Biological effects of radiation





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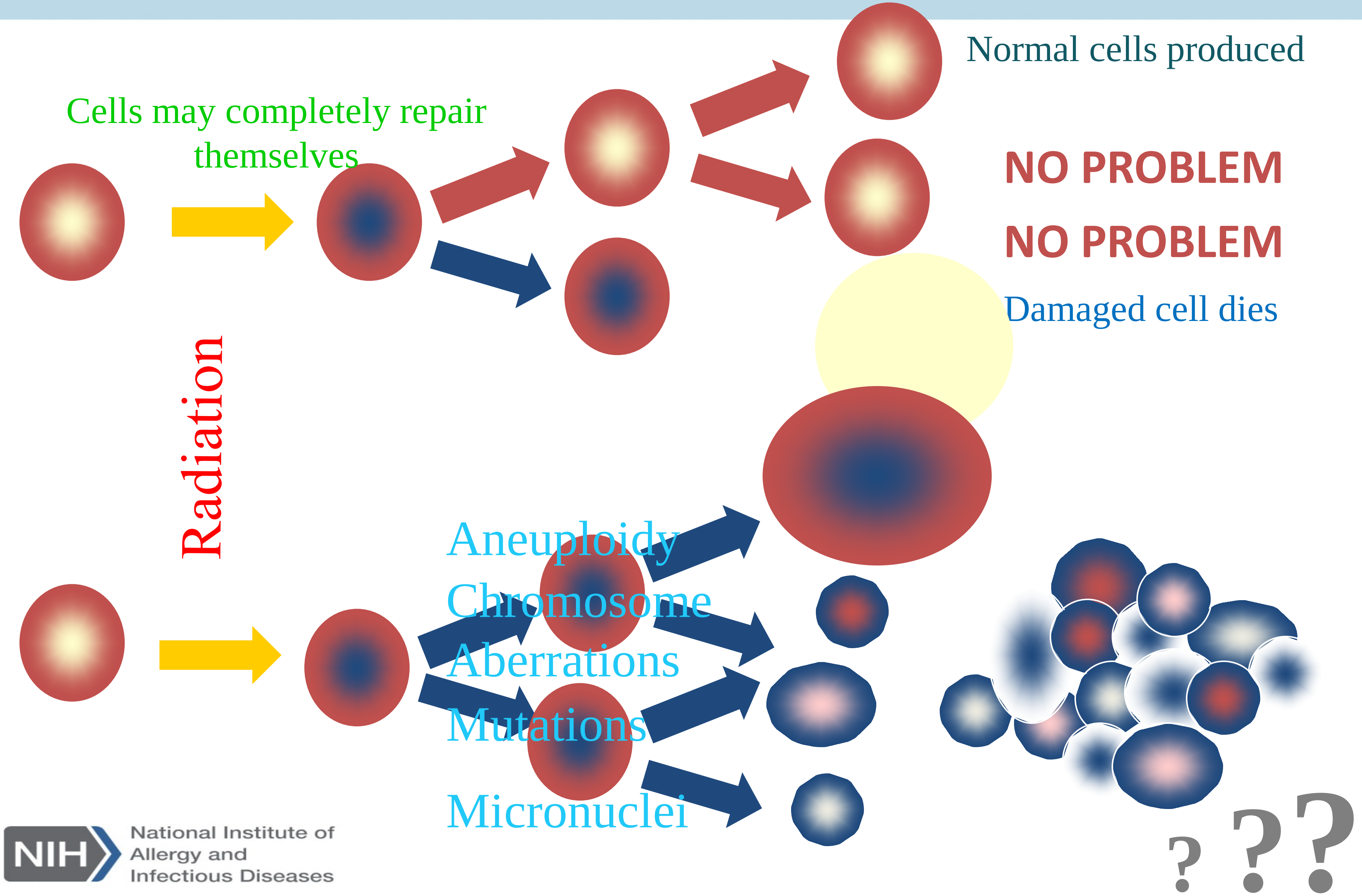
Possible outcomes of radiation damage



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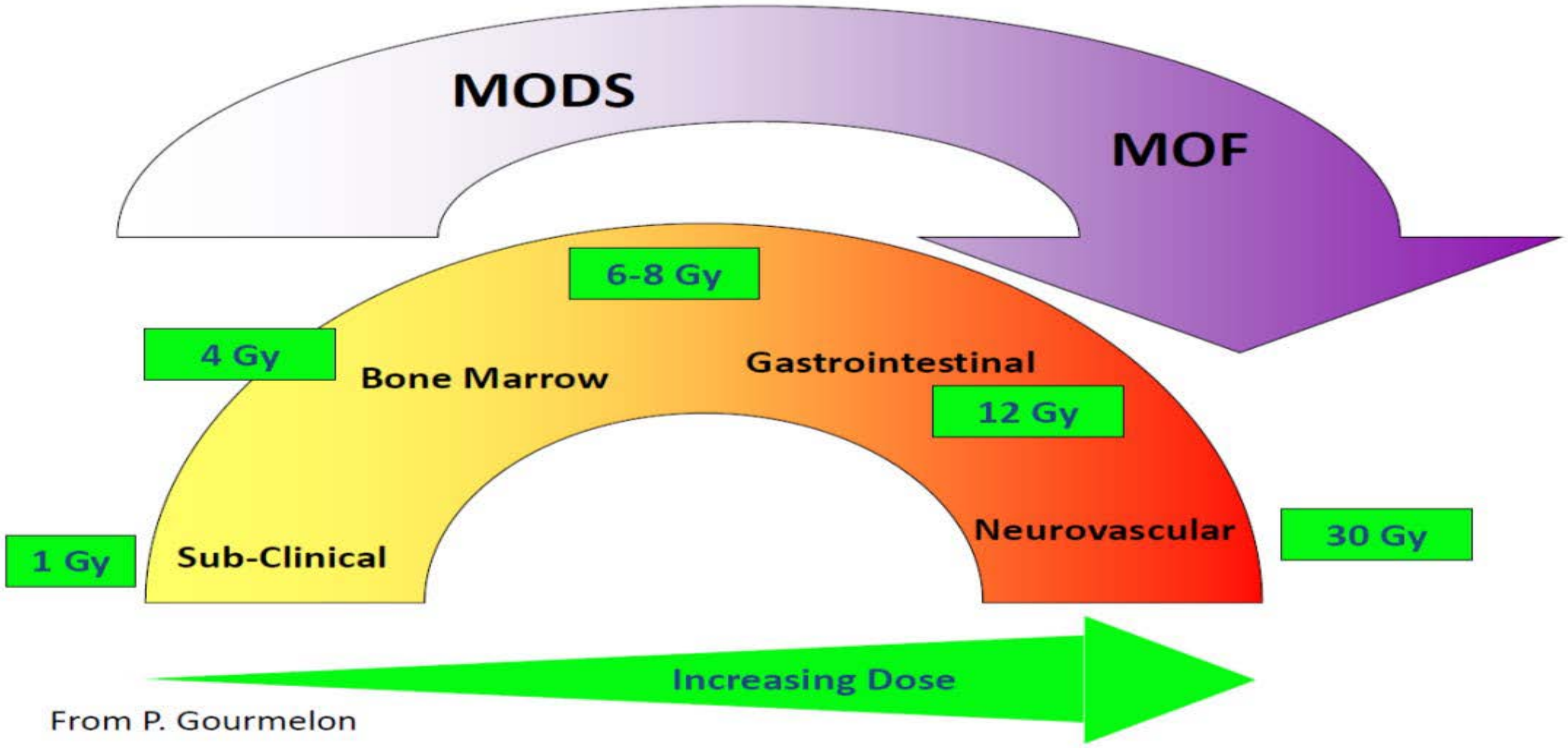
Acute Radiation Syndrome –what is it?



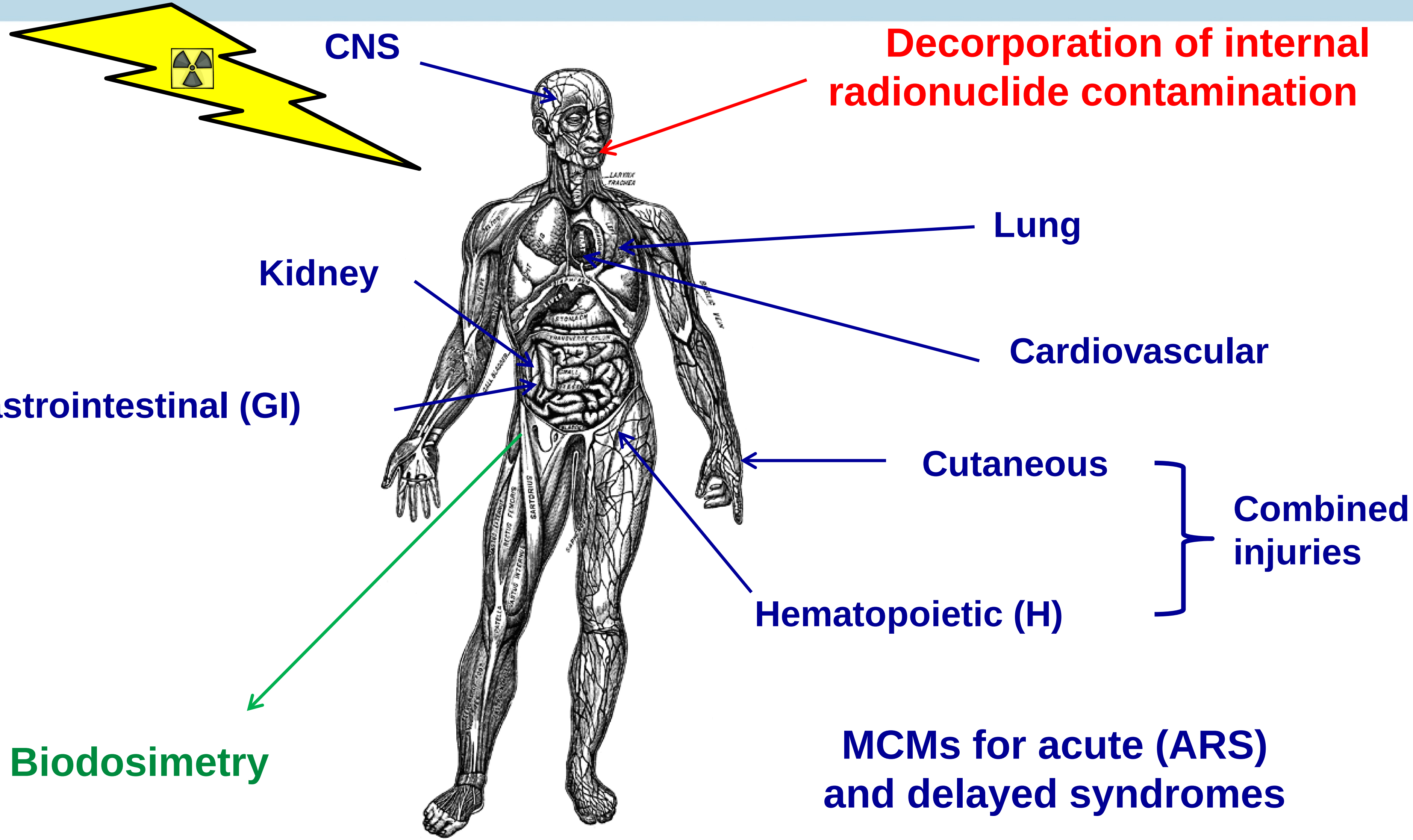
- Radiation dose dependent injuries to cells, tissues, and organs
- Spectrum of injuries and symptoms – multi-organ dysfunction/failure

Tissue sensitivity to radiation

- Lymphocytes
- Granulocytes, Erythrocytes
- Epithelial cells
- Endothelial cells
- Connective tissue
- Bone cells
- Nerve
- Brain
- Muscle

- Bergonie and Tribondeau, 1906

Scientific areas

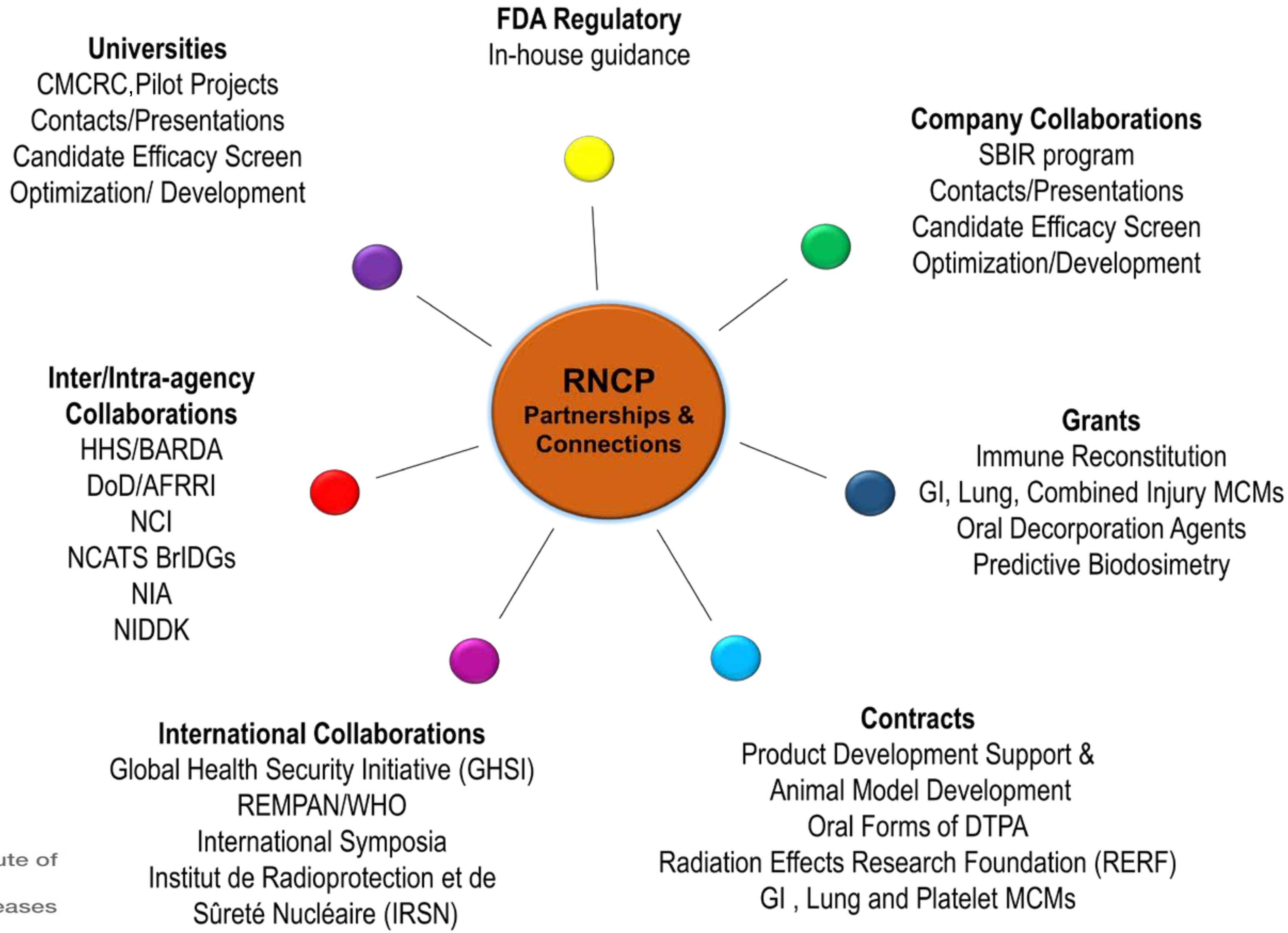


MCMs for acute (ARS) and delayed syndromes

What does RNCP do?

- MCMs to treat or mitigate radiation injury 24 hours post-exposure
- Drugs to remove radioactive materials from the body
- Biodosimetry tools and biomarker identification to determine levels of radiation exposure

NIAID-RNCP: Program Elements



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NIAID Radiation and Nuclear Countermeasures Program Biodosimetry Architecture

Predictive Biodosimetry

Contamination

Decorporation agents

Predictive Biodosimetry

Medical management

>2 Gy

Immediate triage

<2 Gy

Risk assessment

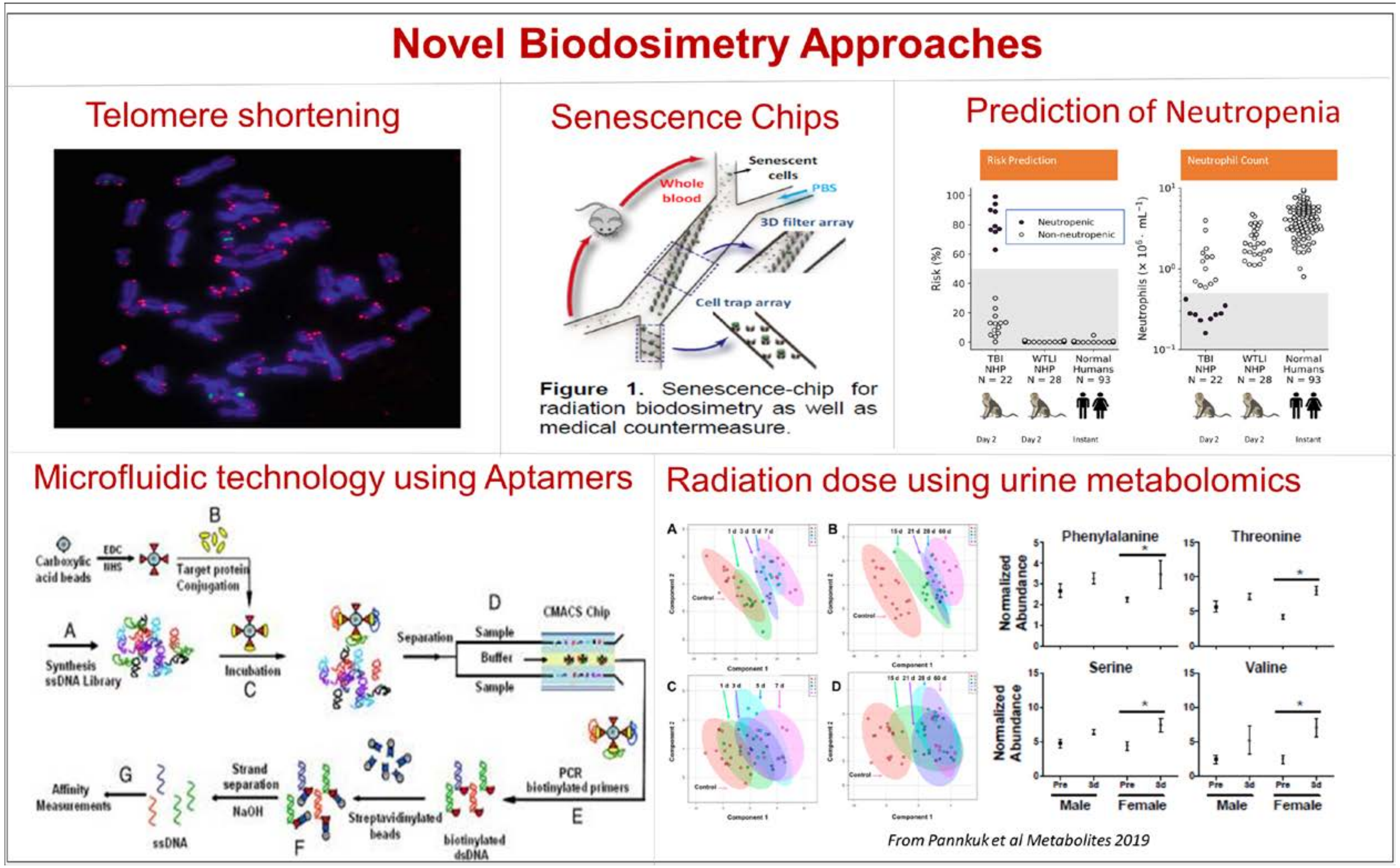
Dose estimation
TBI vs PBI
Specific tissue
Damage

POC devices
Hematology
OSL/EPR
qPCR
Biomarkers

Cytogenetics
Micronucleus
Assay

Predictive Biodosimetry

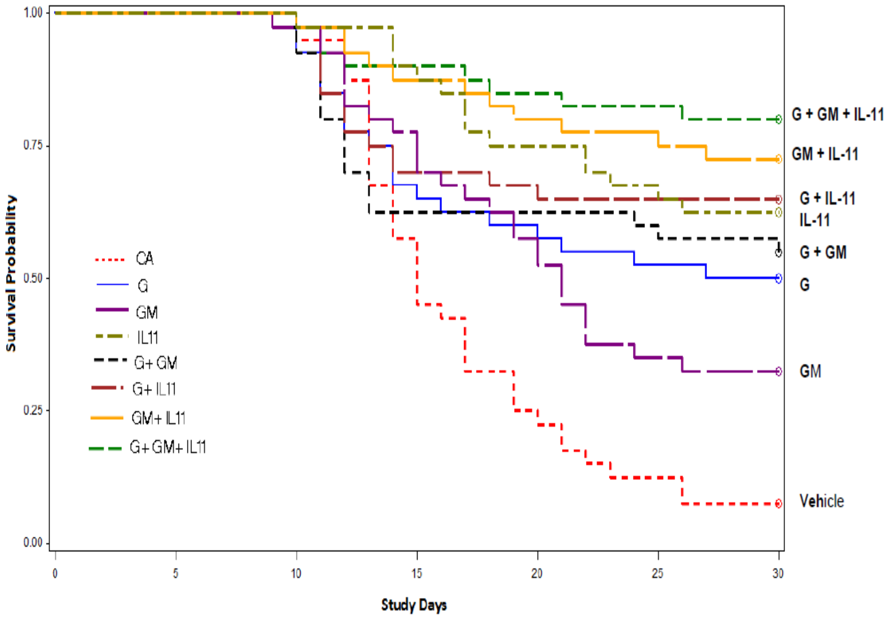
Novel biodosimetry approaches

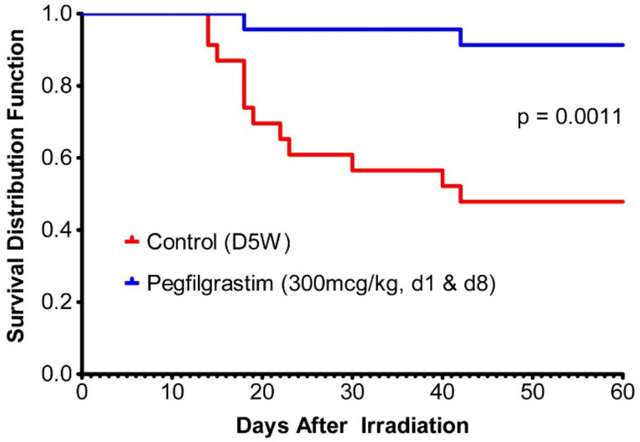


Identify and develop radiation countermeasures for radiation subsyndrome of heme-ARS

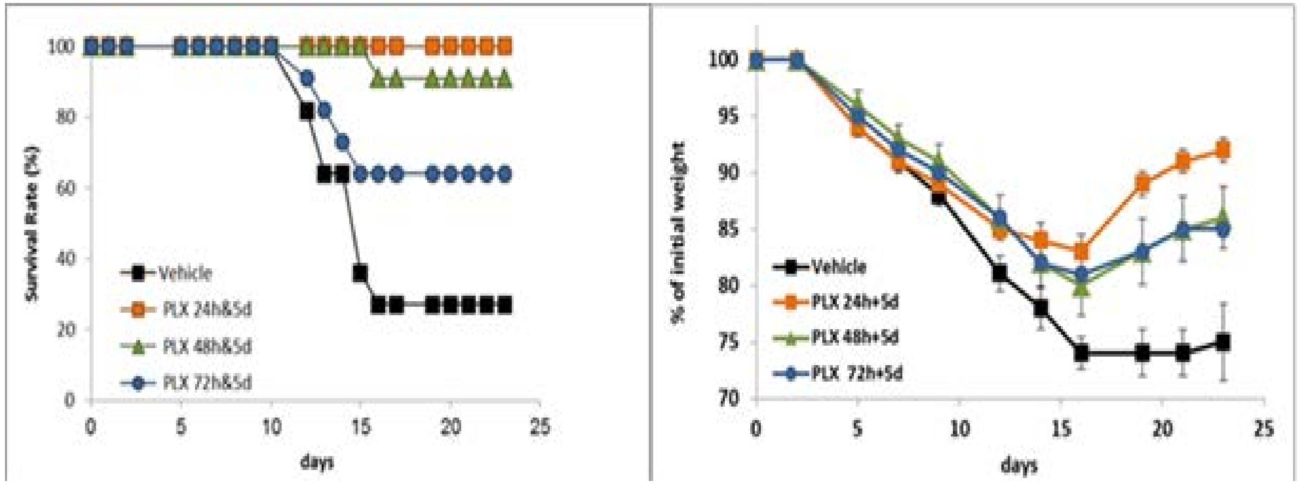
Polypharmacy approach for heme-ARS

12 w/o C57BL/6 mice, 40/group, LD95/30 radiation dose
Single sc injection of PEG-GFs at 24h post-TBI





Heme



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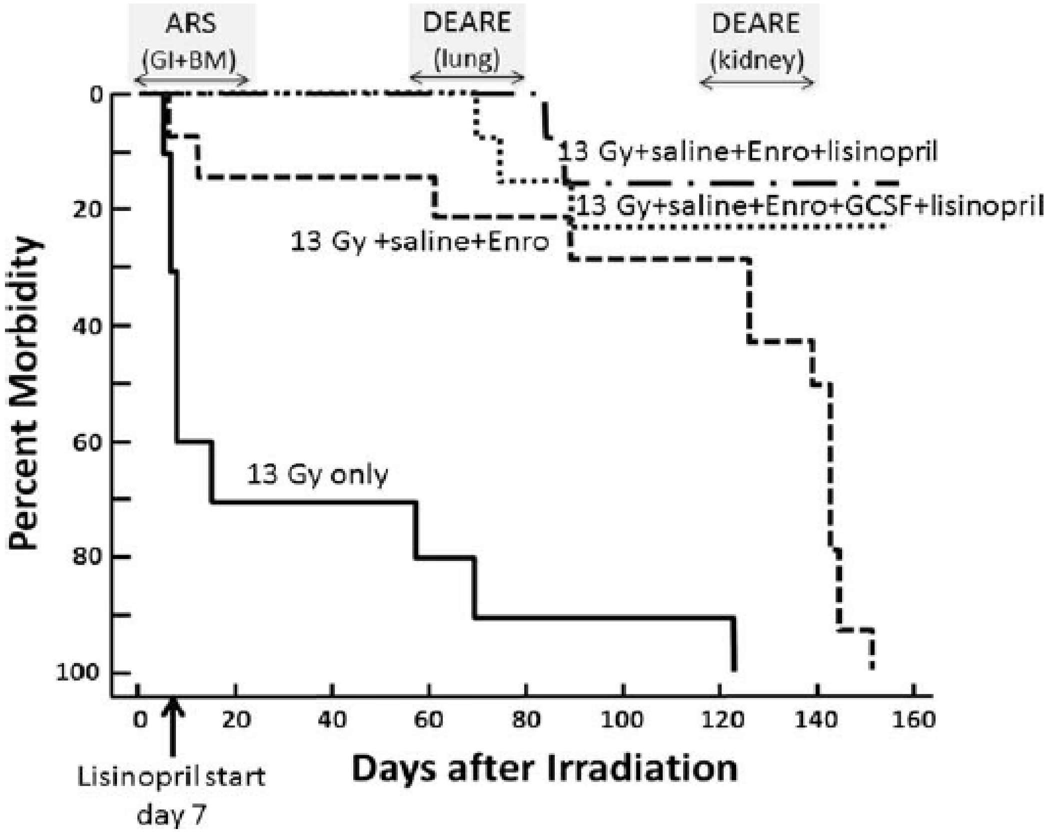
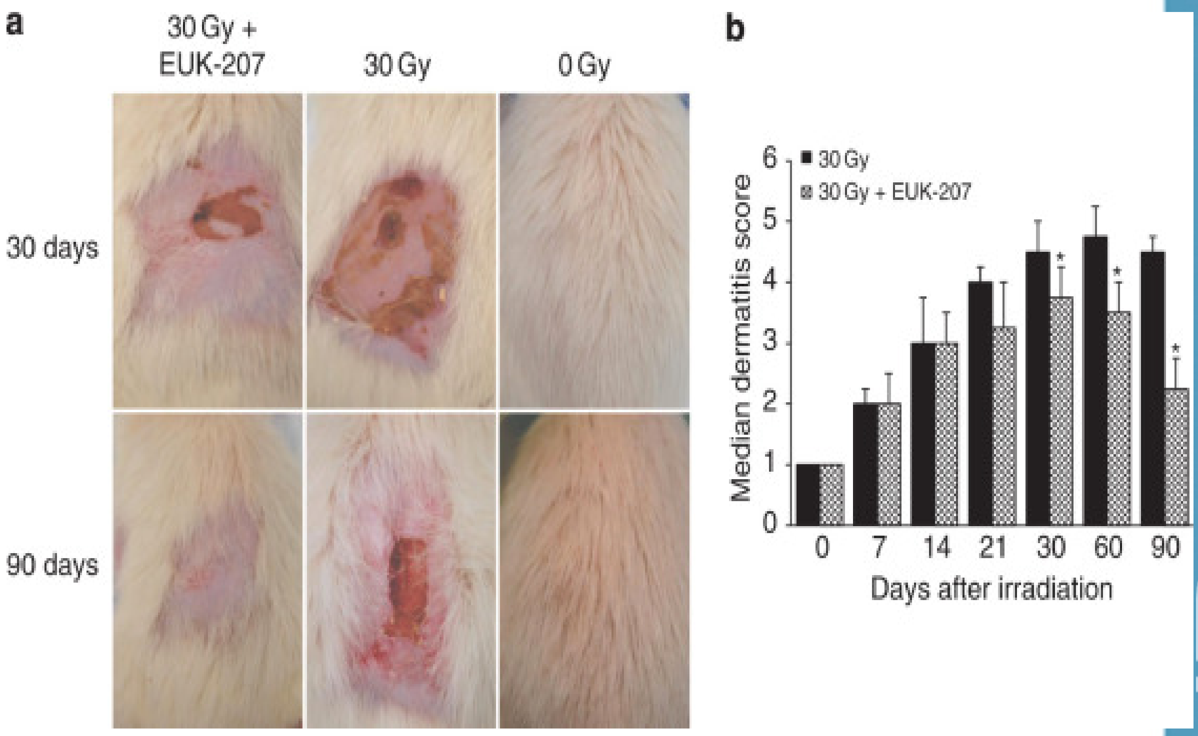
Heme

Identify and develop radiation countermeasures for radiation subsyndromes of Lung, Kidney, Skin



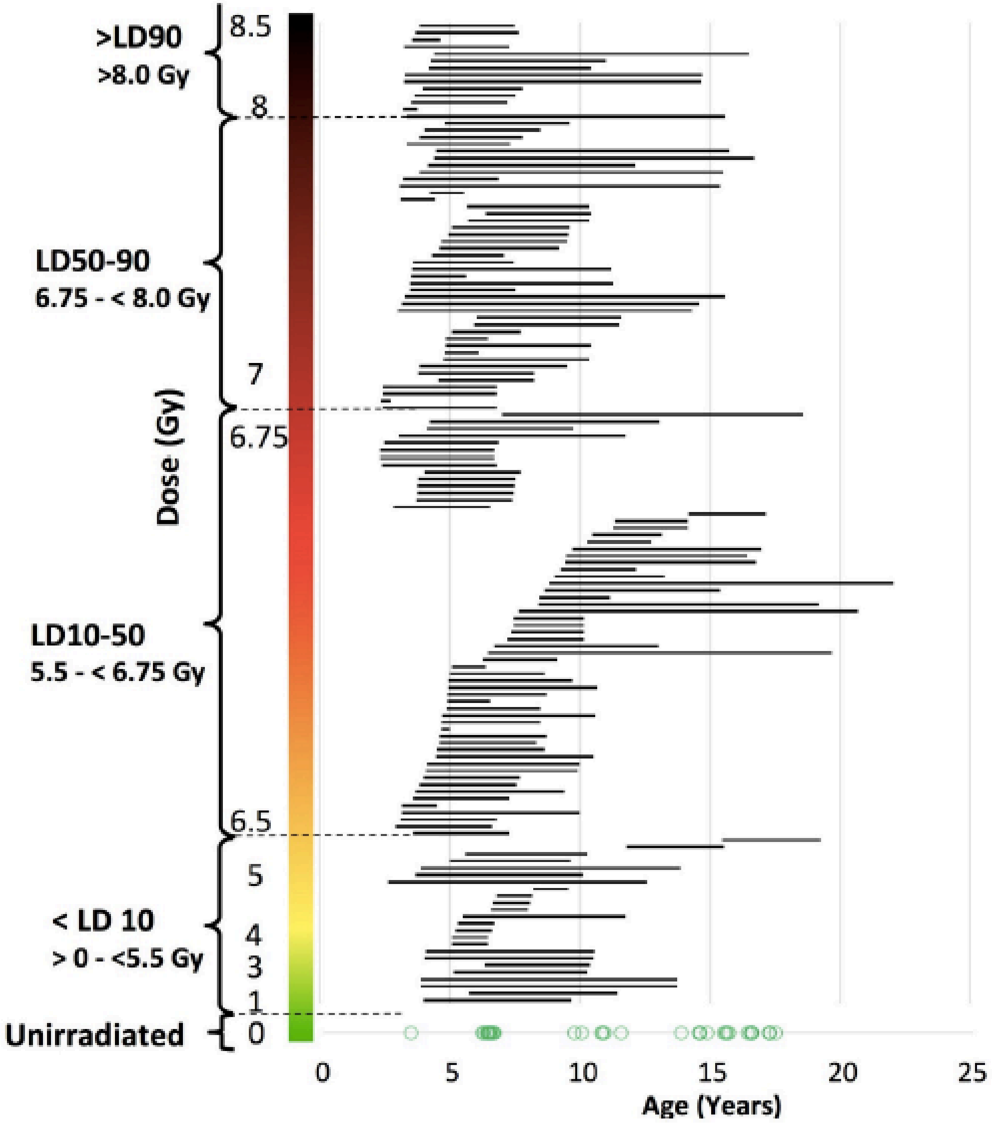


Lung
Renal

Skin-CRI

NHP survivor cohort (Natural history)

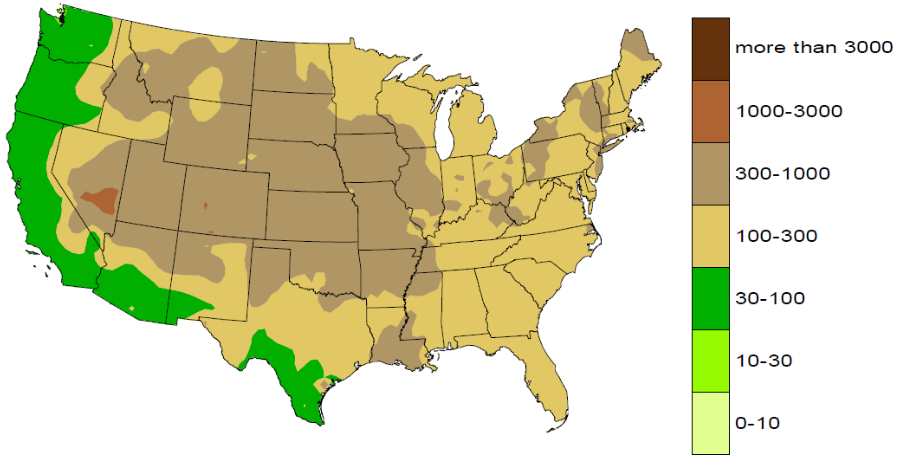
- Cohort initiated in 2005
- Wake Forest only provider
- Animals “adopted” from USG-funded studies
- >140 irradiated NHPs
- >30 unirradiated control NHPs
- Sample/data sharing
- Unanticipated late effects
  - Diabetes
  - Immune blind spots
  - Multiple comorbidities



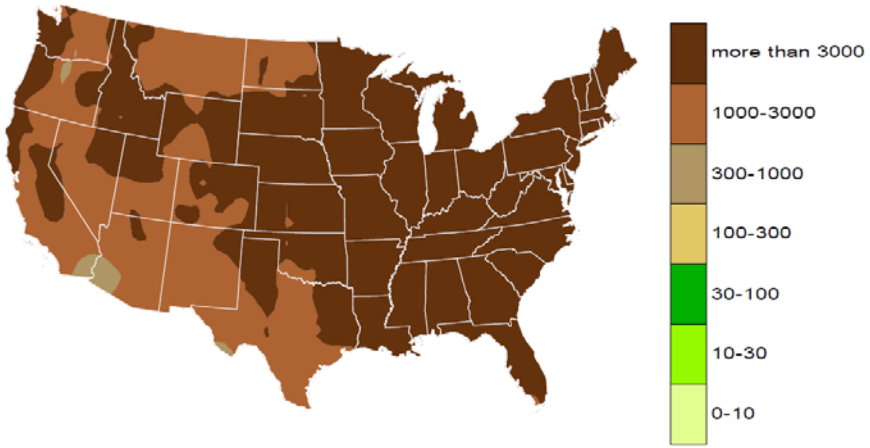
Oral decorporation products

- 3,4,3-LI(1,2-HOPO)
  - LBNL (grant, PDSS Contract)
  - For U and transuranics
- Zn-DTPA Tablets
  - SRI International
  - For transuranics
- C2E2
  - Capture Pharmaceutics (via UK, UNC)
  - For transuranics

Nuclear fallout modeling (IAA with NCI)



Cumulative Cs-137 deposition (Bq/m^2) from NTS



Cumulative Cs-137 deposition (Bq/m^2) from Global fallout

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Long term monitoring, dose reconstruction, and Retrospective Biodosimetry

Chromosome Translocations, Inversions, and Telomere Length for Retrospective Biodosimetry on Exposed US Atomic Veterans

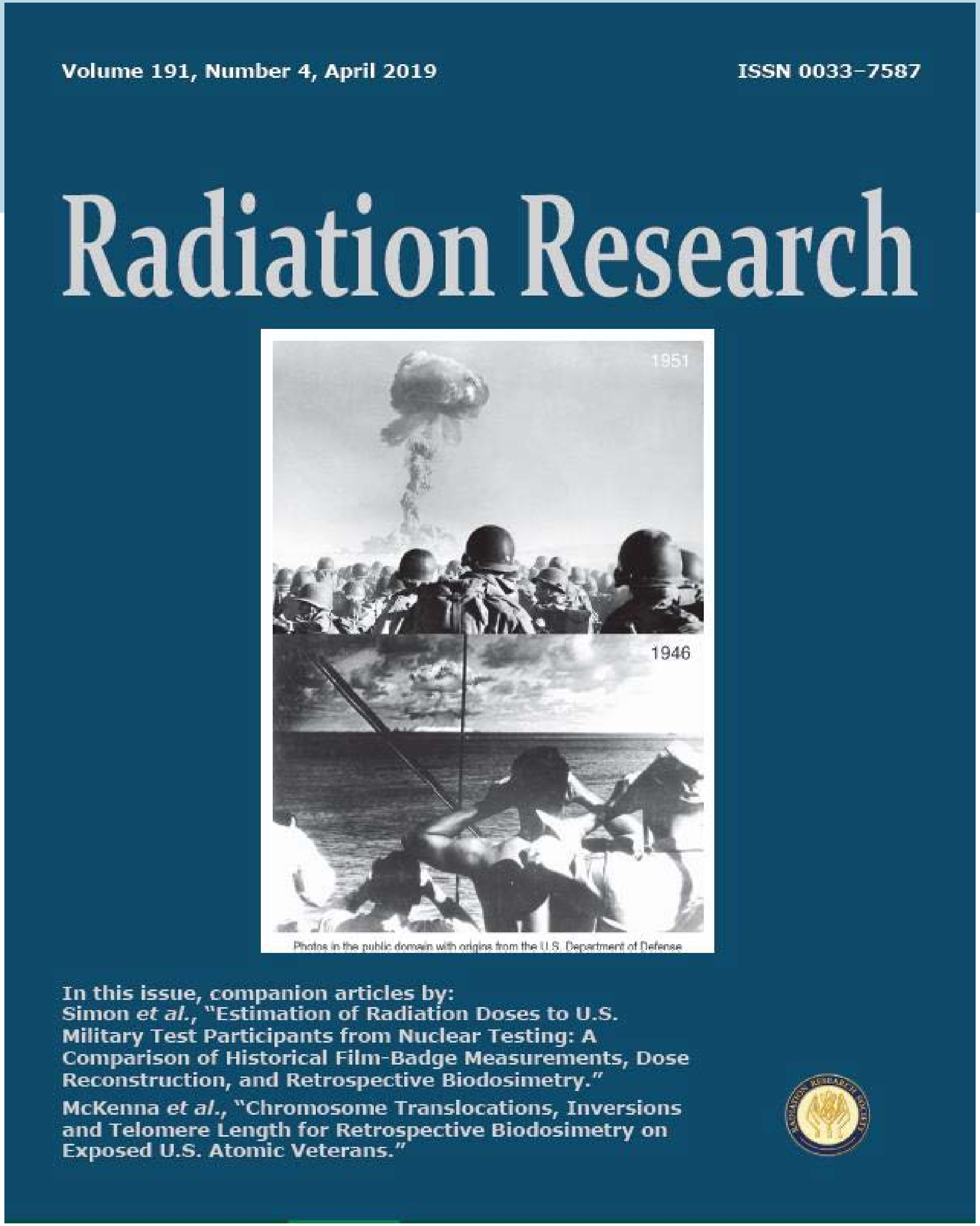
(accepted for publication – Radiation Research)

Miles J. McKenna[1,2,3], Erin Robinson[3], Lynn Taylor[2], Christopher Tompkins[3], Michael N. Cornforth[3,4], Steven L. Simon[5] and Susan M. Bailey[1,2,3]

Estimation of Radiation Doses to U.S. Military Test Participants from Nuclear Testing: A Comparison of Historical Film-Badge Measurements, Dose Reconstruction, and Retrospective Biodosimetry

[journal (Radiation Research) review completed]

Steven L. Simon[1], Susan M. Bailey[2], Harold L. Beck[3], John D. Boice[4], André Bouville[1], Aaron B. Brill[5], Michael N. Cornforth[6], Peter D. Inskip[1], Miles J. McKenna[2], Michael T. Mumma[7], Silvia I. Salazar[8], Abigail Ukwuani[1]


Volume 191, Number 4, April 2019 ISSN 0033-7587

Radiation Research

Photos in the public domain with origins from the U.S. Department of Defense

In this issue, companion articles by:
Simon *et al.*, "Estimation of Radiation Doses to U.S. Military Test Participants from Nuclear Testing: A Comparison of Historical Film-Badge Measurements, Dose Reconstruction, and Retrospective Biodosimetry."
McKenna *et al.*, "Chromosome Translocations, Inversions and Telomere Length for Retrospective Biodosimetry on Exposed U.S. Atomic Veterans."

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RNCP advances

- Product licensures
  - Neupogen®
  - Neulasta®
- IND/IDE approvals
  - 2 MCMs
  - 3 oral decorporation
  - 4 biodosimetry
- 15 pre-IND/pIND sponsor meetings with FDA
- Interactions with 275+ companies
- 29 products transitioned to BARDA

Radiation and emergency response

- **The CDC Public Response Source** at 1-888-246-2675
- **Conference of Radiation Control Program Directors** (CRCPD) at www.crcpd.org or 502-227-4543

Acute Radiation Syndrome (continued from previous page) Reviewed and updated May 20, 2005 Page 2 of 2

- **U.S. Environmental Protection Agency** (EPA) at www.epa.gov/radiation/rert
- **Nuclear Regulatory Commission** (NRC) at www.nrc.gov or 301-415-8200
- **Federal Emergency Management Agency** (FEMA) at www.fema.gov or 202-646-4600
- **Radiation Emergency Assistance Center/Training Site** (REAC/TS) at www.orau.gov/reacts or 865-576-3131
- **U.S. National Response Team** (NRT) at www.nrt.org
- **U.S. Department of Energy** (DOE) at www.energy.gov or 1-800-dial-DOE

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Paul Price, PhD, Regulatory Affairs Officer

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