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Topic: What Emergency Management Professionals Should Know about Antidotes for Radiological Agents

Key words: Radionuclear incidents, internal radioactive contamination, radiological terrorism, thermonuclear detonation, “dirty bomb”, decontamination, radionuclear antidotes, Iodine, DTPA.

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Objectives of this lecture:

- Emphasize the need for more education of health care providers, rescue and public safety personnel for radionuclear incidents and threats
- Review the different radionuclides and their sources which could serve for radioactive contamination, incorporation and radiological terrorism.
- Discuss the need for reviewing the stockpile situation for radionuclear decorporation antidotes.
- Review briefly two examples for incorporation of a radionuclide. One for which decorporation is effective and one for which it is not.

Accidents involving radioactive material and contamination of humans are relatively rare but are of high consequence medically and psychologically. They are low probability and high impact events. After the terrorist attacks of New York and Washington the intelligence services warned of a new threat from radionuclear devices like **radiological dispersal devices (RDD)** such as a **Dirty Bomb**. In the past nuclear power plants and facilities using radioactive material like laboratories were considered to be most likely source of radioactive contamination. The major health threats form radionuclear material arises from contamination, ionizing radiation, incorporation, corpuscular radiation (energy transfer via alpha, beta and neutron, especially along very short distances on a cellular level) and to some extend from the chemical toxicological properties of the radionuclide itself.

The ingestion, injection, inhalation, (skin and mucosal) absorption of a radioactive substance can lead to incorporation of this substance into the human or animal body. The chemical element follows the basic laws of pharmacology; pharmcokinetics and pharmacodynamics. Pharmcokinetics describes processes like absorption, distribution, biotransformation and elimination. The human body and the cellular elements do not distinguish between a radioactive element and a non-radioactive and stable element of the same isotope. An Isotope is one of two or more atoms with the same atomic number but with different numbers of neutrons. A radioisotope is an unstable element that releases radiation as it breaks down. Radioisotopes can be used in imaging tests or as a treatment for cancer. A stable isotope is a chemical isotope that is not radioactive.

Stable isotopes of the same element the same chemical characteristics and therefore behave chemically and physiologically almost identically. The mass differences are due to a difference in the number of neutrons.

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Pharmacokinetics	Interventions, treatment options

• Absorption	Prevent further absorption – Decontamination, reduction of absorption
• Distribution	Reduce uptake in a specific organ. – Thyroid gland -
• Biotransformation	--- ---
• Elimination	Increase elimination via kidney and gut

Example: **Iodine with an Atomic Number or 53**. **Number of electrons: 53**

Stable Iodine: Atoms 53. Neutrons: 74 53 (A) +74 (N) = 127

http://www.chemicalelements.com/elements/i.html

Isotopes of Iodine

Isotope	**Half Life**
I-122	3.6 minutes
I-123	13.2 hours
I-124	4.2 days
I-125	60.1 days
I-126	13.0 days
I-127	Stable
I-128	25.0 minutes
I-129	1.57E7 years
I-130	12.4 hours
I-131	8.0 days
I-132	2.3 hours
I-133	20.8 hours
I-134	52.6 minutes
I-135	6.6 hours
I-136	1.4 minutes

Source:
http**://www.chemicalelements.com/elements/i.html**

Liquid:
1 mL = 65 mg KI

Tablet:

1 Tablet = 65 mg

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I-131 is radioactive, has an 8 day half-life, and emits beta and gamma radiation. Both iodine-129 and iodine-131 are produced by the fission of uranium atoms during operation of nuclear reactors and by plutonium (or uranium) in the detonation of nuclear weapons.

Antidotal therapy with (stable) Iodine (I-127) in form or tablets or Lugol solution should be available in the vicinity of nuclear power plants, medical facilities operating with radioactive Iodine, and in event of a nuclear detonation. (Stable) Iodine works by saturating the uptake mechanism in the thyroid gland and "competes" with radioactive iodine (I-131). Early administration of radionuclear antidotes is the key element for successful therapy.

Iodine is a thyroid blocking agent.

FDA document: Guidance Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) December 2001 Procedural

……This guidance updates the Food and Drug Administration (FDA) 1982 recommendations for the use of KI to reduce the risk of thyroid cancer in radiation emergencies involving the release of radioactive iodine. The recommendations in this guidance address KI dosage and the projected radiation exposure at which the drug should be used.

…..these revised recommendations are in general accordance with those of the World Health Organization (WHO), as expressed in its *Guidelines for Iodine Prophylaxis Following Nuclear Accidents: Update 1999* (WHO 1999).

…. December 15, 1978, FDA announced its conclusion that KI is a safe and effective means by which to block uptake of radioiodines by the thyroid gland in a radiation emergency under certain specified conditions of use……..
The amount of KI recommended at that time was 130 mg per day for adults and children above 1 year of age and 65 mg per day for children below 1 year of age.

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Thermonuclear explosion

A **nuclear explosion** occurs as a result of the rapid release of energy from an uncontrolled nuclear reaction. Fission, fusion. Thermal energy, electromagnetic pulse wave, gamma radiation….

Effects of a nuclear explosion

The energy released from a nuclear weapon comes in four primary categories:

- Blast—40-60% of total energy
- Thermal radiation—30-50% of total energy
- Ionizing radiation—5% of total energy
- Residual radiation—5-10% of total energy

http://en.wikipedia.org/wiki/Nuclear_explosion

Dirty Bomb:

For a dirty bomb detonation the antidotal and decorporation therapy has to take into account the radioisotope used to mix it with the conventional explosive. Possible radioisotopes can be stolen, purchased and produced.

Antidotes and Decorporation Agents

For all antidotes early therapy within hours of exposure is essential

Ammonium chloride	Oral salt (together with Ca++ gluconate) [iv] Acidification of blood	Strontium (Sr) Levels diminish 40- 75%

Ca salts	Interferes with absorption and bone incorporation (iv, po)	Barium (Ba), Sr-90, Radium (Ra) Ra-226

Ca-DTPA **Zn-DPTA**	Chelates transuranic metals (Actinoids) Iv , inhaled (aerosol) DTPA has toxicity (Zn, Mn) chelation.	Plutonium (Pu), Americium (Am) Curium (Cm) Californium (Cf) Neptunium (Np) And certain rare earths Lanthanum (La) ….

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Antidotes and Decorporation Agents

Dimercaprol (British antilewisite, BAL) Deep im	Chelates radioactive and stable nuclides Deep im injection , peanut oil based	Mercury, Lead, Arsenic, Gold, Bismuth, Chromium, Nickel Probably Po-210 (experimental data)

Prussian blue	Oral ion-exchange drug 0.5 mg capsule , Stool turns blue	**Cesium, Thallium,** Rubidium Highly effective for Cesium (Cs-137)

Potassium Iodine (KI)	Oral tablets, oral solution Blocks uptake of radioactive iodine (I-131) Virtually useless if used after 12 hours after contamination	Radioiodine (I-131)

Sodium alginate: A derivative of kelp used in the manufacture of ice cream	Oral alginates efficiently bind strontium in the gastrointestinal tract, and prevent its absorption. The dose is 10 gm powder in a 30 cc vial, add water and drink	Strontium Sr-90

Na bicarbonate	Oral or intravenous NaHCO3 Alkalization of urine which protects the kidney from Uranium toxicity	Uranium (U)

Elements, radionuclide and their Antidotes

- Americium: parenteral Ca-DTPA, Zn-DTPA.
- Cesium: oral Prussian blue.
- Cobalt: nothing too good, but oral penicillamine worth trying.
- Iodine: KI *within about first 4 hours.* Consider PTU.
- Iridium: unknown; try oral penicillamine.
- Palladium: unknown; try oral penicillamine.
- Phosphorus: oral Na phosphate or K phosphate.
- Plutonium: parenteral Ca-DTPA, Zn-DTPA.

- Radium: oral calcium to reduce gastrointestinal absorption and increase urinary
- Excretion. Alginates are also useful to reduce gastrointestinal absorption.
- Strontium: intravenous calcium gluconate, oral ammonium chloride for acidification.
- Alginates are useful to reduce gastrointestinal absorption.
- Tritium: force water to promote diuresis.
- Uranium: Ca-DTPA and Zn-DTPA within *4 hours only.* Na bicarbonate to alkalinize urine.
- Yttrium: parenteral Ca-DTPA, Zn-DTPA

Radionuclides of Maximum concern for RDDs

It is difficult to predict which radionuclides are most likely to be used in an RDD event, but based on accessibility and maximizing terrorist impact; it is not too hard to come up with some educated guesses. Strontium (Sr)-90, yttrium (Y)-90, cesium (Cs)-137, iridium (Ir)-192, cobalt (Co)-60, americium (Am)-241, iodine (I)-125 and 131, uranium (U)-234, 235, and 238, plutonium (Pu)-239, radium (Ra)-226, tritium (hydrogen-3 or H-3), phosphorus (P)-32 and palladium (Pd)-103 are possible candidates. There could always be mixtures of radionuclides, either because the original sealed sources contained a mixture, or because an exploded establishment contained a mixture, or because a terrorist sought to confuse responders and complicate the response situation

Source: http://acnp-cal.org/DMAT-AdmDecorpDrugsIntRadContam12-01-03.pdf
DMAT CA-9 team, Carol Marcus, MD, PhD; UCLA (2004)

DTPA

http://www.fda.gov/bbs/topics/news/2004/NEW01103.html

August 11, 2004

FDA Approves Drugs to Treat Internal Contamination from Radioactive Elements

Internal contamination with plutonium, americium, or curium can occur through a variety of routes including ingestion, inhalation, or direct contact through wounds. The goal of treatment with Ca-DTPA and Zn-DTPA is to enhance the removal of these radioactive contaminants and therefore the risk of possible future biological effects including the development of certain cancers, which may occur years after exposure.

Release of plutonium, americium and curium could occur from laboratory or industrial accidents; or through terrorist attacks using a radiation dispersal device (RDD), commonly known as a “dirty bomb”.

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Facts About DTPA

Source: http://www.bt.cdc.gov/radiation/pdf/dtpa.pdf

Zn-DTPA (**Trisodium** zinc **diethylenetriaminepentaacetate**)

Currently, DTPA is approved by the U.S. Food and Drug Administration (FDA) for chelation of only three radioactive materials: plutonium, americium, and curium.

When given within the first day after internal contamination has occurred, Ca-DTPA is about 10 times more effective than Zn-DTPA at chelating plutonium, americium, and curium. After 24 hours have passed, Ca-DTPA and Zn-DTPA are equally effective in chelating these radioactive materials.

The more quickly a radioactive material or poison is removed from the body, the fewer and less serious the health effects will be. After 24 hours, plutonium, americium, and curium are harder to chelate

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http://orise.orau.gov/images/reacts/dtpa-sm.jpg

SCIENCE 1966;152:655-656

ARTICLES

Strontium Uptake in Rats on Alginate-Supplemented Diet

George E. Harrison [1], Eric R. Humphreys [1], Alice Sutton [1], and Hilda Shepherd [1]

[1] Medical Research Council, Radiobiological Research Unit, Harwell, Didcot, Berkshire, England

Rats were fed a basic diet supplemented with sodium alginate and with tracer amounts of strontium-85 and calcium-45. Absorption of strontium was always inhibited by the alginate to a greater extent than absorption of calcium. Discrimination against strontium was greatest in alginate containing a high proportion of guluronic acid

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Principles of management with internal contamination of radionuclides

The first 1-2 hours after incorporation of a radionuclide maybe the crucial time for effective treatment.

Alkalization of the stomach may cause the formation of relatively insoluble salts (hydroxides). Iron, copper, plutonium. Consider whole bowel irrigation after pH is higher.

Timely therapy is Essential

After absorption the uptake can be reduced by

- Blocking agents (iodine)
- Isotopic dilution (large quantities of the stable isotope)
  (Ca ---- Sr *) (I ----- Tc *)
- Chelating agents: binding chemically and allowing urinary (or intestinal excretion**)**

Facts:

I -131 – thyroid gland
Pu- 239 – bone and liver

Accidental inhalation or injection of I-131 after a nuclear reactor accident (prominent early fission product). Inhaled Iodine reaches equilibrium in body fluid after 30 min and 30% uptake of the uptake in the thyroid gland.

Periodic Table of Elements

Source:

http://universe-review.ca/F12-molecule.htm#inorganichem

Figure 12-26 Periodic Table, Traditional

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Periodic Table of Elements

Representative elements — Transition elements

Alkali metals (Group 1A) · Alkaline earth metals (Group 2A) · Halogens (Group 7A) · Noble gases (Group 8A)

Period number	1 Group 1A	2 Group 2A	3 3B	4 4B	5 5B	6 6B	7 7B	8 8B	9 8B	10 8B	11 1B	12 2B	13 Group 3A	14 Group 4A	15 Group 5A	16 Group 6A	17 Group 7A	18 Group 8A
1	1 H 1.008																	2 He 4.003
2	3 Li 6.941	4 Be 9.012											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
3	11 Na 22.99	12 Mg 24.31											13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.06	17 Cl 35.45	18 Ar 39.95
4	19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.88	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.38	31 Ga 69.72	32 Ge 72.59	33 As 74.92	34 Se 78.96	35 Br 79.90	36 Kr 83.80
5	37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.94	43 Tc 98	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
6	55 Cs 132.9	56 Ba 137.3	57* La 138.9	72 Hf 178.5	73 Ta 180.9	74 W 183.9	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po 209	85 At 210	86 Rn 222
7	87 Fr 223	88 Ra 226	89† Ac 227	104 Rf 261	105 Db 262	106 Sg 263	107 Bh 262	108 Hs 265	109 Mt 266	110 — 269	111 — 272	112 — 277		114 — 289				

*Lanthanides	58 Ce 140.1	59 Pr 140.9	60 Nd 144.2	61 Pm 145	62 Sm 150.4	63 Eu 152.0	64 Gd 157.3	65 Tb 158.9	66 Dy 162.5	67 Ho 164.9	68 Er 167.3	69 Tm 168.9	70 Yb 173.0	71 Lu 175.0
†Actinides	90 Th 232.0	91 Pa 231	92 U 238.0	93 Np 237	94 Pu 244	95 Am 243	96 Cm 247	97 Bk 247	98 Cf 251	99 Es 252	100 Fm 257	101 Md 258	102 No 259	103 Lr 260

Metals · Metalloids · Nonmetals