

Use of Prussian Blue (Radiogardase™) for Treatment of Internal Radiocesium Contamination

August 2005

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Background

Radioactive cesium (radiocesium) has been implicated as a potential radioactive source for terrorist use as a component of a radiological dispersal device (RDD) or “dirty bomb” due to its availability, high dose-rate radioactivity, and pharmacokinetics when inhaled or ingested. Insoluble Prussian blue (Radiogardase™) is an agent that binds cesium in the gastrointestinal tract after the cesium has been inhaled, ingested, or excreted in the bile by the liver, thereby reducing both its primary uptake and gastrointestinal reabsorption. This binding agent has been shown to be effective at dramatically reducing the residence time of radiocesium in the body (Goans 2002), with a consequent reduction in the committed effective dose. Use of Prussian blue for treatment of internal radiocesium has been approved by the U.S. Food and Drug Administration (FDA 2003), and the Assistant Secretary of Defense for Health Affairs has authorized military health care providers to issue a blanket prescription for Prussian blue to appropriate beneficiaries involved in a presumptive radiocesium exposure (DoD, HA Policy 05-007).

WARNING

These guidelines are intended to supplement the guidance for administration of Radiogardase™ as promulgated by the FDA for treatment of internal radiocesium contamination (www.fda.gov/cder/foi/label/2003/021626lbl.pdf). All warnings and precautions contained in the FDA guidance must be observed when administering Prussian blue.

Therapy Guidelines

Initiating therapy. Therapy is most effective when administered as soon as possible after inhalation or ingestion of radiocesium. However, a quantitative determination of internal contamination is highly unlikely to be available within 24 hours of a terrorist incident involving radiocesium. Therefore, a qualitative assessment of the likelihood of internal

contamination will be necessary to determine when to initiate treatment. Those who were close to the incident (e.g., victims in the immediate vicinity and first-responders not wearing personal protective equipment) have a greater likelihood of internal contamination than those who were several hundred yards away and/or upwind from the explosion/release site. It is reasonable to assume exposure for unprotected persons near the incident in the absence of evidence to the contrary.

Additionally, if appropriate radiation detection instrumentation, e.g., a Geiger–Mueller (G-M) tube, is available, then the results of a survey of the victim, conducted by someone familiar with the instrument’s characteristics and operation, may be used to estimate the likelihood of exposure. It is reasonable to assume exposure based on the detection of upper body external radioactive contamination, particularly in the region of the mouth and nose, and on the detection of internal contamination based on any injuries and on bilateral moist nasal swabs preferably obtained within one hour after the incident.

If the victim’s respiratory/hemodynamic status is stable and there is reason to presume exposure occurred, then one or two 30-capsule packages of Prussian blue (500 mg per capsule) should be provided to the victim to initiate a daily dosage regimen consistent with FDA guidance:

- Adults and adolescents: 3 g (six capsules) orally three times daily
- Pediatrics (2-12 years): 1 g (two capsules) orally three times daily

Because Prussian blue is well tolerated (constipation and colored stool are the only consistently reported reactions), treatment of presumptively exposed victims is not contraindicated although judicious use of this agent is advised to ensure an adequate supply to support sustained therapy for victims known to be contaminated internally. Hence, a definitive diagnosis of internal contamination is required to continue treatment for those presumptively exposed.

Assessing the need to sustain therapy. In the event that large numbers of patients begin presumptive therapy, an interim assessment of these individuals may be necessary. Following complete external decontamination, hand G-M scanning of a casualty may reveal a gamma radiation level emanating from the patient that is above background levels. These patients should continue therapy while awaiting whole-body counting and/or excretion-sampling measurements. The clinical decision to continue interim therapy on

other patients should be made on a case-by-case basis after evaluation of the available data.

A quantitative determination of the presence or absence of internal contamination (as well as the magnitude of the exposure) for those who actually inhaled or ingested radiocesium should be conducted as soon as is feasible after the incident. This can be accomplished through direct measurement of radioactivity in the whole body (whole-body counting) or through *in vitro* measurement (radiation counting) of excreta (specifically, urine and feces). Whole-body counting is the preferred method for initial evaluation because it is rapid (typically, a two-minute count will provide an acceptable lower limit of detection), it requires no sample collection and preparation, and it can be done in a field-expedient facility (IAEA 1988). It is imperative that victims be decontaminated externally prior to whole-body counting to prevent false positives or overestimates of exposure. Excreta sampling and counting is more sensitive than whole-body counting and may be conducted either in conjunction with or in lieu of whole-body counting. Care must be exercised in sample collection to prevent contamination that would lead to false positives or overestimates of exposure. Specific guidance on sample collection and shipping should be obtained from the laboratory that will conduct the analysis (e.g., the U.S. Army Center for Health Promotion and Preventive Medicine or the U.S. Air Force Institute for Operational Health). Discontinue therapy for victims with no radiocesium contamination detectable by direct measurement and/or excreta sampling. For victims with radiocesium contamination detectable by direct measurement and/or excreta sampling, continue therapy at the dosages recommended in the FDA labeling instructions. Because evidence has shown that Prussian blue is well tolerated at dosages greater than those recommended in the labeling instructions, consideration may be given to increasing the therapeutic dosages after consulting with a health physicist about the magnitude of the exposure.

Termination of therapy. Serial measurements of internal radioactivity (i.e., weekly whole-body counting and/or excreta sampling) will be necessary to evaluate the efficacy of treatment and to determine when it may be terminated. Therapy should be continued until the whole-body concentration of radiocesium is reduced substantially and should be based on the principle that any radiation exposure should be reduced to as low as is reasonably achievable. Following are reasonable criteria for termination of therapy:

- No further reduction in the radiocesium concentration in the body is observed in serial whole-body counting or excreta sampling.
- There is evidence of an adverse reaction with continuing administration.
- The impact of continued therapy on the available supply of Prussian blue if the dose avoided by continued therapy is negligible, with negligible being an individual committed effective dose of ≤ 0.01 mSv (≤ 1.0 mrem) (NCRP 1993).

Additional Assistance

Further physician assistance regarding treatment for internal radiocesium may be obtained from the senior physician on the Armed Forces Radiobiology Research Institute (AFRRI) Medical Radiobiology Advisory Team (commercial 301-295-9881 or DSN 295-9881) or the director of Military Medical Operations (commercial 301-295-1069/2950 or DSN 295-1069/2950). Or contact the AFRRI Security Desk (commercial 301-295-0530 or DSN 295-0530) and request assistance. Please send comments or suggestions by e-mail to meir@afri.usuhs.mil or write one of the above offices at AFRRI, 8901 Wisconsin Avenue, Bethesda MD 20889-5603.

References

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