

## **DTRA POINT PAPER FOR VBDR REVIEW AND CONCURRENCE**

### **DOSE RECONSTRUCTION FOR CONDITIONS NOT LIKELY INDUCED BY EXPOSURE TO IONIZING RADIATION**

#### **BACKGROUND**

The Defense Threat Reduction Agency (DTRA) is mandated by law to perform a radiation dose assessment (RDA) for any radiogenic disease listed in 38 CFR 3.311(b)(2) which does not otherwise qualify for presumptive service connection under §3.309. For any non-cancer condition not identified as radiogenic in §3.311 (i.e., relating to or caused by exposure to ionizing radiation), the Department of Veterans Affairs (VA) will consider the claim as non-presumptive, provided the claimant has cited or submitted “competent scientific or medical evidence” that the claimed condition was “at least as likely as not” caused by radiation.

As of October 2006, over 98% of 1,313 pending DTRA non-presumptive cases were for diseases that are considered radiogenic in §3.311. However, the dose reconstruction backlog also includes (or has included in the past) a number of cases which involve conditions not listed in §3.311, and 1) for which there is no sound scientific or medical evidence that the conditions are radiogenic (i.e., induced by ionizing radiation) or 2) are considered to be deterministic (threshold) effects that are not likely to be observed at the relatively low doses encountered by veterans of the 1945-1946 occupation of Hiroshima and Nagasaki; veterans who were prisoners of war in those regions when the atomic bombs detonated; and veterans of U.S. sponsored atmospheric nuclear weapons tests from 1945-1962. These include:

- Acute respiratory failure
- Anxiety/depression (these conditions may be psychologically associated with actual or suspected radiation exposure, but are not caused by it)
- Benign prostatic hypertrophy
- Blindness
- “Breathing condition” (*sic*, not otherwise specified)
- Carotid endarterectomy (this is a surgical procedure, not a disease)
- Chronic lymphocytic leukemia (CLL) (this disease is specifically excluded from §3.309 and §3.311)
- Chronic obstructive pulmonary disease
- Cirrhosis of the liver
- Diabetes
- Eye sensitivity (*sic*, not otherwise specified)
- “Heart disease” or “heart condition” (not otherwise specified)
- Hypertension
- Intestinal disorder, mimicking Crohn’s disease
- Jaw bone deterioration
- Loss of taste buds

- “Memory lapses” (*sic*, not otherwise specified)
- Multiple system disease due to immune deficiency (also “multiple chemical sensitivity”)
- Osteoarthritis
- Osteoporosis
- Peripheral neuropathy
- Progressive supranuclear palsy
- Rheumatoid arthritis
- Ruptured disc affecting hip/knee/leg
- Scleroderma
- “Teeth condition” (*sic*, not otherwise specified, including “loss of teeth”)
- Testicular atrophy
- “Underlying disease process manifested by high cholesterol”

Claimed conditions (not listed in §3.311) for which there is scientific evidence of radiogenicity at doses well above those typically encountered by veterans include:

- Anemia/lymphocytopenia/leucopenia/neutropenia (requires a high dose of radiation; in any case, blood counts would have returned to normal long before the veteran consulted a physician)
- “Cerebrovascular accident” (stroke)
- Hypothyroidism

Finally, some conditions (also not listed in §3.311) may be radiogenic at moderate radiation doses that are conceivable for typical veterans. These include myelodysplastic syndrome and myelofibrosis, both considered to be pre-leukemic conditions.

While each veteran is entitled to due process with regard to his/her claim, there are two factors that support the discontinuation of dose reconstruction for cases involving conditions that are not likely caused by radiation exposure: the unsuitability of the veteran’s submitted scientific/medical evidence and the lack of a causal relationship between these conditions and radiation exposure (especially at doses typically encountered by veterans).

## **DISCUSSION**

### *Scientific or Medical Evidence*

If extant in the veteran’s claim file, the sole source of “competent scientific or medical evidence” is usually a letter from a physician (or dentist) that conveys a speculative and/or uncertain opinion about a causal relationship (nexus) between the claimed condition and the veteran’s account of activities during military service. There is generally no attempt by the physician to quantitatively assess the magnitude of the exposure; this is understandable, given that it would be nearly impossible for a clinician to assess radiation exposure (over 40 years after the fact) based on symptoms, physical examination, and commonly available laboratory tests alone. While it may or may not be prudent for a physician to assume that a “high” dose was received (if only for the purposes of supporting the veteran’s compensation claim), there are additional issues concerning the suitability of such evidence.

1. In many cases, the physician's letter does not identify any medical evidence to support the diagnosis of radiation-induced disease, or does not establish a plausible nexus with any degree of certainty. In *Lee v. Brown*,<sup>1</sup> the Court ruled that statements from physicians that are inconclusive (speculative) as to the origin of a disease cannot fulfill the "nexus" requirement to ground a claim. In *Sacks v. West*,<sup>2</sup> the Court ruled that a physician's opinion, using the term "could" without supporting clinical data or other rationale, is too speculative to provide a degree of certainty required for medical nexus evidence. Examples from several pending cases (emphasis added):

"Review of current medical literature regarding people exposed to radiation the [sic] course of radiation accidents as might be comparable to the exposure that this patient suffered documents many other radiation-induced disabilities but does not mention radiation-induced neuropathy. *Although there is little in the medical literature documenting radiation-induced injury, for the purposes of compensation and pension I would suggest that this particular individual may be unique.* I would suggest that it is likely as not that the disability in his lower extremities is related to a radiation induced-neuropathy."

"The veteran suffers from chronic obstructive pulmonary disease, pulmonary fibrosis, and cataracts, which certainly *could have been [sic] caused by* his exposure to radiation from the atomic bomb blasts that he was exposed to while he was in the Army."

"[The veteran] is currently being treated for progressive pulmonary fibrosis of *unclear etiology*. He has a history of radiation exposure while in the military and it is my opinion that this exposure *may very well have caused or contributed to* his current pulmonary condition."

"The damage was *probably caused or else aggravated, at least in part by* the radiation."

"I am writing this letter to state that [the veteran's] osteoporosis *is as likely as not to have been caused by (or at least related to)* his whole-body radiation exposures *in the past.*"

2. While physicians may be qualified to render opinions that are predicated on a complete set of facts, few are qualified to speculate about the magnitude and quality of a radiation dose based only on a patient's personal account. In *LeShore v. Brown*,<sup>3</sup> the Court ruled that evidence which is simply information recorded by a medical examiner, unenhanced by any additional medical comment by that examiner, does not constitute "competent medical evidence" and that a bare transcription of lay history is not transformed into "competent medical evidence" simply because the transcriber happens to be a medical professional. However, the following opinions were based only on a history provided by the veteran, as opposed to any actual evidence regarding the magnitude of radiation exposure (emphasis added):

"The patient reports that while he was serving aboard a Naval ship that he was placed within one mile of an atomic bomb detonation. He was able to see the bones in his arm and the blast caused a newspaper against a steel hull to be imprinted backwards in the bulkhead. *This would indicate to us that he had a significant radiation exposure.* It is, therefore, *reasonable to consider* that this type of exposure *probably has had some implication in* his health conditions."

“On an experimental naval ship in the Marshall Islands, 1953-57. *Apparent radiation exposure, per his history*, while serving tour of duty on that ship; this would represent the etiology of his disease *if that were the case.*”

“This veteran states he witnessed three separate nuclear explosions and was in very close proximity, being about seven miles away. Based on this information...*it would appear that this veteran was exposed to large amounts of radiation...*”

In another case, the physician simply restated the veteran’s account of participation, failing to offer an explicit opinion that the claimed condition is (or could be) the result of exposure to radiation (emphasis added):

“[The veteran] is a patient whom I have followed for a number of years. He has had multiple pulmonary problems which include pulmonary fibrosis. *By his report, and I believe him, he had significant atomic bomb radiation exposure* in 1955 at the Tea Pot Dome explosions in Nevada. He had had progressive fibrosis and had been debilitated by that [sic] requiring high levels of oxygen therapy. *He does in my opinion have a 100% disabled condition secondary to his pulmonary fibrosis.*”

3. In *Reonal v. Brown*,<sup>4</sup> the Court ruled that the weight of a medical opinion is diminished (and perhaps of little or no probative value) when based on an inaccurate factual premise or an examination of limited scope. While examples (and associated factual rebuttals) will not be provided here, several pending non-radiogenic cases are supported by opinions that are based on inaccuracies, errors, and speculation.

4. Finally, the physicians in two cases simply assumed without justification that the patient’s current symptoms/conditions were due to a higher radiation dose than typically indicated by a dose reconstruction predicated on contemporaneous dosimetry, survey data, and other information. As almost all radiogenic diseases can also be caused by other etiologic factors, even in the absence of any radiation exposure above background, summarily dismissing alternate causes of a patient’s disease is not good clinical practice. Examples are (emphasis added):

“The estimated exposure by the Defense Nuclear Agency is significantly less than that expected to cause thyroid hypofunction. By his account, the symptoms that he experienced at the time of his evacuation *would suggest much higher levels of radiation exposure.*”

“[Sophisticated computer modeling] analysis would also require suppositions. Thus *any resulting modeling could be less reliable than practical clinical estimates* used in my own evaluation of [the veteran’s] case based on reliable radiobiological principles, clinical observations in [the veteran’s] case and my extensive education, training and clinical experience on radiation effects in people.”

Unless it can be demonstrated in advance that a veteran’s exposure scenario was extraordinary and unique (i.e., likely to result in an external and/or organ dose exceeding the 99<sup>th</sup> percentile of radiation doses provided to date), unscientific and unsupported medical opinions should not be accepted as justification for the performance of a dose reconstruction for claims involving conditions that are not considered to be radiogenic (i.e., not defined as radiogenic in §3.311).

### *Radiogenic Disease in the Scientific Literature*

The prodromal symptoms most indicative of radiation exposure (e.g., fatigue, nausea, vomiting) do not present below 30 rem (usually at much higher doses) and they may, of course, be caused by factors other than radiation exposure. It is very unlikely that any veteran received an external whole body dose sufficient to cause skin changes, as even transient erythema does not occur unless very large areas of the skin receive doses of at least 200-300 rad or more. At these doses, a subject would become clinically ill within hours of exposure and would almost certainly have consulted a physician. It is possible, however, that beta burns leaving permanent telangiectasiae, erosion, atrophy, and even necrosis could arise from fallout particles retained on the skin. Beta-emitting particles, in this scenario, could give a high dose to the skin while sparing bone marrow and other tissues. This would cause local (skin) injury only, not systemic illnesses.

Anemia, leukopenia, lymphocytopenia, and thrombocytopenia are well-known laboratory findings (vice diseases) that may follow closely after whole body or significant partial body radiation exposure. The threshold dose for such effects is between 20 and 50 rem. As hematopoietic tissue replenishes itself, these effects are transient, though recovery may take up to two years and may not be complete at high but survivable doses. These laboratory findings can be associated with diseases unrelated to radiation exposure, and it is a reasonable expectation that a physician be required to consider non-radiation factors and rule them out. Cytogenetics, fluorescent *in situ* hybridization (FISH) and immunoassays can detect chromosomal damage and changes at even lower dose levels. However, their results are not pathognomonic for radiation injury, nor are they useful in determining therapy. Hence, these highly sophisticated and expensive tests are not routinely ordered for such conditions.

While age-dependent screening doses for common skin cancers are relatively low (as described in the DTRA point paper on expediting skin cancer cases), the radiation doses required to cause non-cancer skin injury are relatively high. According to the Centers for Disease Control and Prevention, the threshold for cutaneous radiation injury is 200 rem.<sup>5</sup> Actinic keratosis, considered to be the earliest stage in the development of skin cancer, is caused by long-term exposure to sunlight; modifying factors include geographical latitude, age, and skin complexion.<sup>6</sup> Should a veteran with actinic keratosis later develop biopsy-proven skin cancer, he/she would clearly be eligible for compensation under §3.311. However, it must be noted that not all patients with skin cancers have pre-existing actinic keratosis, nor do all cases of actinic keratosis progress to skin cancer.

The radiation doses required to cause detectable injury to most other organs are even higher. According to Hall (Table 19.2, pp. 334-335),<sup>7</sup> the doses required to cause injury in 5% of an exposed population at five years post-exposure are:

- Lungs – 1,750 rad
- Stomach – 5,000 rad
- Intestine – 4,000 rad
- Peripheral nerves – 6,000 rad
- Retina (for blindness) – 4,500 rad

- Mature cartilage and adult bone – 6,000 rad (1,000 rad in a growing child; ossification in some bones is not complete by age 18, so theoretically some veterans could develop arthritis in the very improbable case they were exposed to such doses locally).

These data are generally from therapeutic radiation, which is usually administered in daily doses of 180 to 200 rad over several weeks; the acute dose required to produce these effects would therefore be lower by a factor of 2 or more. Based on health physics principles and a wealth of dose reconstruction data compiled by DTRA, it is virtually impossible for a veteran to have received a dose high enough to cause an illness based on damage to these organs.

As noted previously, CLL is categorically excluded from consideration as a radiogenic disease in §3.309 and §3.311. The National Research Council (NRC) has noted that CLL is not covered in other radiogenic disease programs, and it was not included as a radiogenic disease in the 2003 revision of the 1985 National Institutes of Health (NIH) radioepidemiological tables because available data were insufficient to support a relationship between CLL and radiation exposure.<sup>8</sup>

#### *DTRA Dose Reconstruction Data*

DTRA has analyzed the results of 3,667 cases for which dose estimates have been provided to VA or veterans since the inception of the Nuclear Test Personnel Review (NTPR) Program. All of the cases include an external dose estimate, and many cases involve more than one organ dose. This analysis includes doses that have been generated since 2003 using procedures that have been revised in accordance with the recommendations of the NRC; these doses tend to be higher than pre-2003 doses due to the consideration of previously-neglected exposure pathways and the assignment of various uncertainty factors. The tables below present the results of this analysis.\*

Dose	Number	Number/percent exceeding			High (rem)	Explanation of high dose(s)
		10 rem	20 rem	30 rem		
External	3,667	34 (0.9%)	9 (0.2%)	3 (< 0.1%)	84	Rongerik (all three highest)
Organ**	4,087	19 (0.5%)	8 (0.2%)	6 (0.1%)	76	Rongerik (1), unique scenario (2), iodine (3)
Eye	133	9 (7%)	2 (1.5%)	1 (0.8%)	62	Close-up fallout filter work

Of 1,997 separate skin doses assigned (among 913 total individual cases):

Number/percent exceeding					High (rem)	Explanation for high dose(s)
10 rem	50 rem	100 rem	200 rem	500 rem		
408 (20%)	150 (7.5%)	99 (5.0%)	52 (2.6%)	23 (1.2%)	3,500	Operation Redwing

\* In cases where upper bound (95<sup>th</sup> percentile) doses were not provided, mean doses (central estimates) were used in this evaluation.

\*\* Skin and eye doses have been excluded from the analysis due to the significant uncertainty involved in skin dose calculations and the shallow tissue depth used in skin and eye dose determinations (in comparison with the deep dose as it applies to external and internal/organ doses)

The above analysis clearly illustrates the range of external and organ doses (not including skin) that are encountered by veterans, including those who received the highest doses as a result of unique and/or unusual (rare) exposure scenarios. At no time during the existence of the NTPR Program has an external or organ dose (excluding skin) exceeded 84 rem.

### *VHA Medical Opinions*

After a dose estimate is delivered to VA, radiation claims are referred to the Chief, Office of Public Health and Environmental Hazards, Veterans Health Administration (VHA), for an advisory medical opinion. Because the claimed conditions are not considered radiogenic and upper bound radiation doses (external and internal) for the vast majority of veterans are low (often  $\leq 1$  rem), the VHA has consistently rendered the opinion that it is unlikely that a claimed condition (aside from neoplastic disease, which are stochastic rather than deterministic in terms of causation) can be attributed to radiation exposure. For example:

“Damage to the [organ/system] other than neoplastic transformation, if caused by radiation, would be an example of a deterministic effect. Deterministic changes generally are considered to have a threshold. The probability of causing harm in most healthy individuals at doses of less than 10 rem as a result of deterministic effects is close to zero (Institute of Medicine Report, Adverse Reproductive Outcomes in Families of Atomic Veterans: The Feasibility of Epidemiological Studies, 1995, pages 23-24). Usually a threshold dose on the order of hundreds or thousands of rads must be exceeded for the deterministic effect to be expressed (Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Ionizing Radiation, 1999, page 83).”

“In light of the above, in our opinion it is unlikely that the veteran’s disorder... can be attributed to exposure to ionizing radiation in service.”

The VHA position regarding the probability of adverse health outcomes is substantiated by the Health Physics Society, the NRC, and the Radiation Effects Research Foundation, all of which generally agree that adverse health effects at whole body doses below 10 rem have not been demonstrated:

“There is substantial and convincing scientific evidence for health risks following high-dose exposures. However, below 5-10 rem (which includes occupational and environmental exposures), risks of health effects are either too small to be observed or are nonexistent.”<sup>9</sup>

“[T]he BEIR VII lifetime risk model predicts that approximately one individual in 100 persons would be expected to develop cancer (solid cancer or leukemia) from a dose of 100 mSv [10 rem] while approximately 42 of the 100 individuals would be expected to develop solid cancer or leukemia from other causes. Lower doses would produce proportionately lower risks. For example, it is predicted that approximately one individual in 1000 would develop cancer from an exposure to 10 mSv [1 rem].”<sup>10</sup>

“There is no evidence of [noncancer] radiation effects for doses less than about 0.5 Sv [50 rem].”<sup>11</sup>

DTRA has performed an analysis of VHA medical opinions provided since 2003 in response to radiation claims for which DTRA has provided a dose estimate (the NRC published a review of the DTRA dose reconstruction program in 2003 that resulted in major program changes and improvements). The results of this analysis indicate:

- Of 418 medical opinions provided by VHA for DTRA veteran cases involving diseases and conditions other than skin cancer, 230 (55%) of the associated doses were  $\leq 1$  rem, 371 (89%) were  $\leq 5$  rem, and 407 (97%) were  $\leq 10$  rem.
- Of the 11 cases involving doses  $> 10$  rem, seven were less than 20 rem and 10 were less than 45 rem. Only two of these cases received medical opinions favorable to compensation.
- Of the 418 cases, 28 involved one or more conditions not considered radiogenic. None of these received a medical opinion favorable to compensation.

As expected, these data are in close agreement with the DTRA doses reviewed above, and it follows that the chance of successful adjudication is extremely low to non-existent for a condition that is not considered to be radiogenic.

#### *Impact on DTRA and Veterans*

As noted above, there are over 1,200 veterans awaiting decisions on claims that involve legitimate radiogenic conditions (as defined in §3.311), all of which deserve prompt consideration. Expending time and resources on cases that 1) involve conditions not considered to be radiogenic, 2) are founded solely on a medical opinion unsubstantiated by supporting laboratory tests/data or peer-reviewed literature, and 3) have little or no chance of successful adjudication only serve to delay the consideration of reasonable/legitimate cases. In *Grivois v. Brown*,<sup>12</sup> the Court ruled that it was the duty of VA to avoid adjudicating implausible claims at the expense of delaying well-grounded ones. It is, therefore, reasonable to conclude that DTRA has a similar duty to avoid performing dose reconstructions for conditions that are highly unlikely to be attributable to radiation exposure.

A secondary, yet major, impact on DTRA (aside from delaying timely consideration of legitimate claims) is the cost associated with performing unwarranted dose reconstructions. DTRA expends approximately \$9k to \$15k per RDA, and the average processing time (since the NRC recommendations were released in 2003) can range up to three years or more. This expenditure is simply not justified for cases that have little or no chance of successful adjudication.

### **RECOMMENDATIONS**

DTRA recommends the following:

- Pending claims involving conditions that are not considered to be radiogenic should undergo a review by VHA to determine if 1) scientific or medical evidence exists to support the claim and 2) the cited evidence is indeed competent (i.e., supported by laboratory tests, medical data, or scientific literature). If not, then the claim should be

returned to VA for further development and/or a request that the veteran's physician provide such support. If the claim cannot be properly substantiated, then the request for a dose reconstruction should be rescinded.

- All future claims involving conditions not considered to be radiogenic should receive a preliminary review by VHA, as described above, to determine if the condition may be induced by the maximum radiation doses received by veterans with exposure scenarios that are not extraordinary or unique. If not, then a dose reconstruction should not be requested from DTRA.

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<sup>1</sup> 10 Vet. App. 336 (1997)

<sup>2</sup> 11 Vet. App. 314 (1998)

<sup>3</sup> 8 Vet. App. 406, 409 (1995)

<sup>4</sup> 5 Vet. App. 458 (1993)

<sup>5</sup> Centers for Disease Control and Prevention, Cutaneous Radiation Injury: Fact Sheet for Physicians (2005)

<sup>6</sup> American Academy of Dermatology, Actinic Keratosis (2006)

<sup>7</sup> Hall, E.J., Radiobiology for the Radiologist, 6<sup>th</sup> Edition (2006)

<sup>8</sup> National Research Council, Assessment of the Scientific Information for the Radiation Exposure Screening and Education Program (2005)

<sup>9</sup> Health Physics Society, Radiation Risk in Perspective (2004)

<sup>10</sup> National Research Council, BEIR VII: Health Risks from Exposure to Low Levels of Ionizing Radiation (2005)

<sup>11</sup> Radiation Effects Research Foundation, Life Span Study Report 13: Solid cancer and noncancer disease mortality: 1950-1997 (2003)

<sup>12</sup> 6 Vet. App. 136 (1994)