Presentation 13 - Melissa McDiarmid

HEALTH EFFECTS OF DEPLETED URANIUM IN EXPOSED GULF WAR VETERANS – A TEN-YEAR FOLLOW-UP

Melissa A. McDiarmid, M.D., M.P.H.
VA Maryland Health Care System
Baltimore Division

Background

- Friendly Fire incidents - inhalation exposure/wound contamination and embedded shrapnel
- Finding - relation between shrapnel status and elevated urinary uranium first observed in 1994 visit, confirmed in all 4 subsequent visits

Purpose of DU Surveillance Program

- Determine health effects, if any, in exposed population
- Develop methods to measure uranium exposure in novel exposure mode (embedded shrapnel)
- Examine surgical management of shrapnel

Summary of Surveillance Visits

Year	Cases	Non-exposed	Total
1993-4	33		33
1997	29	38	67
1999	21+29 new		50
2001	31+8 new (17 original cases)		39
2003	32		32

A total of 70 individuals involved in friendly fire incidents have been evaluated at Baltimore.

Surveillance Protocol
Detailed Questionnaire

- Medical History
- Social History
- Family History
- Occupational/Exposure History
- Reproductive History
- Partner's History

Surveillance Protocol
Laboratory Studies

- CBC
- Blood Chemistries
- Urinalysis
- Neuroendocrine markers (FSH, LH, Prolactin, Testosterone)
- Urinary Uranium
- Immunologic markers
- Other Uranium Measures

Surveillance Protocol
Special Studies

- Semen analysis
- Chromosomal aberrations
- Sister chromatid exchange

Surveillance Protocol
Additional Surveillance Components

- Physical examination
- Neurocognitive test battery
- Whole body radiation counting
- Risk Communication/Focus Group

Demographic Characteristics for 2001 Cohort

	N	%
RACE		
African-American	12	31
Caucasian	22	56
Hispanic	4	10
Other	1	3
EDUCATION		
0-8 years	1	3
9-12 years	9	23
Some college	22	56
College degree	4	10
Post college	3	8
MARITAL STATUS[a]		
Never married	3	8
Married	31	79
Divorced	4	10
Unknown	1	3
AGE[b]	35.1 ± 0.76	

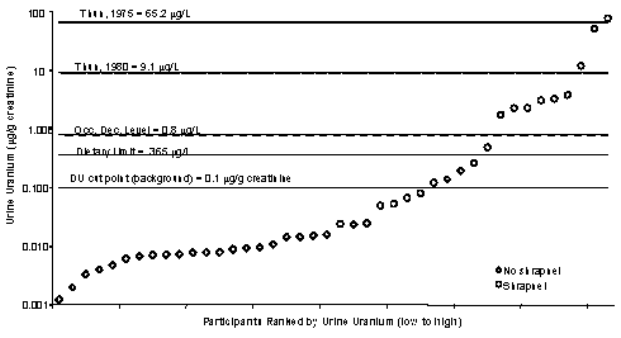
[a] At time of 2001 evaluation
[b] Mean age at time of 2001 evaluation (±SE, standard error of the mean)

Active Medical Problems Summary (2001)

	Low Uranium Group[a]		High Uranium Group[b]		Mann-Whitney Test(p)
	n	%	n	%	
Participants with active problems[c]	26	100	12	92.3	0.15
Injuries[d]	7	26.9	13	100	0.00
Musculoskeletal	17	65.4	7	53.8	0.49
Cardiovascular	10	38.5	2	15.4	0.14
Psychiatric	4	15.4	3	32.1	0.56
Nervous system	5	19.2	3	23.1	0.78
Other[e]	18	69.2	10	76.9	0.61

[a] < 0.10 µg/g creatinine (n=26)
[b] ≥ 0.10 µg/g creatinine (n=13)
[c] Individuals might have more than one problem
[d] Injuries sustained during Gulf War
[e] Gastrointestinal, skin, respiratory, genitourinary

Urine Uranium (2001) N=39



Hematologic Parameters Summary (2001)

Laboratory test (normal range)	Low Uranium Group[a] (mean ± SE)	High Uranium Group[b] (mean ± SE)	Mann - Whitney Test (p)
White Blood Cells (4.8-10.8 K/cm^3)	6.53 ± 0.41	5.85 ± 0.45	0.36
Hematocrit (42-52%)	44.60 ± 0.43	42.59 ± 0.80	0.03
Hemoglobin (14-18 g/dL)	15.40 ± 0.15	14.79 ± 0.32	0.07
Platelets (140-440 K/cm^3)	254.54 ± 13.82	234.08 ± 13.73	0.21
Lymphocytes (%) (15-45%)	36.87 ± 1.99	36.07 ± 1.81	0.80
Neutrophils (%) (40-75%)	50.95 ± 2.09	51.83 ± 1.97	0.74
Basophils (%) (0-2%)	0.78 ± 0.10	0.65 ± 0.07	0.54
Eosinophils (%) (0-4%)	3.60 ± 0.35	3.51 ± 0.44	0.85
Monocytes (%) (2-12%)	7.79 ±0.37	7.94 ± 0.48	0.99

[a] < 0.10 µg/g creatinine (n=26)
[b] ≥ 0.10 µg/g creatinine (n=13)

Renal Function Parameters (2001)

Laboratory test (normal range)	Low Uranium Group[a] (mean ± SE)	High Uranium Group[b] (mean ± SE)	Mann - Whitney Test (p)
Serum creatinine (0.5-1.1 mg/dL)	0.95 ± 0.03	0.85 ± 0.03	0.03
Serum uric acid (3.4-7 mg/dL)	5.94 ± 0.23	5.85 ± 0.51	0.45
Serum calcium (8.4-10.2 mg/dl)	9.17 ± 0.006	9.27 ± 0.137	0.67
Serum PO4 (2.7-4.5 mg.dl)	3.82 ± 0.101	3.82 ± 0.148	0.63
Urine calcium (100-300 mg/24 hr)	183.50 ± 23.8	214.50 ± 26.3	0.35
Urine PO4 (0.4-1.3 g/24 hr)	1.03 ± 0.008	1.15 ± 0.107	0.40

[a] < 0.10 µg/g creatinine (n=26)
[b] ≥ 0.10 µg/g creatinine (n=13)

Renal Function Parameters (2001) cont.

Laboratory test (normal range)	Low Uranium Group[a] (mean ± SE)	High Uranium Group[b] (mean ± SE)	Mann - Whitney Test (p)
Urine beta-2 microglobulin (0-300 µg/g creatinine)[c]	38.53 ± 6.71	36.42 ± 7.46	0.78
Urine retinol binding protein (3-610 µg/g creatinine)	46.13 ± 3.46	65.68 ± 11.11	0.06
Urine creatinine (1.3 -2.6 g/24 hr)	1.99 ± 0.11	2.14 ± 0.10	0.29
Urine total protein (0-92.8 mg/g creatinine)	54.63 ± 4.94	78.69 ± 10.52	0.01

[a] < 0.10 µg/g creatinine (n=26)
[b] ≥ 0.10 µg/g creatinine (n=13)
[c] n = 16 for low uranium group and n = 9 for high uranium group

Neurocognitive Impairment Measures (2001)

Laboratory test	Low Uranium Group[a] (mean ± SE)	High Uranium Group[b] (mean ± SE)	Mann - Whitney Test (p)
A-IIac: Indexes Accuracy	0.16 ± 0.04	0.27 ± 0.07	0.138
A-Iirt: Indexes Speed	0.14 ± 0.03	0.14 ± 0.06	0.886
A-Iitp: Indexes Accuracy per Minute	0.12 ± 0.02	0.17 ± 0.06	0.717
NP3 Index	0.05 ± 0.01	0.09 ± 0.04	0.812

[a] < 0.10 µg/g creatinine (n=26)
[b] ≥ 0.10 µg/g creatinine (n=13)

Neuroendocrine and Thyroid Hormone Parameters (2001)

Laboratory test (normal range)	Low Uranium Group[a] (mean ± SE)	High Uranium Group[b] (mean ± SE)	Mann - Whitney Test (p)
Prolactin (2.1 - 17.7 ng/mL)	18.84 ± 1.60	14.70 ± 2.76	0.06
FSH[c] (.9-15 IU/ml)	4.39 ± 0.50	4.51 ± 0.74	0.95
LH[c] (1.5-9.3 mIU/ml)	5.09 ± 0.51	5.13 ± 1.04	0.48
Testosterone (3-10 ng/ml)	5.64 ± 0.49	4.77 ±0.47	0.28
TSH[c] (0.49-4.67 µIU/ml))	1.99 ±0.24	2.28 ± 0.50	0.89
Free thyroxine (0.71-1.85 ng/dL)	1.66 ± 0.35	1.08 ± 0.07	0.02

[a] < 0.10 µg/g creatinine (n=26)
[b] ≥ 0.10 µg/g creatinine (n=13)
[c] FSH, follicle - stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone

Semen Characteristics (2001)

Clinical parameters (normal range)	Low Uranium Group[a] (mean ± SE)	High Uranium Group[b] (mean ± SE)	Mann - Whitney Test (p)
Days Abstinence (2 – 5 days)	4.8 ± 1.7	4.2 ± 0.9	0.820
Semen Volume (2-5 ml)	2.6 ± 0.4	3.5 ± 0.6	0.167
Sperm Concentration(> 20 million/mL)	102.8 ± 28.6	219.1 ± 70.5	0.126
Total Sperm Count (>40 million)	241.6 ± 66.4	708.6 ± 215.1	0.061
Percent Motile Sperm (>50%)	57.6 ± 4.9	60.5 ± 6.3	0.639
Percent Progressive Sperm [WHO[c] Class A and B] (>50%)	27.3 ± 3.2	25.7 ± 3.7	0.766
Total Progressive Sperm [WHO Class A and B] (>20million)	79.9 ± 22.6	206.8 ± 58.3	0.126
Percent Rapid Progressive Sperm [WHO Class A] (>25%)	17.6 ± 2.7	16.3 ± 2.5	0.586
Total Rapid Progressive Sperm [WHO Class A] (>10 million)	54.9 ± 16.2	134.8 ± 40.5	0.152

[a] < 0.10 µg/g creatinine (n=16)
[b] ≥ 0.10 µg/g creatinine (n=11)
[c] WHO, World Health Organization

Genotoxicity Parameters (2001)

Laboratory test	Low Uranium Group[a] (mean ± SE(n))	High Uranium Group[b] (mean ± SE(n))	Mann - Whitney Test (p)
Mean aberrations/cell	0.003 ± 0.001 (26)	0.01 ± 0.004 (13)	0.027
Mean SCE[c] untreated	5.07 ± 0.32 (25)	4.39 ± 0.37 (13)	0.199
Mean SCE w/Bleomycin 2 µg/ml	5.42 ± 0.32 (23)	5.95 ± 0.71 (11)	0.663
Mean SCE w/Bleomycin 4 µg/ml	6.31 ± 0.60 (20)	5.30 ± 0.42 (11)	0.197
HPRT MF[d]	10.97 ± 0.97 (26)	19.84 ± 4.89 (13)	0.105

[a] < 0.10 µg/g creatinine
[b] ≥ 0.10 µg/g creatinine
[c] SCE, sister chromatid exchange
[d] HPRT MF, hypoxanthine phosphoribosyl transferase mutation frequency

Radiation Dose Estimate from Whole Body Counting

- Nine veterans with whole body measurements above background
- Radiation dose estimates calculated using ICRP 30 Biokinetic model for U
  - 0.01 to 0.11 rem/year
  - 0.61 to 5.33 rem/50 years
- Public dose limit: 0.1 rem/year
- Occupational limit: 5 rem/year

Immunologic Markers (2001)

Laboratory test (normal range)	Low Uranium Group[a] (mean ± SE)	High Uranium Group[b] (mean ± SE)	Mann - Whitney Test (p)
IGG (690-1400 mg/dL)	1239.04 ± 68.13	1243.46 ± 75.46	0.82
IGA (88-410 mg dL)	199.00 ± 16.33	198.69 ± 24.66	0.95
IGM (34-210 mg/dL)	110.19 ± 12.03	96.85 ± 10.03	0.79
Complement C3 (75-140 mg/dL)[c]	126.32 ± 4.66	123.85 ± 8.20	0.56
Complement C4 (10-34 mg/dL)[c]	24.52 ± 1.47	26.62 ± 2.17	0.89
C-reactive protein	0.91 ± 0.04	0.95 ± 0.03	0.76

[a] < 0.10 µg/g creatinine (n=26)
[b] ≥ 0.10 µg/g creatinine (n=13)
[c] N for low uranium group, 25

Depleted Uranium Follow-Up Program Collaborators

- Melissa McDiarmid, MD, MPH
- Katherine Squibb, PhD
- Susan Engelhardt, RN, MN
- Marc Oliver, RN, MPH
- Patricia Gucer, PhD
- Craig Thorne, MD, MPH
- Robert Kane, PhD
- Michael Kabat, PhD
- John Ejnik, PhD
- Robert Ououa, PhD
- Barbara Curbow, PhD
- Larry Anderson, PhD
- Dennis Hoover, PhD
- Richard Albertini, MD
- Bruce Kaup, MD
- Lawrence Brown, MD
- David Jacobson-Kram, PhD