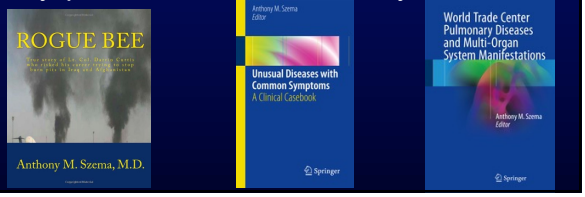
DISCLOSURES

- 9/11 Trauma and Toxicity in Childhood: Longitudinal Health and Behavioral Outcomes CDC NIOSH U01 OH011308 Co-investigator Szema, PI Hoven, Columbia University Global Psychiatric Epidemiology Group
- International Center of Excellence in Deployment Health and Medical Geosciences, Northwell Health, Szema, Director
- RDS2 Solutions, Inc., (RDS2Solutions.com), CEO
- Three Village Allergy & Asthma, PLLC, Managing Member
- Author, ***Rogue BEE; Unusual Diseases with Common Symptoms; World Trade Center Pulmonary Diseases.***



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Disclosure: Dr. Szema is the author of “Rogue Bee” which is marketed by amazon.com and is CEO of a start-up drug company RDS2 Solutions.

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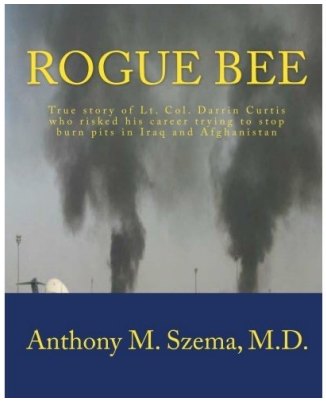

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RDS2 Solutions

Anthony M. Szema, MD, CEO

Long Island High Technology Incubator (LIHTI)
25 Health Sciences Drive, Room 208B, Stony Brook, NY 11794
Tel: (631) 675-6474 FAX: (631) 444-8825
szemasolutions@gmail.com rds2solutions.com

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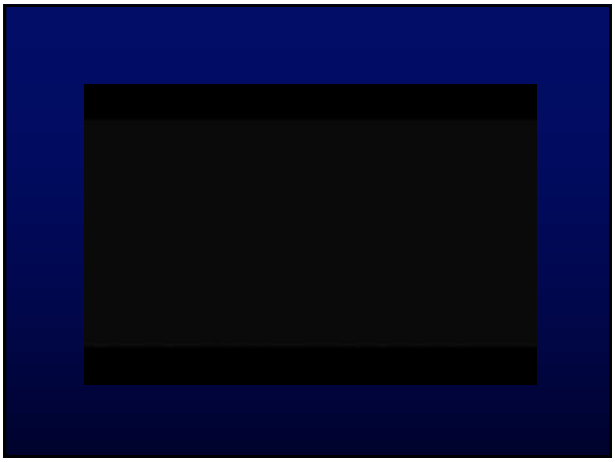

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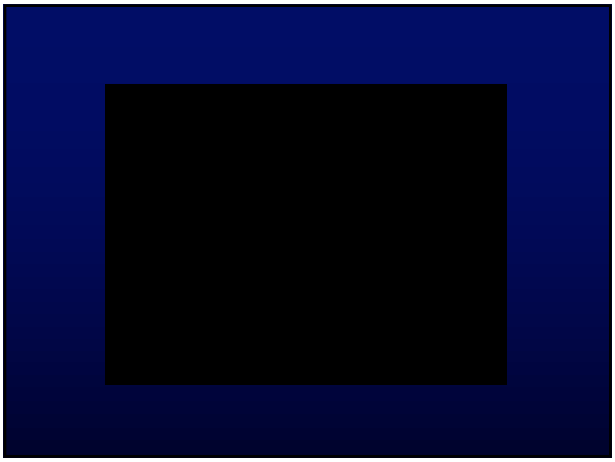

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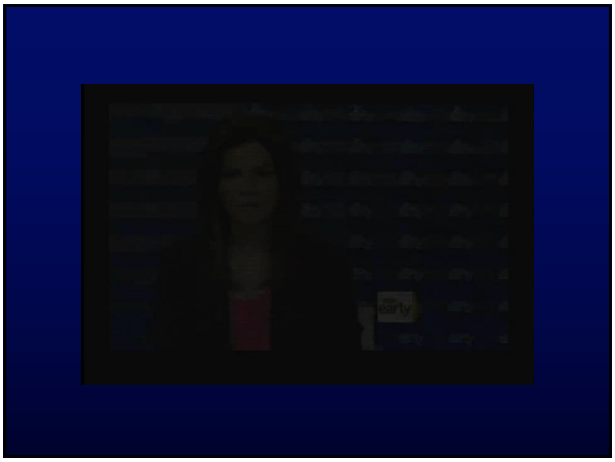

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International Center of Excellence in Deployment Health and Medical Geosciences, Northwell Health

Anthony M. Szema, MD

Northwell Health

DONALD AND BARBARA ZUCKER SCHOOL of MEDICINE AT HOFSTRA/NORTHWELL

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Burn Pit Exposure as a Cardinal Feature

of

Iraq/Afghanistan War Lung Injury

Anthony M. Szema, MD
Asthma Educators Conference 2022
Chattanooga, TN

Northwell Health

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NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ

RESPIRATORY SYMPTOMS NECESSITATING SPIROMETRY AMONG SOLDIERS WITH IRAQ/AFGHANISTAN WAR LUNG INJURY (IAW-LI)

***IN VITRO*, *IN VIVO* MOUSE, AND HUMAN LUNG TISSUE EXPOSED TO DUST FROM IRAQ & AFGHANISTAN**

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NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ

Anthony M. Szema, MD
Michael C. Peters, MD
Kristen M. Weissinger, BA
Christy A. Gagliano, MS
John J. Chen, PhD

Northwell Health

DONALD AND BARBARA ZUCKER SCHOOL of MEDICINE AT HOFSTRA/NORTHWELL

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NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ

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NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ

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NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ

Prolonged exposure to harsh environment

- For a variety of reasons, soldiers have had to be assigned ***extended or multiple tours*** of duty in Iraq.
- As a result, they have been increasingly exposed to unfavorable environmental conditions that are ***dusty*** and harsh.

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Prolonged exposure to harsh environment

- These conditions are unique and are dramatically different from the usual conditions that soldiers are exposed to in the U.S. The average rainfall in Iraq is low (*per annum*), leading to dry soil and dust-filled air (1).
- In Iraq, dust storms are so frequent that the language employs different terms describing the direction of the storm, *e.g.* :

  1) Northern seasonal dust storm, "*shamali*" (شمالی)

  2) Easterly season dust storm, "*sharqi*" (شرقی) which literally means Eastern (2).

Al Asad, Iraq

Dust storm photo taken by U.S. Marine Corps Gunnery Sargent Shannon Arledge 2005

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NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ

Prolonged exposure to harsh environment

- Inhalation of small (10μ) ***particulate*** dust can trigger asthma, even in the absence of allergic sensitization (3).
- Massive, continuous exposure to indoor dust may lead to ***allergic sensitization*** to dust mite antigens, which are risk factors for asthma (4).

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Medic visits for new respiratory illness

14%of medic visits in Iraq

are due to *respiratory complaints*

Personal communication:

Michael E. Kilpatrick, M.D., Deputy Director for Force Health Protection and Readiness Programs in the Office of the Assistant Secretary of Defense for Health Affairs

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Background:

Asthma is a barrier to serving in the military

- Since June 4, 2004, asthma diagnosed after the age of 13 has been an exclusion criterion for military enlistment.
- Therefore, no U.S. military personnel enrolled since that date should have asthma in the absence of a medical waiver.
- This means that asthma should be diagnosed less often than in the general population.

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NEW ONSET OF ASTHMA IN SOLDIERS SERVING IN IRAQ

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New-Onset Asthma in Soldiers Serving in Iraq:

- ***Hypothesis:***
  Deployment to Iraq is a risk factor for asthma.

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New-Onset Asthma in Soldiers Serving in Iraq:

- We expected to find high asthma rates among soldiers serving in Iraq.

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Methods:
Retrospective Ecological Cohort Study

- We analyzed data retrospectively from the Northport Veterans Affairs Medical Center,
- and **compared asthma rates in U.S. Iraq War Veterans** to those rates in veterans who never served in Iraq.

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Methods:

- We analyzed computer records of 6,233, 18-45-year-old subjects who served and were discharged between 3/1/04-5/1/07.
- The subjects were identified from a computerized database and stratified based on whether they had prolonged deployment to Iraq (≥1 year) or were stationed in the United States. All deployed soldiers were exposed to burn pits in Balad.
- Asthmatic soldiers were further classified by International Classification of Disease (ICD) codes for asthma.
- Possible correlation between deployment and disease status was evaluated.

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Methods:

- All patients were examined by Northport VAMC physicians.

  The clinical guidelines at the VAMC clinic for a diagnosis of asthma include:
- Presence of respiratory symptoms (cough, wheeze, dyspnea, exercise-induced shortness of breath).
- Spirometric evidence of airway obstruction with decreased FEV1/FVC or FEF25-75.
- Improvement of symptoms and FEV1 after bronchodilators.

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NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ

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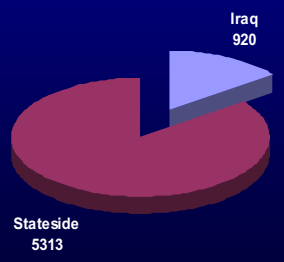
6233 Long Island-Based Soldiers Discharged 2004-7



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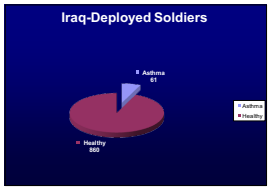
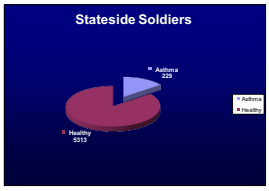
Increased rates of new-onset asthma among Iraq-Deployed Soldiers





6.6% vs. 4.3 %

P = 0.003

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Ethnic Stratification of Soldiers with Asthma

MALES	FEMALES
• 45 Caucasian	2 Caucasian
• 3 Hispanic	3 African-American
• 6 African-American	
• 2 Unknown	

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Results:

Increased likelihood of asthma if serving in Iraq

- Based on these criteria, soldiers deployed to Iraq were diagnosed with asthma more often than stateside soldiers (6.6% *vs.* 4.3%, with a crude Odds Ratio (OR) = 1.58, 95% Confidence Interval (CI) = 1.18-2.11.
- The same conclusions apply when subjects are stratified by gender and age groups.

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Results:

Risk of Being Diagnosed with Asthma Stratified by Gender

Iraq-Deployed Group	Odds Ratio	95% Confidence Interval
Asthma in both genders	1.58	(1.18, 2.11)
Asthma in men	1.60	(1.17, 2.18)

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Table 2. Summary of associations between asthma and deployment to the Persian Gulf

Age group (Years)	Deployment Status	Female (n=1453)			Male (n=4780)		
		Asthma	No Asthma	OR (95% CI)	Asthma	No Asthma	OR (95% CI)
≤25	Persian Gulf	1	21	0.91 [0.11, 7.34]	14	272	1.67 [0.82, 3.41]
	U.S.	12	229		18	585	
26 – 30	Persian Gulf	1	16	1.96 [0.24, 16.24]	15	242	2.22 [1.13, 4.34]
	U.S.	10	313		22	787	
31 – 35	Persian Gulf	1	11	1.74 [0.21, 14.63]	6	97	1.49 [0.60, 3.73]
	U.S.	12	230		25	603	
36 – 40	Persian Gulf	1	5	7.06 [0.73, 68.63]	10	87	2.44 [1.17, 5.07]
	U.S.	7	247		37	784	
>40	Persian Gulf	1	9	1.54 [0.19, 12.67]	11	99	1.74 [0.89, 3.41]
	U.S.	22	304		64	1002	
Homogeneity test (across different age groups)		P-value			P-value		
		0.71			0.90		
		0.96					
Crude OR (all age groups)		1.69 [0.66, 4.36]			1.60 [1.17, 2.18]		
		1.58 [1.18, 2.11]					
Mantel-Haenszel Common OR (95% CI)		1.70 [0.66, 4.40]			1.90 [1.37, 2.63]		
		1.88 [1.38, 2.56]					

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Results:

Increased asthma persists when adjusted for age

- When stratified by age groups, the higher risk for asthma still holds.
- For men, the odds ratios of deployment were significant in the 26-30-year-old and 36-40 year-old age groups.
- The same female age groups also showed higher risks of asthma, though the ORs were not statistically significant because of smaller sample sizes.

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Results:

Reduced FEV1/FVC in Soldiers Serving in Iraq

In the 45 subjects with numerical VA data, spirometric measurements were collected while subjects were taking asthma medications and showed reduced values:

FVC	4.76±1 L
FEV1	3.49±0.19 L
FEV1/FVC	74±5%

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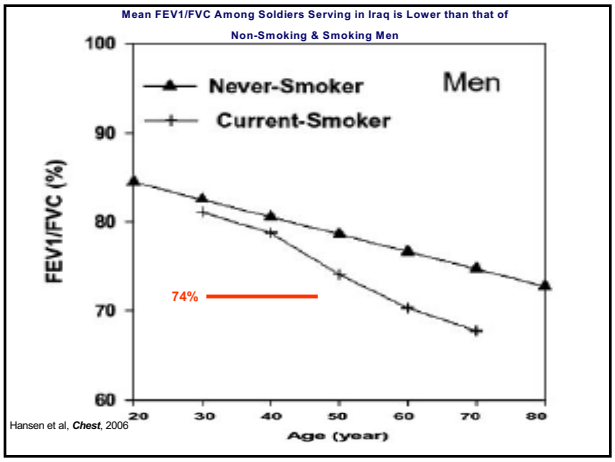

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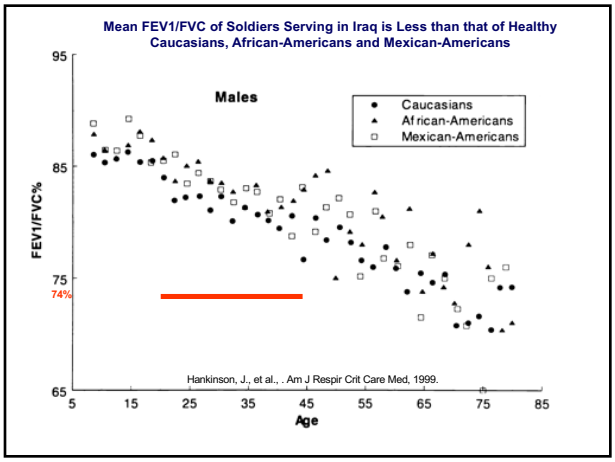

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Results:

Of these 45 veterans with spirometry, all were taking asthma medicines:

Spirometric Data on Asthma Medications Consistent with Asthma

# Subjects	Parameter
14 out of 14	DLco normal
10 out of 22	Bronchodilator response to FEF25-75 > 35%
7 out of 23	FEV1/FVC increased 12% after bronchodilator
8 out of 24	FEV1 increased > 200 ml and 12% after bronchodilator

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Results:

3 of 9 without spirometry were skin prick test + dust mite antigens (with one of these subjects + cat and another + dog). All of these three atopic patients noted wheezing when they contacted dust or their other agent noted on + skin test.

# of Subjects	Clinical History
9	Multiple asthma attacks/week
6	Exercise-induced bronchospasm
1	Several intubations for asthma and + methacholine challenge
1	Samter's triad (AERD) (asthma, polyps, aspirin sensitivity)

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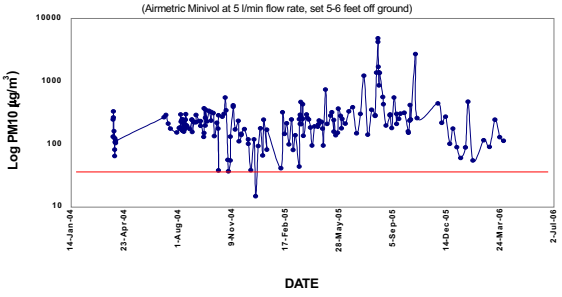
Air pollution levels in ambient air, Balad, Iraq

(Airmetric Minivol at 5 l/min flow rate, set 5-6 feet off ground)



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NEW ONSET OF ASTHMA IN SOLDIERS SERVING IN IRAQ

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Summary:

Deployment to Iraq is associated with an increased likelihood of being diagnosed with asthma.

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RESEARCH TEAM

- **SUNY Stony Brook**
  - Kristen Weissinger (Ph.D. Student, University of Rhode Island, Summer SUNY assistant to Dr. Szema)
  - Michael Peters, M.D. (SUNY Stony Brook '07)
  - Emily Rosa (Health Care Administration Undergraduate, Penn State University, Summer Student at SUNY)
  - John Chen, Ph.D., (Statistician, Assistant Professor of Preventive Medicine)
  - Sayyed Hamidi, M.D., Research Assistant Professor of Medicine
- **U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPPM)**
  - Coleen Weese, M.D., M.P.H., Program Manager, Environmental Medicine
  - Maj. James R. Sheehy, P.E., USCENTCOM Project Manager, Deployment Environmental Surveillance Program
- **Department of Defense (DOD)**
  - Michael E. Kilpatrick, M.D., Deputy Director For Force Health Protection and Readiness Programs in the Office of the Assistant Secretary of Defense for Health Affairs
  - Col. George P. Johnson, M.D., M.P.H., M.H.A., Director, Force Health Assessment and Readiness DASD (Health Affairs)

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New-onset asthma among soldiers serving in Iraq and Afghanistan

Anthony M. Szema, M.D.,[1,2] Michael C. Peters, M.D.,[1,2] Kristen M. Weissinger, B.A.,[3]
Christy A. Gagliano, M.S.,[1] and John J. Chen, Ph.D.[2]

ABSTRACT

Since June 4, 2004, asthma diagnosed and symptomatic after the age of 12 years has been an exclusion criterion for military enlistment unless exempted via *medical waiver. The Department of Defense determined that 13% of U.S. Army Medic visits in Iraq are for new-onset acute respiratory illness; case reports of veterans with asthma that began in Iraq and Afghanistan War zones have surfaced. This prompted our study to determine whether new asthma is diagnosed more frequently among Iraq/Afghanistan War troops versus stateside-based troops. Retrospective review of asthma diagnoses among computerized charts for military personnel discharged from active duty and examined between March 1, 2004 and May 1, 2007, at the Veterans Affairs Medical Center (VAMC), Northport, NY, classified soldiers by (1) deployment status—whether they were stationed in Iraq/Afghanistan for a 1-year tour of duty or stationed in the United States, and (2) VA diagnosis of asthma per International Classification of Disease codes. Associations between deployment and asthma statuses were evaluated/stratified by gender/age group. Eligibility criteria entailed (1) residence in Long Island, (2) aged 18–45 years, and (3) both U.S. military service and discharge dates between March 1, 2004 and May 1, 2007. Out of 6233 patients who served between 2004 and 2007 and were followed at the Northport VAMC, 290 new-onset/prevalent asthma cases were identified. Deployment to Iraq was associated with a significantly higher risk of asthma compared with stateside soldiers (6.6% versus 4.3%; with a crude odds ratio, 1.58; 95% CI, 1.18, 2.11). These associations persist when stratified by gender and age group. Deployment to Iraq and Afghanistan is associated with new-onset asthma. Etiologic studies, surveillance, incidence, epidemiology, and assessing response to therapy are recommended.*

(Allergy Asthma Proc 31:e67–e71, 2010; doi: 10.2500/aap.2010.31.3383)

Since June 4, 2004, asthma diagnosed and symptomatic after age 12 has been an exclusion criterion for military enlistment unless exempted *via* medical waiver (<2% of requests granted).[1] Iraq/Afghanistan deployment exposes soldiers to harsh environmental conditions.[2,3] Extremes of temperature and humidity range from 120°F (summer) to below freezing (January). Rainfall occurs from December to April and can reach 100 cm annually. Spring flash floods affect the Tigris–Euphrates delta. During summer, wind prevails: dry soil and dust fill the air.[2] The local language uses terms "shamal" for northern seasonal dust storm and "sharqi" for eastern seasonal dust storm.[3] Inhalation of fine particulate matter with a diameter <2.5 μm (PM2.5) or a diameter <10 μm (PM10) in size, in the absence of allergic sensitization, may cause lung injury that mimics asthma.[4]

Exposure to indoor dust in Army trailers during the rainy season may lead to IgE-mediated allergic sensitization to dust-mite antigens, a risk factor for asthma.[5] IgE is the *sine qua non* of allergy. Conditions faced by soldiers are unprecedented because they live in confined spaces (trailers) unless on patrol.

The Department of Defense determined that 13% of U.S. Army Medic visits in Iraq are for new-onset acute respiratory illness (Michael E. Kilpatrick, M.D., Deputy Director for Force Health Protection and Readiness Programs in the Office of the Assistant Secretary of Defense for Health Affairs, personal communication).

Roop *et al.* reported that active-duty soldiers and Department of Defense contractors—both nonasthmatic and asthmatic patients—had increased respiratory symptoms of wheezing, cough, and sputum production; chest pain/tightness; and allergy symptoms during deployment to Iraq compared with predeployment.[6] In the Israeli Army, service in combat units is associated with increased frequency of asthma among not only those with prior diagnoses but also *de novo* cases, with 25% relative excess for maintenance unit workers versus clerical workers.[7] There is a precedent for considering someone to be at risk for new-onset asthma rather than at risk for reactivation or aggravation of asthma. The National Institute for Occupational Safety and Health SENSOR surveillance case definition for work-related asthma considers someone with a history of asthma who has neither had symptoms nor

From the [1]Veterans Affairs Medical Center, Northport, New York, [2]State University of New York at Stony Brook School of Medicine, Stony Brook, New York, and [3]The University of Rhode Island, Kingston, Rhode Island
Supported by the VAMC, Northport, New York
Address correspondence and reprint requests to Anthony M. Szema, M.D., VAMC Northport, 79 Middleville Road, Northport, NY 11768
E-mail address: anthony.szema@stonybrook.edu

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RESPIRATORY SYMPTOMS NECESSITATING SPIROMETRY AMONG SOLDIERS WITH IRAQ/AFGHANISTAN WAR LUNG INJURY (IAW-LI)

Anthony M. Szema, MD
Walid Salihi, DO
Khalil W. Savary, AB
John J. Chen, PhD

Northwell Health

DONALD AND BARBARA ZUCKER SCHOOL of MEDICINE AT HOFSTRA/NORTHWELL

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Table 1. Comparisons of veterans deployed to Iraq/Afghanistan *vs.* those who were not

	Iraq/Afghanistan (n=1816)	Non Iraq/Afghanistan (n=5335)	p-value*
Age (year): mean (std. dev.)	33.85 (9.23)	35.38 (10.08)	<0.001
Smoker: n (%)	292 (16.1)	178 (3.3)	<0.001
Diagnosed with asthma: n (%)	113 (6.2)	38 (0.7)	<0.001
With Spirometry: n (%)	263 (14.5)	98 (1.8)	<0.001
Female: n (%)	158 (8.7)	918 (17.2)	<0.001
TBI: n (%)	499 (27.5)	219 (4.1)	<0.001
PTSD: n (%)	610 (33.6)	198 (3.7%)	<0.001

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Table 2. Comparisons of veterans with *vs.* without a spirometry evaluation

	With Spirometry (n=361)	Without Spirometry (n=6790)	p-value*
Age (year): mean (std. dev.)	37.04 (10.85)	34.88 (9.83)	<0.001
Smoker: n (%)	126 (34.9)	344 (5.1)	<0.001
Deployed in Iraq/Afghanistan: n (%)	263 (72.9)	1553 (22.9)	<0.001
Female: n (%)	47 (13.0)	1029 (15.2)	0.16
TBI: n (%)	334 (92.5)	384 (5.7)	<0.001
PTSD: n (%)	153 (42.4)	655 (9.6)	<0.001

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Table 3. Comparisons of means (standard deviations) of FEV1, FVC, FEV1/FVC, at rest, age, height and weight between veterans in the two groups who had a spirometry

	Non Iraq/Afghanistan (n=98)	Iraq/Afghanistan (n=263)	p-value
Age (year)	38.67 (11.92)	36.43 (10.37)	0.11
Height (in)	68.90 (3.60)	69.10 (3.29)	0.64
Weight (pd)	193.30 (35.45)	193.75 (34.39)	0.92
FEV1	3.43 (0.87)	3.68 (0.79)	0.009
FVC	4.44 (1.14)	4.73 (0.94)	0.029
FEV1/FVC	77.53 (7.99)	77.97 (7.42)	0.63

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CME Available for this Article at ACOEM.org

Respiratory Symptoms Necessitating Spirometry Among Soldiers With Iraq/Afghanistan War Lung Injury

Anthony M. Szema, MD, FCCP, Walid Salihi, DO, Khalil Savary, AB, and John J. Chen, PhD

Learning Objectives

- Outline previous findings on asthma and lung function abnormalities among soldiers returning from Iraq and Afghanistan.
- Summarize the new data on respiratory symptoms necessitating spirometry in soldiers returning from Iraq/Afghanistan, compared to those posted elsewhere.
- Review the hazardous exposures possibly associated with lung injury in soldiers serving in Iraq or Afghanistan, and the authors' recommendations for mitigating these hazards.

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DECEMBER 16, 2010 • THE VILLAGE TIMES HERALD • PAGE A5

Local doctor, researchers aid soldiers nationwide

Setauket MD leads team uncovering airborne dangers in Middle East

BY ELANA GLOWATZ
eglowatz@timesreviewpapers.com

Before 2004, the people who visited Dr. Anthony Szema's allergy clinic at the Northport Veterans Affairs Medical Center were typically 80-year-old men. But suddenly, Dr. Szema said, "there were all these 18-year-old boys and girls there. Kids."

Veterans who served in Iraq and Afghanistan have complained to Dr. Szema, 45, of shortness of breath, chest pain and difficulty exercising. This led Dr. Szema, the chief of allergy at NVAMC, along with a team of residents and medical students, to research the number of soldiers who were deployed to the Middle East and now have pulmonary problems.

The team sifted through medical files and found the number of veterans who were symptomatic enough to receive a spirometry test, which measures volume and air flow, was significantly higher for those who were deployed to Iraq or Afghanistan compared to those who remained stateside. Walid Salihi, a resident on Dr. Szema's team, said two percent of the veterans registered at NVAMC who remained stateside received a spirometry test, while the same test was given to 11 percent of people who had served overseas.

The statistics do not include soldiers who had symptoms such as shortness of breath but were not tested, which could mean the real percentage is greater. "What is it about being in Iraq and Afghanistan that makes the numbers higher?" Dr. Szema asked.

The lung problems could have a number of different causes. Dr. Szema, who lives in East Setauket and is a faculty member at the Stony Brook University School of Medicine, listed sandstorms, smoke from bombs, regional allergens and burn pits as possible culprits.

'What is it about Iraq and Afghanistan that makes the numbers higher?'
— DR. ANTHONY SZEMA

The sandstorms could create problems because of the particles in the dust.

Capt. Mark Lyles, chair of medical sciences and biotechnology at the U.S. Naval War College, found in the grains silicates of metals such as aluminum, zinc, copper, nickel, iron, lead and more. The dust also contained fungi and bacteria, which, with the metals, would get into soldiers' eyes, food and skin. It's an even bigger problem because "in those temperatures and in that dry humidity, most people breathe through their mouth," Lyles said. The protectants of the nose, such as nasal hairs, are bypassed and the particles have "a direct shot into the lung and mouth." These metals and viruses could have an effect not just on the respiratory system, but on the nervous system as well.

Burn pits could also be at the root of the pulmonary problem because of what the soldiers inhale. A burn pit is where the military throws waste such as plastics, other garbage and even medical waste, such as body parts. The materials are soaked in jet fuel and ignited. The burned fuel and garbage releases toxins that nearby soldiers breathe. "Should you be inhaling all this stuff?" Dr. Szema said. "The answer is no."

Congressman Tim Bishop (D-Southampton), after looking into the health effects of burn pits on the troops, worked on legislation since signed into law that prohibits the use of them, unless the secretary of defense says no other alternatives, such as incinerators, exist.

"One of the sad realities of war is that when our troops venture off our bases, they are exposed to peril," but they should not face that on their own bases, Bishop said. One of the next steps for the congressman is to make exposure to burn pits a presumptive cause of certain illnesses that are known to be related. "We have an obligation to those who serve our country. We have an obligation to care for them."

But for now, Dr. Szema said, with his research, the causes of the veterans' pulmonary issues are speculative. "We only showed that the doctors are saying you have asthma." Tests on these symptomatic veterans from Iraq and Afghanistan showed fewer than half of them had conditions that were reversible with an inhaler. This points to an airway obstruction or lung injury, Dr. Szema said.

'We have an obligation to those who serve our country. We have an obligation to care for them'
— CONGRESSMAN TIM BISHOP

The next step in the research, fourth-year medical student Khalil Savary said, is to prove the pulmonary problems of these veterans can be linked to a specific set of circumstances. The goal is to be able "to say these Americans are coming back from this specific location and they are having this effect," Savary, who is on Dr. Szema's research team, said, and the effect is not happening anywhere else.

In order to better study the effects of burn pits, sandstorms and other factors on the health of soldiers in Iraq and Afghanistan, Dr. Szema would like to see more standardized testing. Periodically while overseas and when troops return home, the doctor said, he wants them to receive spirometry and a two-mile run test to measure lung function.

As far as prevention goes, for the military as well as all others, Dr. Szema said it is important to stay away from things that burn, including marshmallow roasts, he joked. Humans are meant to inhale "21 percent oxygen, 79 percent nitrogen and that's it."

Photo by Elana Glowatz

Walid Salihi, left, and Dr. Anthony Szema from Stony Brook University Medical Center and the Northport VA Medical Center.

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CME AVAILABLE FOR THIS ARTICLE AT ACOEM.ORG

Overview and Recommendations for Medical Screening and Diagnostic Evaluation for Postdeployment Lung Disease in Returning US Warfighters

Cecile Rose, MD, MPH, Joseph Abraham, ScD, MS, Deanna Harkins, MD, MPH, Robert Miller, MD, Michael Morris, MD, Lisa Zacher, MD, Richard Meehan, MD, Anthony Szema, MD, James Tolle, MD, Matthew King, MD, David Jackson, PhD, John Lewis, PhD, Andrea Stahl, PhD, Mark B. Lyles, DMD, PhD, Michael Hodgson, MD, MPH, Ronald Teichman, MD, MPH, Walid Salihi, DO, Gregory Matwiyoff, MD, Gregory Meeker, MS, Suzette Mormon, MPH, RN, Kathryn Bird, MD, MSPH, and Coleen Baird, MD, MPH

Objective: To review inhalational exposures and respiratory disease risks in US military personnel deployed to Iraq and Afghanistan and to develop consensus recommendations for medical screening and diagnostic referral. **Methods:** A Working Group of physicians and exposure scientists from academia and from the Departments of Defense and Veterans Affairs was convened in February 2010. **Results:** Despite uncertainty about the number of people affected and risk factors for adverse pulmonary outcomes in this occupational setting, the Working Group recommended: (1) standardized approaches to pre- and postdeployment medical surveillance; (2) criteria for medical referral and diagnosis; and (3) case definitions for major deployment-related lung diseases. **Conclusions:** There is a need for targeted, practical medical surveillance for lung diseases and for a standardized diagnostic approach for all symptomatic deployed personnel.

Learning Objectives

- Become familiar with published data on inhalational exposures and respiratory disease risks in U.S. military personnel deployed to Iraq and Afghanistan, as reviewed by the Working Group.
- Summarize the Working Group's recommendations on standardized pre- and post-deployment medical surveillance, criteria for medical referral and diagnosis, and case definitions for deployment-related lung diseases.
- Identify areas of disagreement with the Working Group recommendations in the accompanying "clarification" by the Department of Defense.

In the last few years, evidence has emerged that US military personnel deployed to Iraq and Afghanistan may be at risk for developing respiratory symptoms and, in some cases, disabling chronic lung diseases including asthma and constrictive bronchiolitis (CB). Although no specific risk factors other than "deployment to southwest Asia" have been definitively linked to these health outcomes, concerns have been raised about exposures to various airborne contaminants.[1] Specific inhalation exposures of concern include emissions from open-air burn pits, desert dust particulate matter (PM), industrial fires and emissions, and vehicular exhaust.

From the Department of Medicine (Drs Rose, Meehan, and Bird), National Jewish Health and University of Colorado Denver; US Army Public Health Command (Drs Abraham, Harkins, and Baird), Aberdeen Proving Ground, Md; Vanderbilt University School of Medicine (Drs Miller, Tolle, and King), Nashville, Tenn; Department of Medicine (Drs Morris and Zacher), Brooke Army Medical Center, Ft Sam Houston, Tex; SUNY Stony Brook School of Medicine (Drs Szema and Salihi), Stony Brook, and Veterans Affairs Medical Center, Northport, NY; US Army Center for Environmental Health Research (Drs Jackson, Lewis, and Stahl), Ft Detrick, Md; US Naval War College (Dr Lyles), Washington, DC; Occupational Health, Office of Public Health (Dr Hodgson), VHA, Department of Veterans Affairs, Washington, DC; War Related Illness and Injury Study Center (Dr Teichman), VA New Jersey Health Care System, Department of Veterans Affairs, East Orange, NJ; Navy Medical Center (Dr Matwiyoff), San Diego, Calif; and US Geological Survey (Mr Meeker and Ms Mormon), Denver, Colo.

Author Rose received a Department of Defense grant in 2011; she receives royalties from a contribution to a chapter in an online journal on silicosis. She and her coauthors have no relationships/conditions/circumstances that present potential conflict of interest.
The JOEM Editorial Board and Planners have no financial interest related to this research.
The opinions expressed herein represent those of the authors and do not represent those of the Department of Veterans Affairs or the Department of Defense.
Address correspondence to: Cecile Rose, MD, MPH, National Jewish Health, 1400 Jackson St, Denver, CO 80206 mail to: rosec@njhealth.org

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Prompted by these concerns, a Working Group of pulmonologists, occupational and preventive medicine specialists, industrial hygienists, and exposure scientists from several academic medical centers, the Department of Defense (DoD), and the Department of Veterans Affairs was convened in February 2010.[2] These physicians and scientists, six of whom had previously deployed to southwest Asia, reviewed known and potential respiratory health outcomes and information about potential risk factors. The Working Group discussed the exposure parameters that might confer increased risk for postdeployment lung disease such as the type, severity, and duration of exposure, deployment for extended periods or multiple times, proximity and duration of exposure to burn pits or fires, reported frequency of exposure to desert dust storms, and particular job duties. The Working Group noted that factors such as general climactic conditions (heat and humidity) as well as individual factors (ie, smoking status, body mass index) in addition to deployment exposures may contribute to respiratory disease risk. Given potential adverse pulmonary outcomes, the Working Group recommended: (1) standardized pre- and postdeployment medical surveillance approaches (Table 1); (2) criteria for medical referral and diagnosis; and (3) case definitions for key deployment-related lung diseases. These recommendations along with a summary of major respiratory exposure hazards, lung diseases of concern, and future needs and directions are described in this article.

EPIDEMIOLOGY

Since 2001, approximately two million US military personnel have deployed to Iraq or Afghanistan in support of Operation Iraqi Freedom (OIF) or Operation Enduring Freedom (OEF), respectively. Reports of increased acute respiratory illnesses in deployed troops began surfacing in 2004, when a survey of 15,000 troops deployed to southwest Asia found that 69.1% reported respiratory illnesses, with 17% requiring medical care while deployed, a doubling of precombat

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IN VITRO, *IN VIVO* MOUSE, AND HUMAN LUNG TISSUE EXPOSED TO DUST FROM IRAQ & AFGHANISTAN

Anthony M. Szema, MD
Andrea D. Harrington, MS
Millicent P. Schmidt, MS
Anthony Lanzirotti, PhD
Richard J. Reeder, PhD
Martin A.A. Schoonen, PhD
Sayyed A. Hamidi, MD
Sergey Lyubsky, MD

BROOKHAVEN NATIONAL LABORATORY

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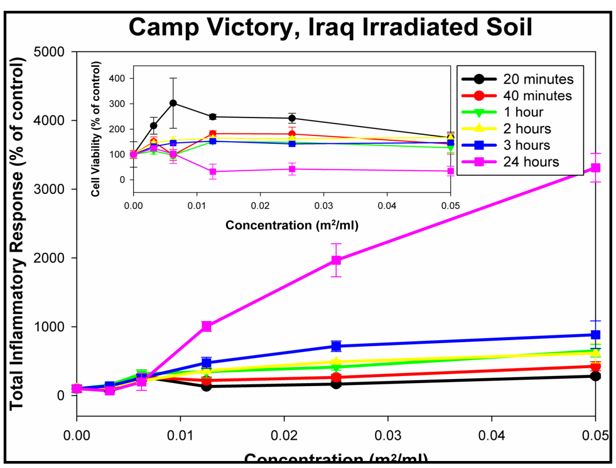

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GSA Annual Meeting & Exposition
9–12 October 2011, Minneapolis, Minnesota USA

Paper No. 107-6
Presentation Time: 10:15 AM

THE UNSEEN CASUALTIES OF URBAN WARFARE – CELLULAR INJURY INDUCED BY PARTICLE INHALATION IN THE WAR on TERROR

HARRINGTON, Andrea D., The Institute of Environmental Medicine, New York University, 57 Old Forge Road, Tuxedo, NY 10987, Harrinan@gmail.com, SZEMA, Anthony M., Veterans Affairs Medical Center, Northport, NY 11768, TSIRKA, Styliani-Anna E., Pharmacology, Stony Brook University, 192T8, Health Sciences Center, z=8651, Stonybrook, NY 11794, and SCHOONEN, Martin A.A., Geosciences, Stony Brook University, 220 ESS, Earth and Space Sciences, Stonybrook, NY 11790

The focus of this study is on the role of particulate matter in the development of lung illnesses of soldiers deployed in Iraq and Afghanistan. Of the soldiers who develop lung illnesses, the majority have adult onset asthma, while others have constrictive bronchiolitis. These types of diseases are inflammatory based. Therefore it is important to evaluate if the soils induce the generation of reactive oxygen species (ROS) or up-regulate cellular ROS (toxicity versus mutagenicity). Furthermore, the chest x-rays of these soldiers do not show significant particulate accumulation, which may be explained by particle dissolution, ROS generation, and subsequent disease development. The origins of particulate exposures in an urban warfare setting, include, but are not limited to: natural minerals, building debris, and particulates generated by ammunition explosions. While some soldiers know their exposure source, many do not. However, one of the constant contributions is the exposure to natural soil dust, often at extreme exposure burdens. Soil dust is a complex mixture of mineral constituents, organic matter, as well as microbes. In this study we focused on the possible role of the mineral constituents in generating ROS. Besides dust collected in Iraq and Afghanistan, we also studied inorganic model systems and standard soils for comparison. Soils from Iraq and Afghanistan were characterized using X-ray diffractometry, X-ray fluorescence spectroscopy, and scanning electron microscopy. The dominant mineral components are calcite and quartz. The dust has several weight per cent iron and less than one weight per cent manganese. Because iron and manganese can promote the formation of ROS, a model system with calcite, quartz and varying amounts of iron and manganese was studied in detail. An array of cellular and acellular assays, largely developed in our group over the last five years, were used to evaluate the ability of the dust, standard soils, and model systems to generate ROS. The initial results show that the dust from Camp Victory in Iraq promotes the up-regulation of ROS in epithelial cells, but more experiments will be conducted over the next months to confirm these results.

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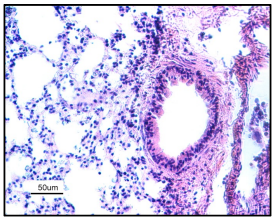
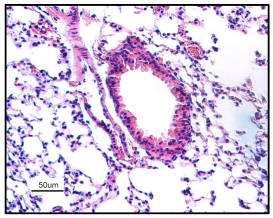
Dust Instillation in C57BL/6 Mice

Left: One-year-old male C57BL/6 mouse was anesthetized with pentobarbital 100 mg/kg i.p., tracheotomized, and instilled with bronchoalveolar lavage fluid containing 1 gram of burn pit dust from Camp Victory, Iraq in 1 ml sterile water, the immediately inflation fixed in formalin for hematoxylin and eosin staining. Peribronchiolar lymphocytes are seen.

Right: Age and gender-matched mouse instilled with 1 gm rutile dust from Georgia in 1ml water did not lead to airway inflammation.



Lung -Iraq Dust



Lung -Rutile Dust

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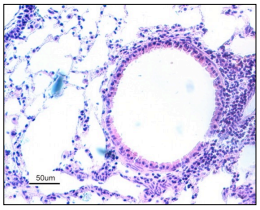
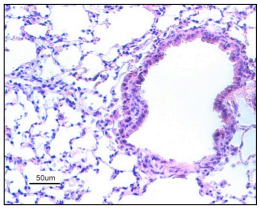
Dust Instillation in VIP KO Mice

Left: One-year-old male VIP KO mouse was anesthetized with pentobarbital 100 mg/kg i.p., tracheotomized, and instilled with bronchoalveolar lavage fluid containing 1 gram of burn pit dust from Kandahar, Afghanistan in 1 ml sterile water, the immediately inflation fixed in formalin for hematoxylin and eosin staining. Peribronchiolar lymphocytes are seen.

Right: Age and gender-matched mouse instilled with 1 gm rutile dust from Georgia in 1ml water did not lead to airway inflammation.



Lung-Afghanistan



Lung-Georgia Dust

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A SOLDIER EXPOSED TO DUST FROM IRAQ

Anthony M. Szema, MD
Andrea D. Harrington, MS
Millicent P. Schmidt, MS
Anthony Lanzirotti, PhD
Richard J. Reeder, PhD
Martin A.A. Schoonen, PhD
Sayyed A. Hamidi, MD
Sergey Lyubsky, MD

BROOKHAVEN NATIONAL LABORATORY

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This case concerns a previously-healthy, fit-for-deployment, active duty soldier who served in Iraq.

This 40-year-old gentleman was part of the emergency response team at the World Trade Center on September 11, 2001 but did not have clinical respiratory sequellae.

He later was a senior quarter master for equipment repair supervising the laundry and bath staff in Camp Anaconda Balad, Baghdad, and Kuwait.

He denied exposure to grinding apparati or industrial paint, though inhaled smoke which comprised, in part, vaporized humvees from detonated Improvised Explosive Devices. Burn Pits operated daily during his tour of duty Feb. 2003-May 2004. He occasionally smoked cigars. Sandstorms were common.

This ex-smoker noted cough and chest wall pain for several years since returning. Physical exam was notable for wheezing despite taking prednisone 20 mg/day for 6 months.

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- Spirometry in 2004 showed FEV-1/FVC 3.72/4.35=85% (103% predicted) with a DLco 86% and TLC 5.73 (78%) that did not change after a bronchodilator.
- In January 2010, FEV-1/FVC=3.36/3.96=84% (111% predicted) without improvement after a bronchodilator.
- In April 2011, his DLco was 60% after 6 months of prednisone, 20 mg daily. His pulse oximetry on room air went from 99 to 97% saturated after 1 minute of jumping jacks, associated with dyspnea which forced him to discontinue exercise.

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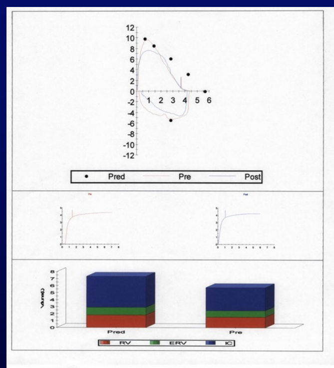

Normal flow volume loops were documented in 2004.
9-21-04

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	Pre-Bronch Actual	Pred	%Pred	SD	LLN	Post Bronch Actual	%Chng
----- SPIROMETRY -----							
FVC (L)	4.35	5.62	77	0.64	4.69	4.21	-3
FEV1 (L)	3.72	4.58	81	0.49	3.82	3.68	-1
FEV1/FVC (%)	85	83	103		69	87	2
FEF 25% (L/sec)	9.29	8.57	108		7.16	7.59	-18
FEF 50% (L/sec)	5.53	6.10	91		5.09	6.33	14
FEF 75% (L/sec)	1.80	3.20	56		2.67	1.79	-1
FEF 25-75% (L/sec)	4.63	4.61	100	0.96	3.85	4.83	4
FEF Max (L/sec)	9.53	9.80	97		8.18	7.58	-20
FIVC (L)	4.15					3.83	-8
FIF Max (L/sec)	5.28					4.68	-11
MEP (cmH2O)	57	232	25		194		
MIP (cmH2O)	-70	-125	56		-104		
----- LUNG VOLUMES -----							
SVC (L)	4.23	5.62	75	0.64	4.69		
IC (L)	3.29	4.40	75		3.67		
ERV (L)	0.94	1.22	77		1.02		
TGV (L)	2.44	3.64	67	0.72	2.91		
RV (Pleth) (L)	1.50	1.79	84	0.37	1.43		
TLC (Pleth) (L)	5.73	7.31	78	0.79	5.85		
RV/TLC (Pleth) (%)	26	24	109	4	19		
Trapped Gas (L)							
----- DIFFUSION -----							
DLCOunc (ml/min/mmHg)	30.09	35.03	86	6.00	28.02		
DLCOcor (ml/min/mmHg)		35.03		6.00	28.02		
DL/VA (ml/min/mmHg/L)	5.70	4.79	119		3.83		
VA (L)	5.28	7.31	72	0.79	6.10		

9-21-04
A normal diffusing capacity 86% (119% when adjusted for alveolar lung volume) was present in 2004. This decreased by 2010. FEV1 and FVC were 4.58 and 5.62 liters, respectively.

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LUNG VOLUMES

	Units	Predicted	Pre Drug Reported	Pre Drug % Predicted	Post Drug Reported	Post Drug % Predicted	%Change
TLC	L,btps	5.91	4.78	81	5.01	85	5
FRC	L,btps	3.24	1.87	58 <	1.78	55 <	-4
IC	L,btps	2.67	2.92	109	3.23	121 >	11
VC	L,btps	4.25	3.86	91	4.00	94	4
RV	L,btps	1.66	0.92	55 <	1.01	61 <	10
ERV	L,btps	1.59	0.96	60 <	0.77	49 <	-18
RV/TLC	%	28.03	19.18	68 <	20.12	72 <	5
VTG	L,btps		1.87		1.81		-3
Vtg (frequency)	/min		72.83		88.82		22

AIRWAYS RESISTANCE

	Units	Predicted	Pre Drug Reported	Post Drug Reported	%Change
RAW	cmH2O/L/s	0.20 - 2.50	3.62	3.11	-14
SGaw	L/s/cmH2O	0.11 - 0.40	0.15	0.18	20
Raw (frequency)	/min		97.56	113.21	16

SPIROMETRY

	Units	Predicted	Pre Drug Reported	Pre Drug % Predicted	Post Drug Reported	Post Drug % Predicted	%Change
FVC	L,btps	4.25	4.09	96	4.14	97	1
FEV1	L,btps	3.26	3.48	107	3.60	110	3
FEV1/FVC	%	76.70	85.00	111	86.98	113	2
FEFmax	L/s	9.22	10.92	118	12.69	138 >	16
FEF25-75%	L/s	4.00	4.49	112	5.17	129 >	15
MVV	L/min,btps	139.28	142.96	103	157.76	113	10

DIFFUSION CAPACITY

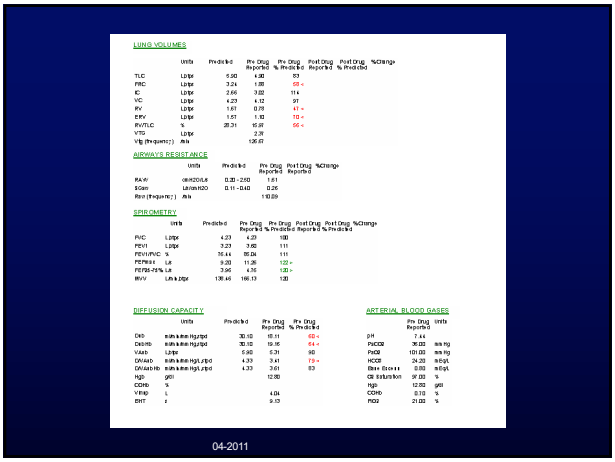
	Units	Predicted	Pre Drug Reported	Pre Drug % Predicted
Dsb	ml/min/mm Hg,stpd	30.28	18.41	61 <
DsbHb	ml/min/mm Hg,stpd	30.28	19.15	63 <
VAsb	L,btps	5.91	5.38	91
D/VAsb	ml/min/mm Hg/L,stpd	4.35	3.42	79 <
D/VAsbHb	ml/min/mm Hg/L,stpd	4.35	3.56	82
Hgb	g/dl		13.30	
COHb	%		0.60	
Vinsp	L		4.21	
BHT	s		10.44	

ARTERIAL BLOOD GASES

	Pre Drug Reported	Units
pH	7.46	
PaCO2	40.00	mm Hg
PaO2	88.00	mm Hg
HCO3	27.90	mEq/L
Base Excess	4.20	mEq/L
O2 Saturation	96.90	%
Hgb	13.30	g/dl
COHb	0.60	%
FIO2	21.00	%

10-21-10
The prior diffusing capacity of 86% (119% when adjusted for alveolar lung volume) in 2004 is now 61% (79% when adjusted for alveolar lung volume). FEV1 and FVC were 4.58 and 5.62 liters, respectively in 2004. In 2010 the FEV1 and FVC decreased to 3.48 and 4.09, respectively and the total lung capacity was 4.78, in contrast to 5.73 liters in 2004.

63



LUNG VOLUMES

	Units	Predicted	Pre Drug Reported	Pre Drug % Predicted	Post Drug Reported	Post Drug % Predicted	%Change
TLC	L/btps	5.90	4.90	83			
FRC	L/btps	3.24	1.88	58 <			
IC	L/btps	2.66	3.02	114			
VC	L/btps	4.23	4.12	97			
RV	L/btps	1.61	0.78	48 <			
ERV	L/btps	1.57	1.10	70 <			
RV/TLC	%	28.31	15.91	56 <			
VTG	L/btps		2.39				
Vtg (frequency)	#/s		126.67				

AIRWAYS RESISTANCE

	Units	Predicted	Pre Drug Reported	Post Drug Reported	%Change
RAW	cmH2O/L/s	0.30 - 2.60	1.61		
SGaw	L/s/cmH2O	0.11 - 0.40	0.26		
Rint (frequency)	#/s		110.09		

SPIROMETRY

	Units	Predicted	Pre Drug Reported	Pre Drug % Predicted	Post Drug Reported	Post Drug % Predicted	%Change
FVC	L/btps	4.23	4.23	100			
FEV1	L/btps	3.23	3.62	111			
FEV1/FVC	%	76.44	85.64	111			
FEF75/25	L/s	3.33	11.26	122 >			
FEF25-75%	L/s	3.96	4.56	120 >			
IRV	Liters btps	136.44	166.13	122			

DIFFUSION CAPACITY

	Units	Predicted	Pre Drug Reported	Pre Drug % Predicted	
DLO	milliliters/mg/dyd	30.10	16.11	53 <	
DLO/VA	milliliters/mg/dyd	30.10	19.95	64 <	
VAeb	L/btps	5.90	5.31	90	
DM/eb	milliliters/mg/L/btps	4.33	3.41	79 <	
DM/eb/Hb	milliliters/mg/L/btps	4.33	3.61	83	
Hgb	g/dl		12.80		
COHb	%				
VTmb	L		4.04		
BHT	s		9.13		

ARTERIAL BLOOD GASES

	Pre Drug Reported	Units
pH	7.44	
PaCO2	36.00	mm Hg
PaO2	101.00	mm Hg
HCO3	24.20	mEq/L
Base Excess	0.80	mEq/L
O2 Saturation	97.00	%
Hgb	12.80	g/dl
COHb	0.10	%
PiO2	21.00	%

04-2011

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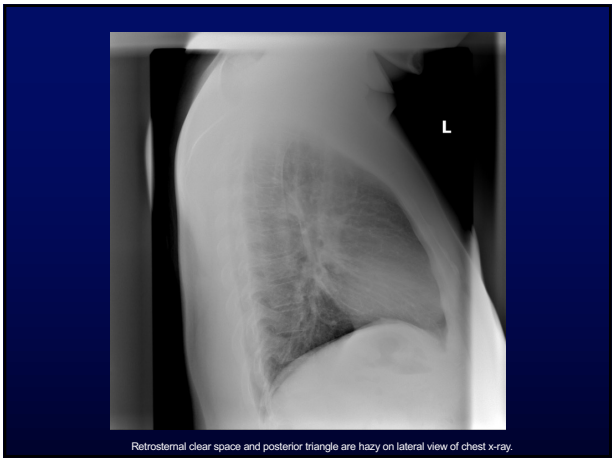
Hazy interstitial infiltrates are seen on chest x-ray in 2009 prior to open lung biopsy.

65



Retrosternal clear space and posterior triangle are hazy on lateral view of chest x-ray.

66


Ground glass opacities seen on chest CT in 2009.

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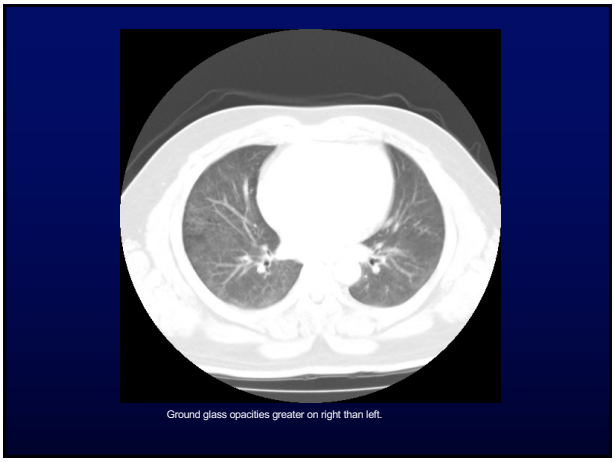
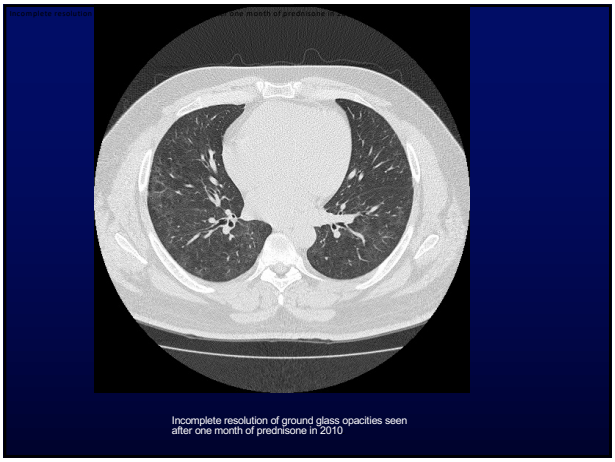

Ground glass opacities greater on right than left.

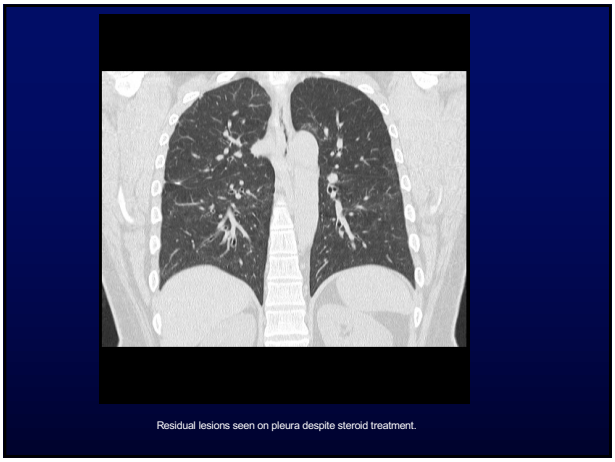
68


Hazy opacification seen bilaterally.

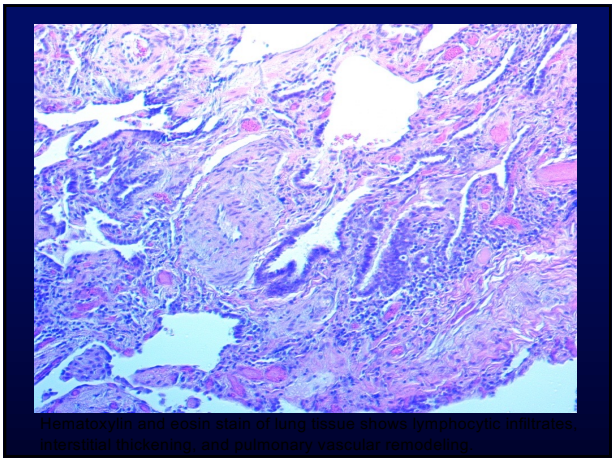
69


Incomplete resolution of ground glass opacities seen after one month of prednisone in 2010

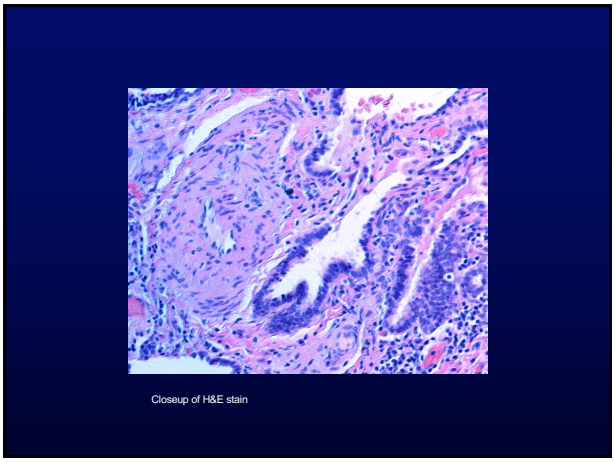
70


Residual lesions seen on pleura despite steroid treatment.

71

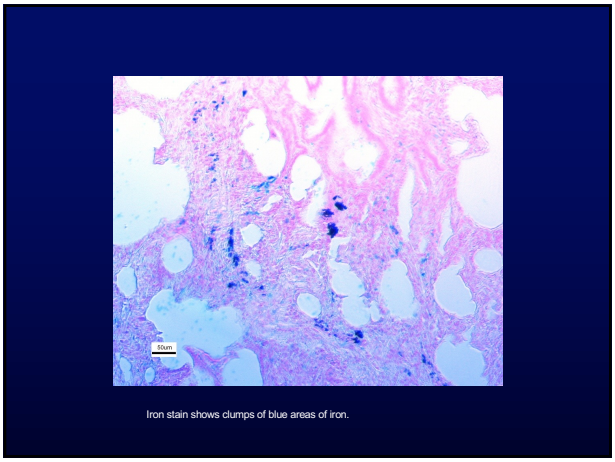

Hematoxylin and eosin stain of lung tissue shows lymphocytic infiltrates, interstitial thickening, and pulmonary vascular remodeling

72



Closeup of H&E stain

73



Iron stain shows clumps of blue areas of iron.

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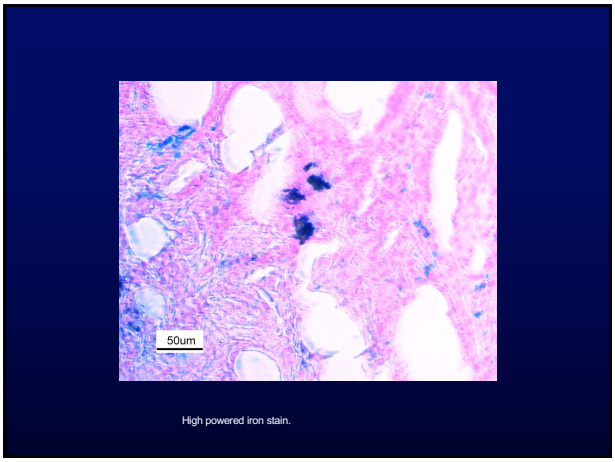
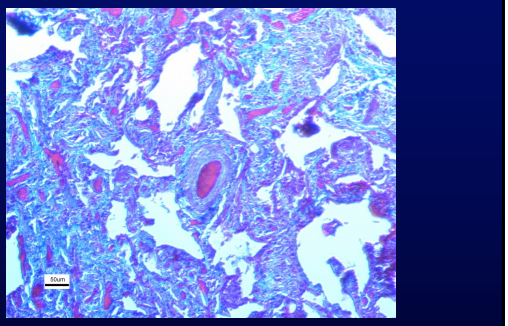


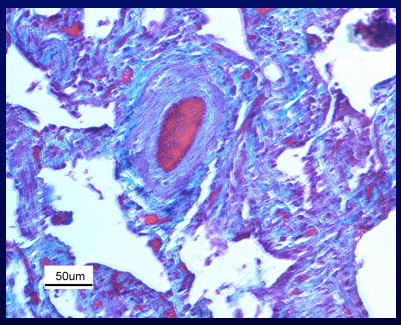
High powered iron stain.

75



Masson trichrome stain shows collagen in thickened interstitium along with pulmonary vessel thickening.

76



High powered view of Masson trichrome stain.

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Micro-X-ray Fluorescence

- A lung section was analyzed at the micro-X-ray fluorescence beamlines X26A/X27A at the National Synchrotron Light Source at Brookhaven National Laboratory to detect metals and to determine their spatial distribution.
- Calcium, sulfur, and zinc were found to be distributed uniformly, as expected from their presence throughout tissue.
- In contrast, titanium, iron, and copper, and less commonly chromium and nickel, were localized in discrete regions, often as spots (< 25 μm) or as bands of multiple spots.
- Iron and titanium were commonly co-localized, with Fe/Ti element ratios in the range 3.9-13.3.
- Some spots high in iron and titanium in element distribution maps correspond to dark particles seen in corresponding light micrographs and may represent dust particles.

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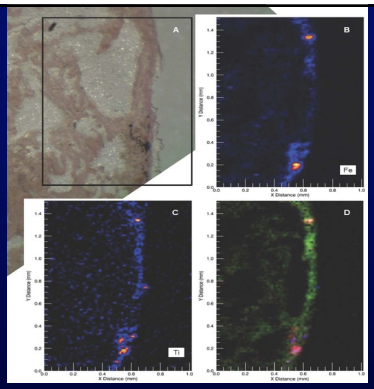

Figure 1. (a) Light microscope image of tissue thin section with corresponding micro-X-ray fluorescence element maps of (b) iron, (c) titanium, and (d) combined iron (red), titanium (blue), and calcium (green) with color intensity/hue saturation representing fluorescence intensity. Data were acquired at X-27A at Brookhaven National Laboratory's National Synchrotron Light Source with an incident beam energy of 17.2 keV. Not identical scales for titanium and iron colocalization (autoscaled to account for highest observed concentrations.

79

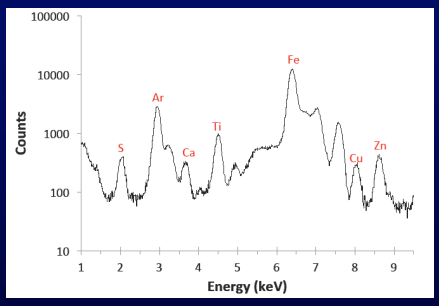

Figure 2. Energy dispersive spectrum of a representative Fe/Ti hotspot; intensity comparison with thin section standards yields a mean elemental Fe/Ti ratio averaging 7.1.

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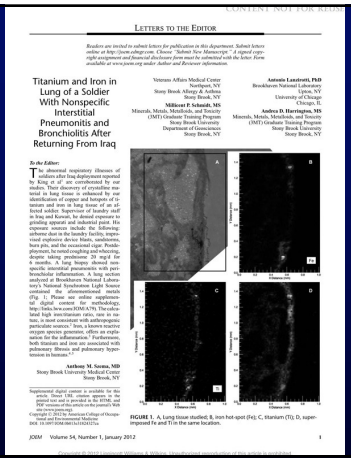

LETTERS TO THE EDITOR

Titanium and Iron in Lung of a Soldier With Nonspecific Interstitial Pneumonitis and Bronchiolitis After Returning From Iraq

Anthony M. Szema, MD
Stony Brook University Medical Center
Stony Brook, NY

FIGURE 1. A, Lung tissue studied; B, iron hot-spot (Fe); C, titanium (Ti); D, superimposed Fe and Ti in the same location.

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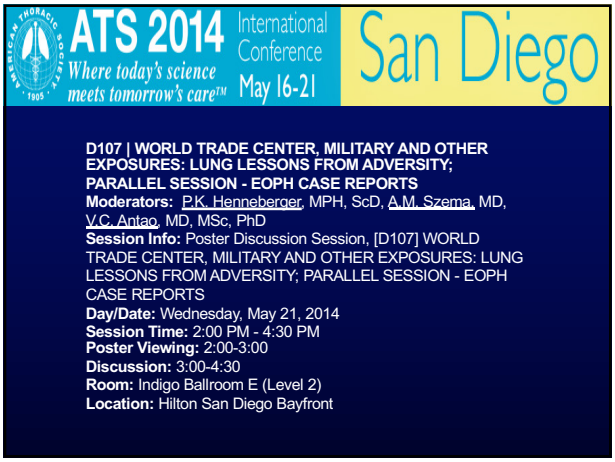
ATS 2014
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May 16-21
San Diego
D107 | WORLD TRADE CENTER, MILITARY AND OTHER EXPOSURES: LUNG LESSONS FROM ADVERSITY; PARALLEL SESSION - EOPH CASE REPORTS
Moderators: P.K. Henneberger, MPH, ScD, A.M. Szema, MD, V.C. Antao, MD, MSc, PhD
Session Info: Poster Discussion Session, [D107] WORLD TRADE CENTER, MILITARY AND OTHER EXPOSURES: LUNG LESSONS FROM ADVERSITY; PARALLEL SESSION - EOPH CASE REPORTS
Day/Date: Wednesday, May 21, 2014
Session Time: 2:00 PM - 4:30 PM
Poster Viewing: 2:00-3:00
Discussion: 3:00-4:30
Room: Indigo Ballroom E (Level 2)
Location: Hilton San Diego Bayfront

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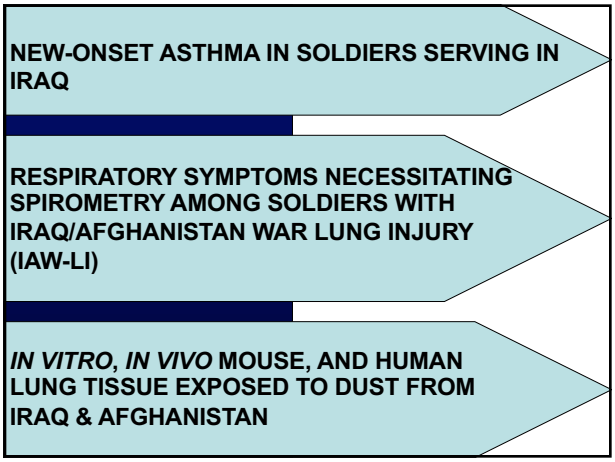
NEW-ONSET ASTHMA IN SOLDIERS SERVING IN IRAQ
RESPIRATORY SYMPTOMS NECESSITATING SPIROMETRY AMONG SOLDIERS WITH IRAQ/AFGHANISTAN WAR LUNG INJURY (IAW-LI)
IN VITRO, *IN VIVO* MOUSE, AND HUMAN LUNG TISSUE EXPOSED TO DUST FROM IRAQ & AFGHANISTAN

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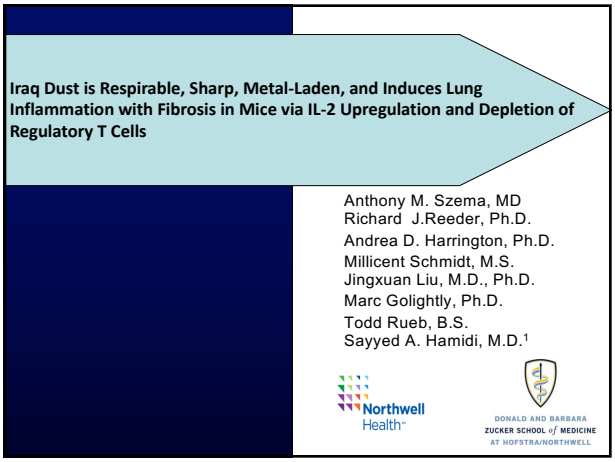
Iraq Dust is Respirable, Sharp, Metal-Laden, and Induces Lung Inflammation with Fibrosis in Mice via IL-2 Upregulation and Depletion of Regulatory T Cells
Anthony M. Szema, MD
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Marc Golightly, Ph.D.
Todd Rueb, B.S.
Sayyed A. Hamidi, M.D.[1]
Northwell Health
DONALD AND BARBARA ZUCKER SCHOOL of MEDICINE AT HOFSTRA/NORTHWELL

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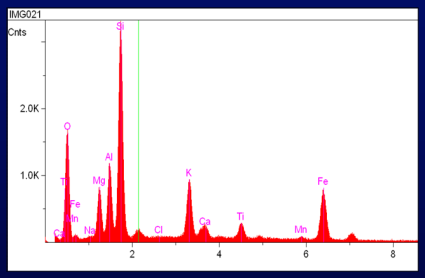
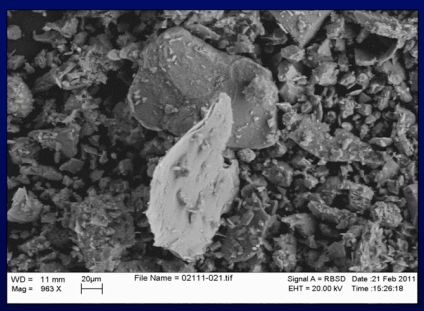


Energy-dispersive X-ray analysis of representative particle in Iraq dust sample, indicating elements detected.

85



Electron micrograph of Camp Victory, Iraq, dust sample shows variable particle sizes, including fraction less than5µm (respirable). Particles are angular with sharp edges.

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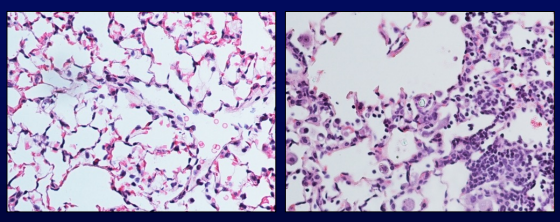
No dust at 400X with normal histology in C57BL/6 mouse lung; Montana dust with significant inflammation.

No Dust: 400 X **Montana Dust: 400 X**



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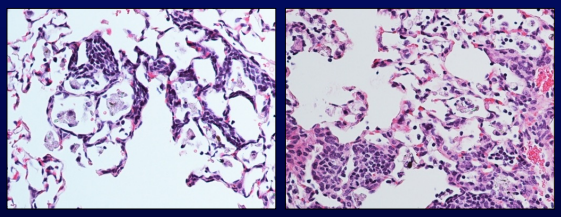
Iraq dust with septate thickening, interstitial inflammation, incompletely phagocytosed crystals;.

San Joaquin, California dust with a focal lymphocytic accumulation in the lower right hand corner of the field.

Iraq Dust: 400X **San Joaquin Dust: 400X**



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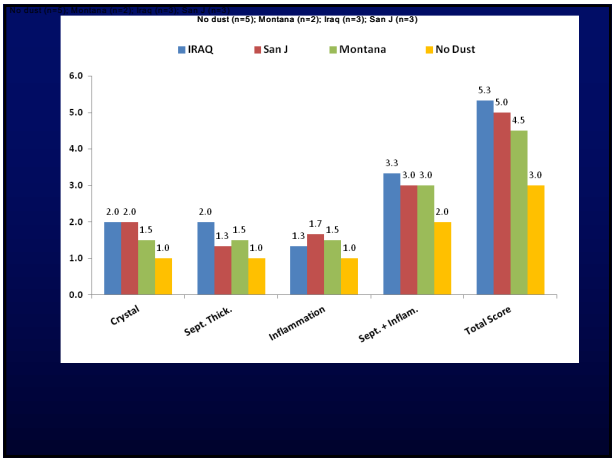

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P values based on t-test

The highest total lung injury score was in the Iraq dust-exposed group, with more crystals, which were polarizable, consistent septate thickening, and inflammation, both airway and interstitial.

	Crystal	Septate Thickening	Inflammation	Septate + Inflammation	Total Score
WT/Mont	0.117	0.117	0.117	0.117	0.117
WT/Iraq	0.000	0.000	0.220	0.002	0.000
WT/Sanj	0.055	0.220	0.034	0.055	0.055
Mont/Iraq	0.272	0.272	0.789	0.724	0.537
Mont/Sanj	0.591	0.789	0.789	1.000	0.806
Iraq/Sanj	1.000	0.116	0.519	0.643	0.795

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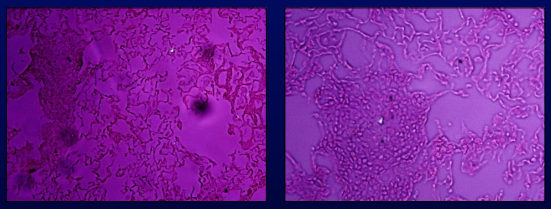
Polarizable crystals are bright white seen in Iraq dust-exposed lungs.

200X Magnification **400X Magnification**



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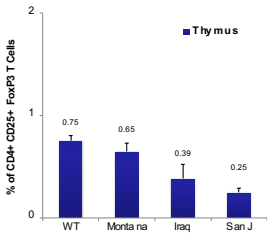
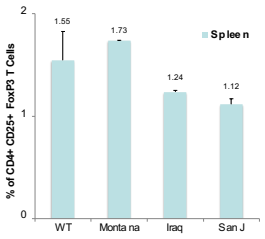
Flow Cytometric Analysis of Cells in Animals Exposed to Dust

Thymus



Spleen



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Flow cytometry Statistical Analysis
1= No dust (n=5); 2= Montana (n=3); 3= Iraq (n=3); 4= San J (n=3)
ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Thymus_CD4CD25	Between Groups	11.300	3	3.767	2.820	.099
	Within Groups	12.020	9	1.336		
	Total	23.320	12			
Spleen_CD4CD25	Between Groups	.957	3	.319	2.211	.156
	Within Groups	1.298	9	.144		
	Total	2.255	12			
Thymus_CD4CD25_FoxP3	Between Groups	.576	3	.192	9.452	.004
	Within Groups	.183	9	.020		
	Total	.759	12			
Spleen_CD4CD25_FoxP3	Between Groups	.652	3	.217	1.233	.353
	Within Groups	1.586	9	.176		
	Total	2.237	12			

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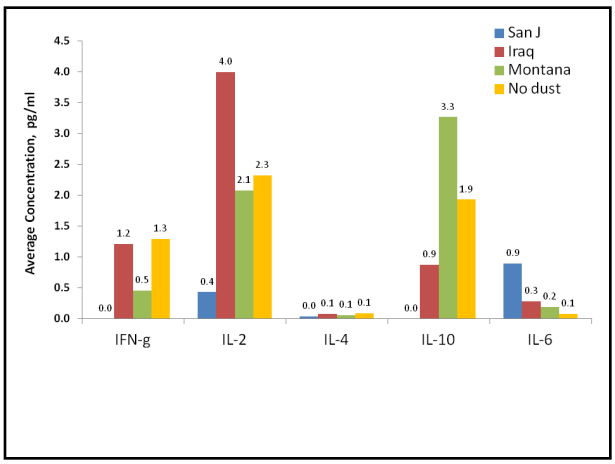

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P value based on unpaired t-test

	IFN-g	IL-2	IL-4	IL-10	IL-6
WT/Mont	0.569	0.708	0.738	0.515	0.527
WT/Iraq	0.942	0.236	0.924	0.487	0.106
WT/Sanj	0.275	0.006	0.401	0.221	0.263
Mont/Iraq	0.211	0.433	0.789	0.106	0.579
Mont/Sanj	0.272	0.011	0.696	0.047	0.588
Iraq/Sanj	0.009	0.093	0.421	0.017	0.533

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CME AVAILABLE FOR THIS ARTICLE AT ACOEM.ORG

Iraq Dust Is Respirable, Sharp, and Metal-Laden and Induces Lung Inflammation With Fibrosis in Mice via IL-2 Upregulation and Depletion of Regulatory T Cells

Anthony M. Szema, MD, Richard J. Reeder, PhD, Andrea D. Harrington, PhD, Millicent Schmidt, MS, Jingmuan Liu, MD, PhD, Marc Golightly, PhD, Todd Rueb, BS, and Sayyed A. Hamidi, MD

Learning Objectives

- Review the findings of previous descriptions of Iraq-Afghanistan war lung injury, including the lung biopsy findings.
- Outline the new findings on the characteristics in samples of Iraq dust that may contribute to respiratory symptoms in returning veterans.
- Review the histologic and immunopathologic findings in mice exposed to Iraq dust samples.

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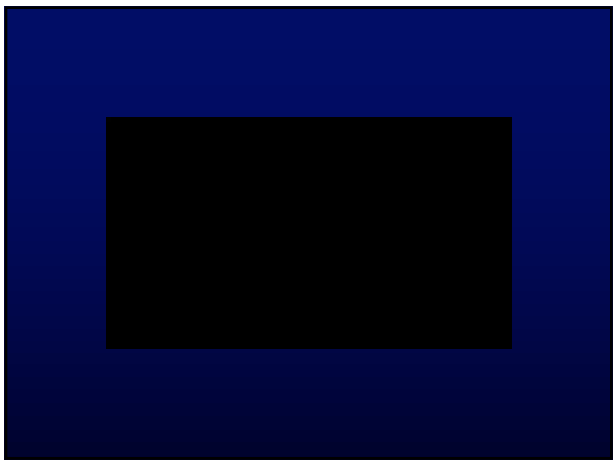

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Preliminary Analysis of Burnpits360 Database

Anthony M. Szema, MD
Jonathan Li, BS
Laura Viens, MD, MPH
Bhumika Patel, MD

Northwell Health

DONALD AND BARBARA ZUCKER SCHOOL of MEDICINE AT HOFSTRA/NORTHWELL

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Mutli-organ system complaints among soldiers in Burnpits360 Database

Symptom	Frequency, of 639	Percent (%)
Shortness of Breath (SOB), mild	193	30.2
SOB, moderate	130	20.3
SOB, severe	44	06.9
SOB, unspecified	114	17.8
Cough	227	35.5
Any Respiratory symptoms	429	67.1
Blurred vision	96	15.0
Headaches	236	36.9
Memory loss	260	40.8
Fatigue	331	51.9
Weight loss	25	3.9
Joint pain	317	49.6
Myalgia	302	47.3
Low testosterone	112	17.5
Low vitamin D	88	13.8
Hypertension	172	26.9
Skin lesions	76	11.9
Chest pain	155	24.3
Fibromyalgia	33	5.2
Infertility	12	1.9
Abdominal pain	141	22.1
Abdominal distension	112	17.5
GERD	137	21.4
Nausea	116	18.2
GI bleed	44	6.9
Diarrhea	95	14.9
Any GI symptoms	292	45.7

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Self-Reported Burn Pit Exposure & Cancer

- 14% of soldiers in the Burnpits 360 database report a diagnosis of cancer
- The most common cancers are bladder and testicular (eight persons each)

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Article

Proposed Iraq/Afghanistan War-Lung Injury (IAW-LI) Clinical Practice Recommendations: National Academy of Sciences' Institute of Medicine Burn Pits Workshop

American Journal of Med's Health
2017, Vol. 11(6) 1653–1663
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Anthony Szema, MD[1,2], Niely Mirsaidi, BA[2], Bhumika Patel, MD[2], Laura Viens, MD, MPH[2], Edward Forsyth, MD[2], Jonathan Li, BS[2], Sophia Dang, BA[2], Brittany Dukes, BS[2], Jheison Giraldo, BS[2], Preston Kim, and Matthew Burns, MPhil[2]

Abstract

High rates of respiratory symptoms (14%) and new-onset asthma in previously healthy soldiers (6.6%) have been reported among military personnel post-deployment to Iraq and Afghanistan. The term Iraq/Afghanistan War-Lung Injury (IAW-LI) is used to describe the constellation of respiratory diseases related to hazards of war, such as exposure to burning trash in burn pits, improvised explosive devices, and sandstorms. Burnpits360.org is a nonprofit civilian website which voluntarily tracks medical symptoms among soldiers post-deployment to the Middle East. Subsequent to initiation of the Burnpits360.org website, the Department of Veterans Affairs started the Airborne Hazards and Open Burn Pit registry. This paper: (a) analyzes the latest 38 patients in the Burnpits360.org registry, validated by DD214 Forms; (b) compares strengths and weaknesses of both registries as outlined at the National Academy of Sciences Institute of Medicine Burn Pits Workshop; (c) further characterizes the spectrum of disease in IAW-LI; (d) describes the risk factors of affected populations; (e) summarizes current practices regarding management of the condition; and (f) defines future research objectives.

Keywords

Burn pits, improvised explosive devices, IED, pollen, dust, particulate matter, PM, Iraq/Afghanistan War-Lung Injury, Iraq, Afghanistan, Lung Injury, IAW-LI, constrictive bronchiolitis, vascular remodeling, impulse oscillometry, IOS, exercise-induced pulmonary hypertension, lung biopsy, quality of life, health awareness, public health

Adverse environmental exposures in the Middle East region include: 1) burning trash in open air "burn pits" ignited with JP-8 jet fuel; 2) improvised explosive devices (IEDs) with associated "blast overpressure" or shock waves (with the capacity to aerosolize metals); 3) aeroallergens; and 4) massive sandstorms consisting of sharp, respirable, metal-laden,

Subsequently, the Department of Veterans Affairs (VA) established the Airborne Hazards and Open Burn Pit (AH&OBP) registry to monitor health effects due to airborne hazard exposure during deployment. This registry collected data from veterans and active duty service members using a voluntary self-assessment questionnaire

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EXPERIMENTAL LUNG RESEARCH
2018, VOL. 44, NO. 3, 153–166
https://doi.org/10.1080/01902148.2018.1459957

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ORIGINAL ARTICLE

Check for updates

Rux largely restores lungs in Iraq PM-exposed mice, Up-regulating regulatory T-cells (Tregs)

David Lin[a], Jonathan Li, B.S[b,o], Rabail Razi, M.D[c], Niha Qamar, M.D[c], Laurie Levine, A.A.S[d], Thomas Zimmerman, D.V.M[d], Sayyed A. Hamidi, M.D, M.P.H, M.B.A[e], Millicent Schmidt, Ph.D.[f], Marc G. Golightly, Ph.D[g], Todd Rueb, B.S[g], Andrea Harrington, Ph.D.[h], Merrill Garnett, D.D.S[i], Frank Antonawich, Ph.D[i,j], Steven McClain, M.D[o], Edmund Miller, Ph.D[p], Courtney Cox[n], Po Hsuan Huang[n], and Anthony M. Szema, M.D[k,l,m,n]

[a]New York University School of Dental Medicine, New York, NY; [b]Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA; [c]M. D. with Distinction in Research Program, Stony Brook University School of Medicine, Stony Brook, NY; [d]Division of Laboratory Animal Resources, Stony Brook University, Stony Brook, NY; [e]Internal Medicine Residency Program, Bronx VA Medical Center, Bronx, NY; [f]Stony Brook University, Department of Geosciences Minerals Metals and Metalloids Toxicity Program; [g]Flow Cytometry Laboratory, Department of Pathology, Stony Brook University School of Medicine, Stony Brook, NY; [h]Department of Environmental Medicine, New York University, New York, NY; [i]Garnett McKeen Laboratory, Bohemia, NY; [j]Department of Biology, St. Joseph's College, Patchogue and Brooklyn, NY; [k]Department of Occupational and Environmental Medicine, Preventive Medicine, and Epidemiology (Population Health), Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY; [l]Department of Technology and Society, College of Engineering and Applied Sciences, Stony Brook University, Stony Brook, NY; [m]The Stony Brook Medicine SUNY at Stony Brook Internal Medicine Residency Program at John T. Mather Memorial Hospital, Port Jefferson, NY; [n]Three Village Allergy and Asthma, PLLC, South Setauket, NY; [o]McClain Laboratories, Smithtown, NY; [p]Molecular Medicine and Medicine, Division of Pulmonary and Critical Care, Feinstein Institute for Medical Research, Great Neck, NY

ABSTRACT

Background Military personnel post-deployment to Iraq and Afghanistan have noted new-onset respiratory illness. This study's primary objective was to further develop an animal model of Iraq Afghanistan War Lung Injury (IAW-LI) and to test a novel class of anti-injury drug called RuX. **Methods** Particulate Matter (PM) samples were obtained in Iraq then characterized by spectromicroscopy. C57BL/6 mice underwent orotracheal instillation with PM, followed by drinkable treatment with RuX. Lung histology, inspiratory capacity (FlexiVent), thymic/splenic regulatory T cell (Treg) number, and whole-lung genomics were analyzed. **Results** Tracheal instillation of Iraq PM led to lung septate thickening and lymphocytic inflammation. PM-exposed mice had suppression of thymic/splenic regulatory T-cells (Tregs). Drinking RuX after PM exposure attenuated the histologic lung injury response, improved lung inspiratory capacity, and increased Tregs. Pooled whole lung genomics suggest differences among gene expression of IL-15 among control, PM, and PM + RuX groups. **Conclusions** RuX, a ruthenium and alpha-lipoic acid complex, attenuates lung injury by improving histology and inspiratory capacity via upregulation of Tregs in Iraq PM-exposed C57BL/6. Plausible genomic effects may involve IL-15 whole lung gene expression.

ARTICLE HISTORY
Received 30 June 2017
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KEYWORDS
Burn pits; dust; fibrosis; iraq; inflammation; lung injury; mice; particulate matter; rux

Introduction/background

Military personnel deployed to regions with harsh environmental conditions often incur physiologic tolls beyond the repercussions of combat itself. Numerous studies have reported that servicemen and women, both during and after deployment to Iraq and Afghanistan (Operations Iraqi Freedom/Enduring Freedom/New Dawn), have new and distinct respiratory illnesses, which were not diagnosed prior to deployment. A screening process rules out potential servicemen and women diagnosed with major respiratory illness prior to deployment.[1–6] Therefore, most studies have associated these illnesses to widespread exposure to hazardous airborne particulate matter (PM) in these severe, desert environments.

Respiratory illness

In an initial 2004 survey, over 69% of troops deployed to Southwest Asia reported respiratory distress,[7] with 24% reporting at least one acute respiratory illness

CONTACT Dr. Anthony M. Szema, M.D aszema@northwell.edu Donald and Barbara Zucker School of Medicine at Hofstra/Northwell Stony Brook University College of Engineering and Applied Sciences, Department of Technology & Society, and Epidemiology, Hempstead, NY 11549; (2) Stony Brook University,

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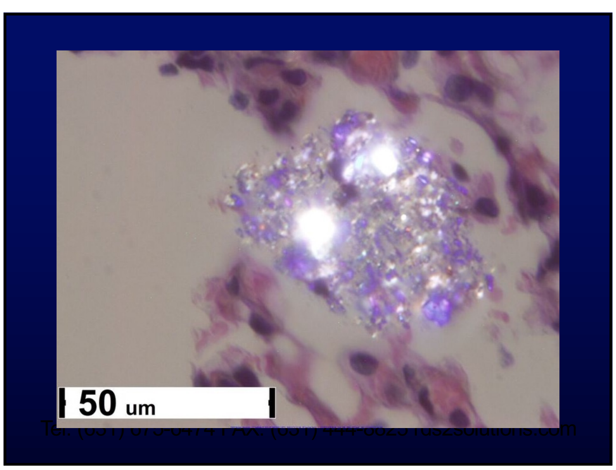

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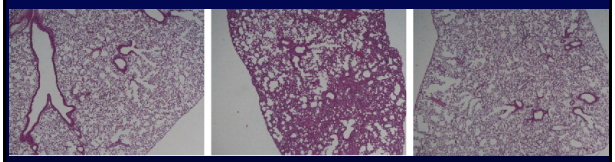
(Left) Lung from female C57BL/6 2-month-old untreated control mouse (40X magnification) with normal histology (H&E stain).

(Center) Lung from 2-month-old female C57BL/6 mouse 3 weeks after 50 microliters orotracheal instillation of Camp Victory Iraq PM 0.00 mg/ml. (40X magnification, H&E stain). There is prominent septal thickening, inflammation and loss of airspaces.

(Right) Lung from 2-month-old female C5757BL/6 mouse 3 weeks after 50 microliters or Camp Victory, Iraq PM 100 mg/ml. RuX was dosed by adding it in the water bottle immediately after orotracheal instillation of PM (40X magnification, H&E stain). The lung is histologically near normal despite exposure to PM.



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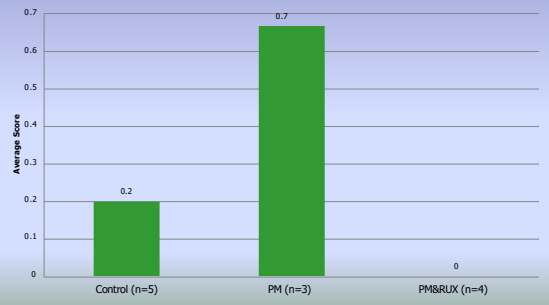
Results

- **Histology**



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Results

- **Flexivent**
- **Deep Inflation Perturbation Estimate of Physiologic Total Lung Capacity (TLC)**

Estimate of Inspiratory Capacity	(ml)
Control	0.867+-0.181
PM	0.312+-0.083
PM+RUX	0.482+-0.010

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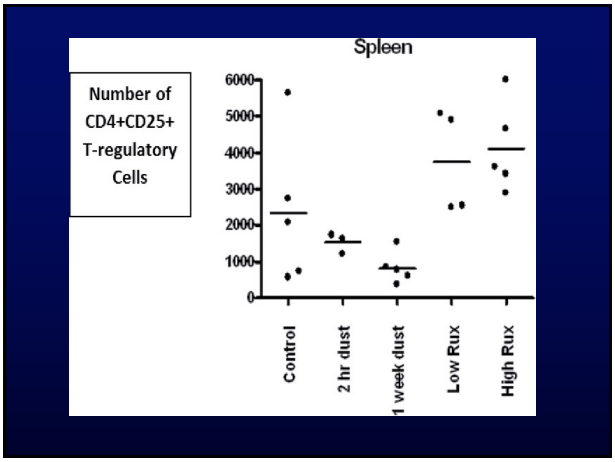

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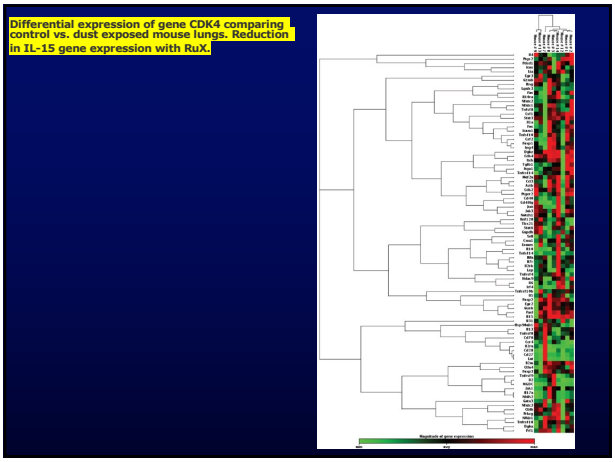

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Summary & Conclusions

- Pro-fibrotic gene programs are upregulated in lung with Camp Victory, Iraq PM exposure.
- Septal thickening is seen in all PM-exposed lungs.
- Reduced inspiratory capacity occurs with PM-exposure.

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Summary & Conclusions

- RUX largely attenuates histologic changes and improves inspiratory capacity, supporting the concept Iraq PM is pro-oxidant.

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Research Team

Jonathan C. Li, B.S., EMT, Three Village Allergy
David Lin NYU undergraduate
Tom Zimmerman, D.V.M., DLAR, Stony Brook
Laurie Levine, A.A.S., DLAR Stony Brook
Frank Antonawich, Ph.D., Garnett McKeen Lab
Merrill Garnett, D.D.S., Garnett McKeen Lab
Joseph Lasky, M.D., Tulane Pulmonary Division
Thomas Kennedy, M.D., M.P.H., New Orleans VA
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Richard Reeder, Ph.D., Geosciences, Stony Brook

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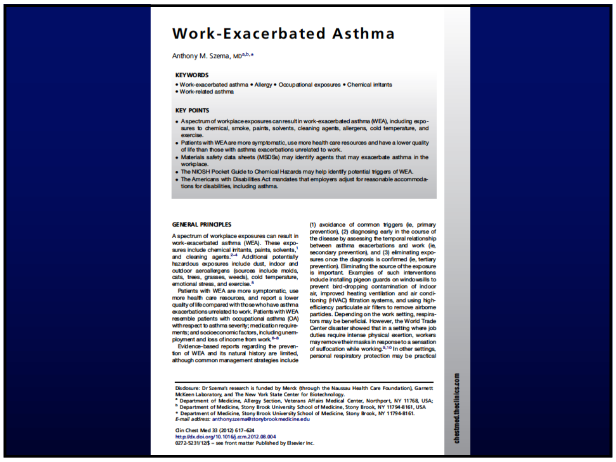

Work-Exacerbated Asthma

Anthony M. Szema, MD[a,b,*]

KEYWORDS
- Work-exacerbated asthma • Allergy • Occupational exposures • Chemical irritants
- Work-related asthma

KEY POINTS
- A spectrum of workplace exposures can result in work-exacerbated asthma (WEA), including exposures to chemical, smoke, paints, solvents, cleaning agents, allergens, cold temperature, and exercise.
- Patients with WEA are more symptomatic, use more health care resources and have a lower quality of life than those with asthma exacerbations unrelated to work.
- Materials safety data sheets (MSDSs) may identify agents that may exacerbate asthma in the workplace.
- The NIOSH Pocket Guide to Chemical Hazards may help identify potential triggers of WEA.
- The Americans with Disabilities Act mandates that employers adjust for reasonable accommodations for disabilities, including asthma.

GENERAL PRINCIPLES

A spectrum of workplace exposures can result in work-exacerbated asthma (WEA). These exposures include chemical irritants, paints, solvents,[1] and cleaning agents.[2–4] Additional potentially hazardous exposures include dust, indoor and outdoor aeroallergens (sources include molds, cats, trees, grasses, weeds), cold temperature, emotional stress, and exercise.[5]

Patients with WEA are more symptomatic, use more health care resources, and report a lower quality of life compared with those who have asthma exacerbations unrelated to work. Patients with WEA resemble patients with occupational asthma (OA) with respect to asthma severity; medication requirements; and socioeconomic factors, including unemployment and loss of income from work.[6–8]

Evidence-based reports regarding the prevention of WEA and its natural history are limited, although common management strategies include (1) avoidance of common triggers (ie, primary prevention), (2) diagnosing early in the course of the disease by assessing the temporal relationship between asthma exacerbations and work (ie, secondary prevention), and (3) eliminating exposures once the diagnosis is confirmed (ie, tertiary prevention). Eliminating the source of the exposure is important. Examples of such interventions include installing pigeon guards on windowsills to prevent bird-dropping contamination of indoor air, improved heating ventilation and air conditioning (HVAC) filtration systems, and using high-efficiency particulate air filters to remove airborne particles. Depending on the work setting, respirators may be beneficial. However, the World Trade Center disaster showed that in a setting where job duties require intense physical exertion, workers may remove their masks in response to a sensation of suffocation while working.[9,10] In other settings, personal respiratory protection may be practical

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[a] Department of Medicine, Allergy Section, Veterans Affairs Medical Center, Northport, NY 11768, USA;
[b] Department of Medicine, Stony Brook University School of Medicine, Stony Brook, NY 11794-8161, USA
* Department of Medicine, Stony Brook University School of Medicine, Stony Brook, NY 11794-8161.
E-mail address: anthony.szema@stonybrookmedicine.edu

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Review Article
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Occupational Lung Diseases among Soldiers Deployed to Iraq and Afghanistan

Anthony M Szema[1,2*]
[1] New York State Center for Biotechnology Stony Brook University School of Medicine, Stony Brook, NY 11794, USA
[2] Chief, Allergy Section, Veterans Affairs Medical Center, Northport, NY, 11768, USA

Abstract

Military personnel deployed to Iraq and Afghanistan, from 2004 to the present, has served in a setting of unique environmental conditions. Among these are exposures to burning trash in open air "burn pits" lit on fire with jet fuel JP-8. Depending on trash burned–water bottles, styrofoam trays, medical waste, unexploded munitions, and computers–toxins may be released such as dioxins and n-hexane and benzene. Particulate matter air pollution culminates from these fires and fumes. Additional environmental exposures entail sandstorms (Haboob, Shamal, and Sharqi) which differ in direction and relationship to rain. These wars saw the first use of improvised explosive devices (roadside phosphate bombs),as well as vehicle improvised explosive devices (car bombs), which not only potentially aerosolize metals, but also create shock waves to induce lung injury via blast overpressure. Conventional mortar rounds are also used by Al Qaeda in both Iraq and Afghanistan. Outdoor aeroallergens from date palm trees are prevalent in southern Iraq by the Tigris and Euphrates rivers, while indoor aeroallergen aspergillus predominates during the rainy season. High altitude lung disease may also compound the problem, particularly in Kandahar, Afghanistan. Clinically, soldiers may present with new-onset asthma or fixed airway obstruction. Some have constrictive bronchiolitis and vascular remodeling on open lung biopsy - despite having normal spirometry and chest xrays and CT scans of the chest. Others have been found to have titanium and other metals in the lung (rare in nature). Still others have fulminant biopsy-proven sarcoidosis. We found DNA probe–positive Mycobacterium Avium Complex in lung from a soldier who had pneumonia, while serving near stagnant water and camels and goats outside Abu Gharib. This review highlights potential exposures, clinical syndromes, and the Denver Working Group recommendations on post-deployment health.

Keywords: Burn pits; Aeroallergenaspergillus; Bronchiolitis; Mycobacterium avium complex

Abbreviations

IED: Improvised Explosive Device; VIED: Vehicle Improvised Explosive Device; MAC: Mycobacterium Avium Complex; ABPA: Allergic Broncho Pulmonary Aspergillosis; CHUS: Containerized Housing Units; IAW-LI; Iraq Afghanistan War Lung Injury

Summary for Table of Contents

Occupational lung diseases have emerged as a problem among soldiers deployed to Iraq and Afghanistan. Clinical presentations are different from prior wars and require pulmonologists to have an enhanced knowledge base regarding concepts such as burn pits, improvised explosive devices, blast overpressure, sandstorms and allergy. Denver Working Group recommendations offer a framework for evaluating war fighters with Iraq Afghanistan War Lung Injury (IAW-LI).

Introduction

For a variety of reasons, U.S. soldiers deployed to Iraq between the years 2004-2011, and Afghanistan from 2004-present, have been assigned extended or multiple tours of duty, often 1 year or longer at a time. As a result, they have been increasingly exposed to unfavorable environmental conditions, which are dusty and harsh. (Figure 1)

For most of the Iraq war, widespread use of incinerators was not available, and at the largest air base in Balad, a ten acre open air burn pit operated daily by burning all trash between 2003-December 2009, lit by jet fuel called JP-8 (Figure 2, Fumes from Camp Anaconda, Balad, Iraq). In Afghanistan, there are many small bases without incinerators, so trash is burned with JP-8 in burn pits as well, leading to aerosolized particulate matter air pollution. JP-8 releases benzene when burned at

ROGUE BEE
Anthony M. Szema, M.D.

Figure 1: Attachment from book Rogue Bee by Anhtony Szema, Createspace 2010

*Corresponding author: Anthony M. Szema, MD, Chief, Allergy Section, Veterans Affairs Medical Center, 79 Middleville Road, Northport, NY 11768; Assistant Professor of Medicine and Sugery, Principal Investigator, New York State Center for Biotechnology, Stony Brook University School of Medicine, Stony Brook, NY 11794; E-mail: anthony.szema@stonybrookmedicine.edu

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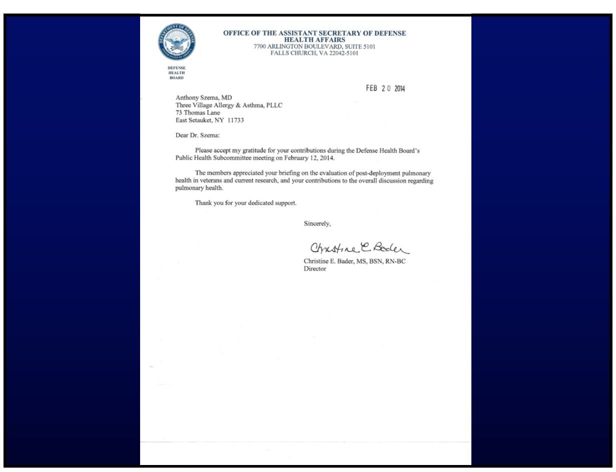

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DEFENSE HEALTH BOARD

FEB 20 2014

Anthony Szema, MD
Three Village Allergy & Asthma, PLLC
73 Thomas Lane
East Setauket, NY 11733

Dear Dr. Szema:

Please accept my gratitude for your contributions during the Defense Health Board's Public Health Subcommittee meeting on February 12, 2014.

The members appreciated your briefing on the evaluation of post-deployment pulmonary health in veterans and current research, and your contributions to the overall discussion regarding pulmonary health.

Thank you for your dedicated support.

Sincerely,

Christine E. Bader

Christine E. Bader, MS, BSN, RN-BC
Director

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$240,000 in Educational Grants and Research Funding

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•Harvard Apparatus	•$1,000
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RESEARCH TEAM

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- Sergey Lyubsky, MD, PhD, VAMC Northport
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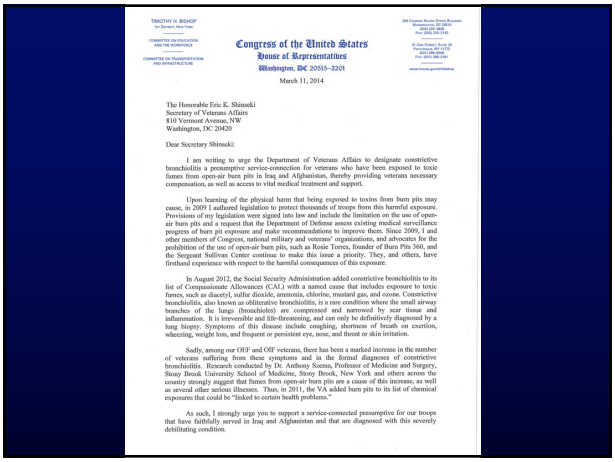

TIMOTHY H. BISHOP
1st District, New York

COMMITTEE ON EDUCATION AND THE WORKFORCE

COMMITTEE ON TRANSPORTATION AND INFRASTRUCTURE

Congress of the United States
House of Representatives
Washington, DC 20515–3201

March 11, 2014

The Honorable Eric K. Shinseki
Secretary of Veterans Affairs
810 Vermont Avenue, NW
Washington, DC 20420

Dear Secretary Shinseki:

I am writing to urge the Department of Veterans Affairs to designate constrictive bronchiolitis a presumptive service-connection for veterans who have been exposed to toxic fumes from open-air burn pits in Iraq and Afghanistan, thereby providing veterans necessary compensation, as well as access to vital medical treatment and support.

Upon learning of the physical harm that being exposed to toxins from burn pits may cause, in 2009 I authored legislation to protect thousands of troops from this harmful exposure. Provisions of my legislation were signed into law and include the limitation on the use of open-air burn pits and a request that the Department of Defense assess existing medical surveillance progress of burn pit exposure and make recommendations to improve them. Since 2009, I and other members of Congress, national military and veterans' organizations, and advocates for the prohibition of the use of open-air burn pits, such as Rosie Torres, founder of Burn Pits 360, and the Sergeant Sullivan Center continue to make this issue a priority. They, and others, have firsthand experience with respect to the harmful consequences of this exposure.

In August 2012, the Social Security Administration added constrictive bronchiolitis to its list of Compassionate Allowances (CAL) with a named cause that includes exposure to toxic fumes, such as diacetyl, sulfur dioxide, ammonia, chlorine, mustard gas, and ozone. Constrictive bronchiolitis, also known as obliterative bronchiolitis, is a rare condition where the small airway branches of the lungs (bronchioles) are compressed and narrowed by scar tissue and inflammation. It is irreversible and life-threatening, and can only be definitively diagnosed by a lung biopsy. Symptoms of this disease include coughing, shortness of breath on exertion, wheezing, weight loss, and frequent or persistent eye, nose, and throat or skin irritation.

Sadly, among our OEF and OIF veterans, there has been a marked increase in the number of veterans suffering from these symptoms and in the formal diagnoses of constrictive bronchiolitis. Research conducted by Dr. Anthony Somma, Professor of Medicine and Surgery, Stony Brook University School of Medicine, Stony Brook, New York and others across the country strongly suggest that fumes from open-air burn pits are a cause of this increase, as well as several other serious illnesses. Thus, in 2011, the VA added burn pits to its list of chemical exposures that could be "linked to certain health problems."

As such, I strongly urge you to support a service-connected presumptive for our troops that have faithfully served in Iraq and Afghanistan and that are diagnosed with this severely debilitating condition.

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DeGette And Bishop Announce "Helping Veterans Exposed To Toxic Chemicals" Act
Jun 27, 2013
Press Release
Burn Pit Toxic Exposure Illnesses Will Be Studied, Treated at Defense Centers of Excellence Under New Bill

WASHINGTON – Today, U.S. Reps. Diana DeGette (D-CO) and Tim Bishop (D-NY) were joined by representatives from veteran advocacy groups, physicians, and family members of veterans to announce new bipartisan legislation to address the health crisis among Iraq and Afghanistan veterans who were exposed to open-air burn pits and other airborne hazards during their service overseas. Original cosponsors of the legislation also include Congressmen Walter Jones (R-NC) and Jim Cooper (D-TN).

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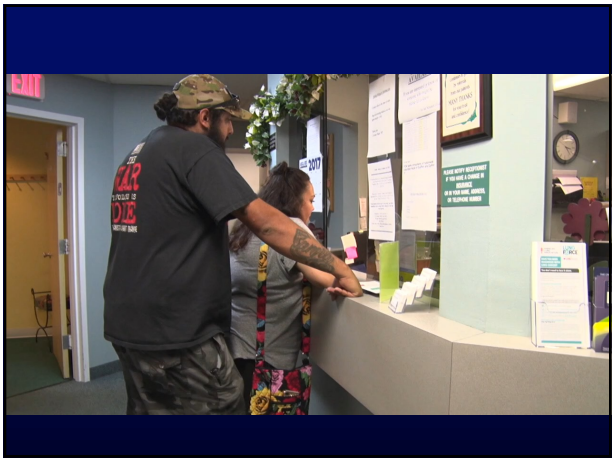

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- 13th International Congress on Combustion By-Products and Their Health Effects, New Orleans, LA, May 15-18, 2013
- Mount Sinai School of Medicine, Department of Preventive Medicine Grand Rounds, January 10, 2014 and May 28, 2013
- Soldier/Veteran Seminar at National Defense University December 19, 2012
- VISN3 Primary Care Conference Bronx VA September 12, 2012
- Dartmouth-Hitchcock Medical Center Chief Resident' s Morbidity & Mortality conference at the VA Hospital in White River Junction, VT on Wednesday, September 28. 2011
- CHEST Hawaii 2011
- AAAAI Session at CHEST 2010Toronto, November 2, 2010

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(1) Which of the following is true of previous studies of respiratory problems in soldiers returning from Iraq or Afghanistan, as reviewed by Szema et al?

a) Soldiers returning from Iraq/Afghanistan have higher rates of new-onset asthma than stateside troops.
b) Even on asthma medications, lung function values are similar to those of asthma patients in the general population.
c) The findings of this clinical syndrome are consistent with fixed airway obstruction due to lung injury.
d) All of the above are true.

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b) Even on asthma medications, lung function values are similar to those of asthma patients in the general population.
c) The findings of this clinical syndrome are consistent with fixed airway obstruction due to lung injury.
d) All of the above are true.

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(2) In the study, the rate of smoking among control soldiers who did not go to Iraq/Afghanistan was about 3 percent. Approximately what percentage of the Iraq/Afghanistan veterans were smokers?

a) 16 percent
b) 11 percent
c) 7 percent
d) 3 percent (no significant difference)

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- (3) About 2 percent of the soldiers posted elsewhere had respiratory symptoms leading to spirometry. About what percentage of Iraq/Afghanistan veterans underwent spirometry?
- a) 33 percent
- **b) 14.5 percent**
- c) 6 percent
- d) 2 percent (no significant difference)

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- a) 33 percent
- **b) 14.5 percent**
- c) 6 percent
- d) 2 percent (no significant difference)

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(4) Which of the following is *not* true of the possible etiologic mechanisms, as discussed by Szema et al?

a) Exposure to sand and toxic dust
b) Burning jet fuel and trash in 'burn pits'
c) Shock waves to the lung caused by improvised explosive devices
d) The differences are probably fully explained by the higher rate of smoking among soldiers deployed to Iraq/Afghanistan.

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(4) Which of the following is *not* true of the possible etiologic mechanisms, as discussed by Szema et al?

a) Exposure to sand and toxic dust
b) Burning jet fuel and trash in 'burn pits'
c) Shock waves to the lung caused by improvised explosive devices
d) The differences are probably fully explained by the higher rate of smoking among soldiers deployed to Iraq/Afghanistan.

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(5) Which of the following is among the prevention/control measures recommended by Szema et al?

a) Installation of incinerators
b) Recycling plastic
c) Spirometry performed before and after deployment
d) All of the above

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(5) Which of the following is among the prevention/control measures recommended by Szema et al?

a) Installation of incinerators
b) Recycling plastic
c) Spirometry performed before and after deployment
d) All of the above

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In memory of Mentor, Distinguished SUNY Professor Sami I. Said, M.D.

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Surfing and research require *mentoring*, the right environment and equipment, teamwork, and persistence!

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International Center of Excellence in Deployment Health and Medical Geosciences, Northwell Health
Anthony M. Szema, M.D., Director

Account 502001

TAX ID 11-2965575

Northwell Health Foundation
2000 Marcus Avenue
2nd Floor
New Hyde Park, NY 11042

"Unrestricted educational and research grant for Dr. Anthony Szema and International Center of Excellence in Deployment Health and Medical Geosciences"

Attn: Robert Lane, Vice-President, Principal Gifts

PHONE: 516-321-6000

foundation@northwellhealth

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