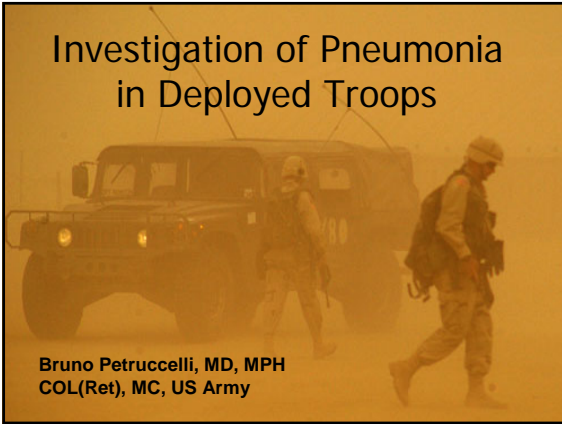


Investigation of Pneumonia in Deployed Troops



Bruno Petruccelli, MD, MPH
COL(Ret), MC, US Army

The views expressed during this presentation are those of the speaker, and do not necessarily represent the policies or position of the Department of Defense.

Operation Iraqi Freedom, 2003

- U.S. Forces
- 19 cases of severe respiratory disease
 - 2 deaths
- EPICON launched
 - Active case finding
 - Questionnaire to determine risk factors

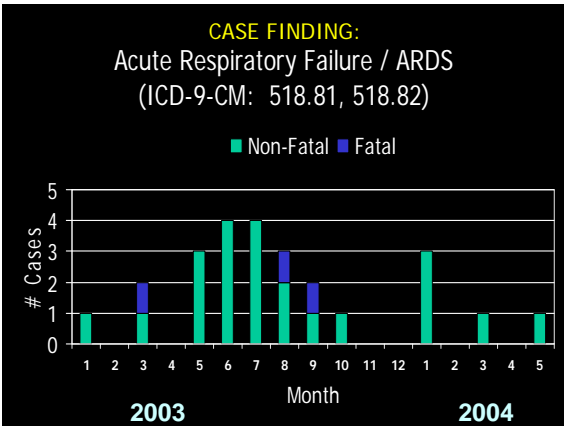
Severe Acute Pneumonia

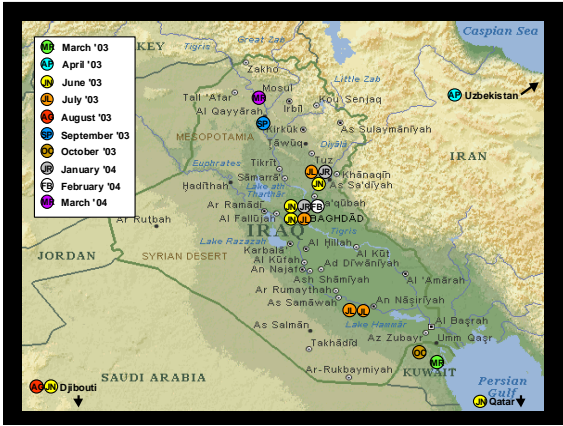
- ### Epidemiological Consultation (EPICON)
- Landstuhl, Germany
 - Late March 2003: 2 patients in ICU
 - 17 June 2003: First pneumonia death, reports of additional ICU patients
 - 12 July 2003: Second pneumonia death
 - 17 July 2003: Army Surgeon General Tasking
 - Confirm severe pneumonia outbreak
 - 3 teams deployed
 - Iraq
 - Germany (Landstuhl)
 - United States

- ### Method
- Questionnaire, database development
 - Case finding
 - Clinician interviews
 - Review of charts, radiographs, laboratory tests
 - Case interviews (surrogate for the two deaths)
 - Autopsy review
 - Follow-up clinical evaluations for 13 severe patients at WRAMC
 - Labs, PFTs, PPD, CXR, pulmonary / allergy evaluations
 - Revised questionnaire
 - Tobacco analysis

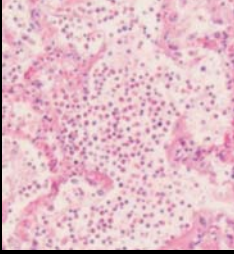
- General
 - CBC
 - Metabolic profile
 - C - reactive protein
 - Erythrocyte sed. rate
- Microbiology
 - Sputum, Blood, Urine Cults.
 - Stool O & P
- Miscellaneous
 - Anti-nuclear antibody
 - Eosinophil cationic protein
 - Hypersensitivity pneumonitis panel
 - Quantitative immunoglobulins
 - Rheumatoid factor
- Serology (infections)
 - Adenovirus Group
 - *Bordetella pertussis*
 - *Chlamydia* spp.
 - Coxsackie B (1-6)
 - *Coxiella burnetii*
 - Hantavirus
 - Histoplasma
 - Respiratory Syncytial Virus
 - Influenza A and B
 - Legionella (serum, urine)
 - *Mycoplasma pneumoniae*
 - Parainfluenza (1,2,3)
 - Rickettsial agents
 - SARS
 - *Stongyloides* spp.
 - *Toxocara* spp.
 - *Wuchereria* spp.

Findings





Demographics

Age	Yrs	Rank	N (%)
Median	22		
Range	19-47	≤ E4	24 (86)
		E5 - E9	3 (11)
		Officer	1 (3)
	Gender		
		Male	26 (93)
		Female	2 (7)
Race			
		White	27 (96)
		Afr-Am	1 (4)

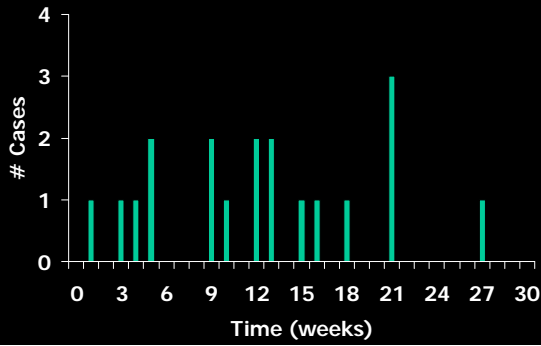
Demographics

Service	
Army	22 (78)
Navy	1 (4)
Marine Corps	5 (18)
Component	
Active	15 (54)
Reserves	6 (21)
National Guard	7 (25)

Military Occupation

Infantry	3
Armor	2
Artillery	2
Engineer	3
Mechanic	1
Truck driver	2
Fuel/Supply	1
Communications	3
Medical	2

Severe Pneumonia: Time from Arrival in Theater to Onset



Distribution of Symptoms (n=16)

fevers or chills	15	vomiting	4
shortness of breath	12	diarrhea	4
fatigue	11	confusion	4
cough	10	sore throat	3
muscle or joint pain	9	sputum	3
chest pain	7	nasal congestion	2
abdominal pain	6	syncope	1
		hemoptysis	0
		rash	0

Overview of Clinical Course (n=16)

- Symptoms & signs
 - Fever, respiratory distress
 - CXR w/ bilateral infiltrates (10 with pleural effusions)

- Antibiotics
 - Levofloxacin 88%
 - Ceftriaxone 65%
 - Doxycycline 59%
 - Imipenem 59%
 - Macrolide 47%
 - Vancomycin 24%

- Steroids given to 8 patients



Medical History

- Generally unremarkable
- No asthma
- Prescription medications
 - Simvastatin (1)
 - Malaria prophylaxis: medication and compliance varied
 - One with latent TB infection; non-compliant with INH
- Over-the-counter medications and supplements
 - Ibuprofen or aspirin as needed (3)
 - Vitamins (3)
 - Creatine (1)
 - OTC stimulant to stay awake (1)

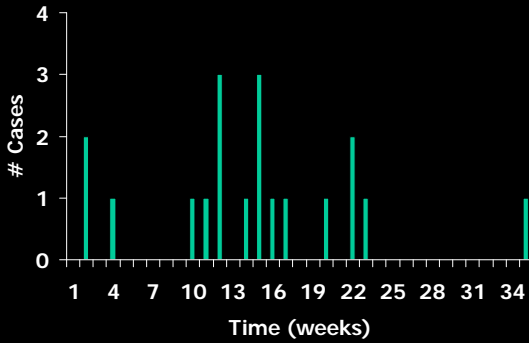
Lab Findings

- Elevated WBC count (Median 13, range 7.3 – 37)
 - 10 patients with elevated eosinophil fraction
- Culture
 - *Streptococcus pneumoniae* (1) – sputum
 - *Acinetobacter baumannii* (1) – BAL fluid
- Urine antigen
 - *Streptococcus pneumoniae* (1)
- Serology
 - *Coxiella burnetii* (3)
 - *Legionella* spp. (1)
 - Low titers to various respiratory pathogens
 - Fungal & parasitic antibodies negative
- Immunology
 - Serum immunoprecipitation to tobacco leaf extracts negative
 - Most patients evidenced atopy by skin testing

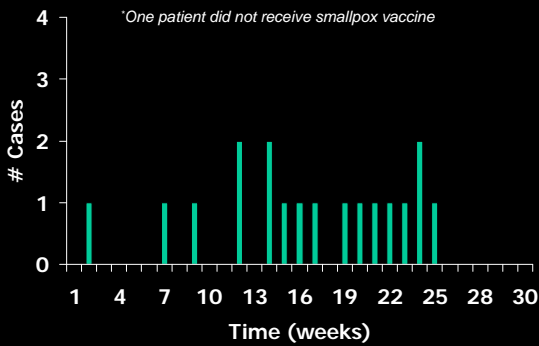
Risk Factors Query

- No common exposures prior to illness
 - Occupational risk factors (daily duties, chemicals, munitions, fuel, etc)
 - Environmental risk factors (water, food, habitat, pollutants, etc)
 - Infectious risk factors (contact with locals, insects, animals, etc)
 - Medications
- Smoking history
 - 16 smokers
 - 7 smoked both foreign and US tobacco
 - 9 began smoking during this deployment

Time Elapsed from Last Anthrax Immunization to Illness



Time Elapsed from Last Smallpox+ Immunization to Illness



Summary of Findings

- Higher rate of severe pneumonia compared to Army basic training posts
- No clear epidemiologic link
 - No relation in person, place or time
 - No common exposures identified
- Variety of possible infectious etiologies
- 10 cases with elevated eosinophils
 - New-onset smoking a possible risk factor
 - No common infectious cause, including parasites
 - No specific medication(s) unique to eos. patients
- No evidence of tobacco contamination

Pneumonia with Elevated Eosinophils

Tissue involvement	
Lung ² ± blood	4
Blood only	6
Smoking	
New-onset	9
Chronic	1
Total	10

²Bronchoscopic alveolar lavage fluid (3)
³Pleural fluid (1)
 Tissue from autopsy (1)

	Elevated Eosinophils ¹	
	Yes	No
Non-smoker	0	3
New-onset smoker	9	0
Chronic smoker	1*	6

¹Blood absolute count >600 cells/ μ l; pleural fluid and BAL fluid >5%
 *Unique from the other chronic smokers in that his tobacco use notably increased during deployment

Time from illness onset to elevated eosinophils
 Mean = 7.5 days, median = 6.5 days, range 4-14 days

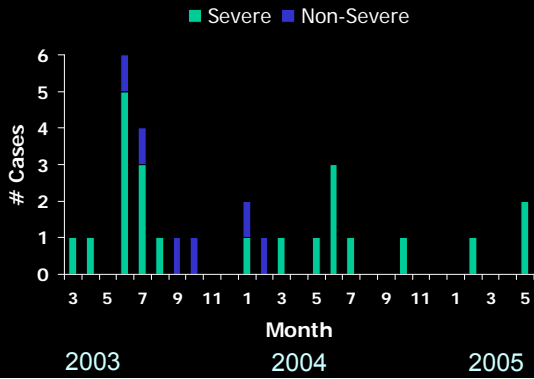
Acute Eosinophilic Pneumonia (AEP)

AEP Case Definition

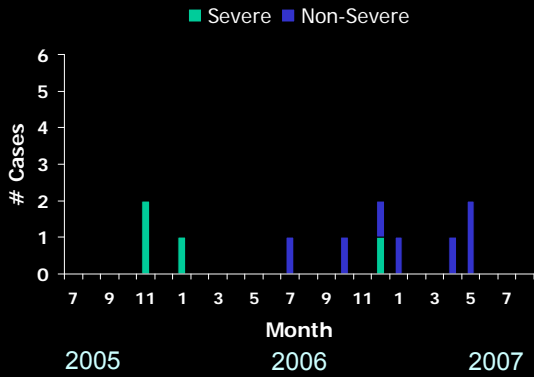
- Febrile prodrome
- Acute onset of respiratory symptoms
- Chest film w/ infiltrates
- Definite case: Either lung biopsy with eosinophilic infiltration or BAL with $\geq 5\%$ eos.
- Probable case: Never underwent BAL or lung biopsy but developed unexplained peripheral eosinophilia (total count $> 250/\text{mcl}$ AND eosinophils $\geq 10\%$ of differential)



AEP Epidemic Curve (first 27 months)



AEP Epidemic Curve (past 27 months)



Smoking history of non-severe^a and severe^b
AEP patients during OIF, March 2003 - June 2005

Cigarette smoking	Non-Severe	Severe	Total
New	4	19	23
Increased quantity	0	3	3
Chronic	2	0	2

^aNon-severe=did not require mechanical ventilation

^bSevere=required mechanical ventilation

Acute Eosinophilic Pneumonia (AEP)

- Etiology undetermined
- Evidence suggests one or more inhalational exposures in a predisposed individual
- Not an infection, but may present in conjunction with, or as a result of, infectious agents
- Initiation of tobacco smoking, or a significant increase in the quantity of tobacco smoked, appears to be a major risk factor

AEP Treatment

- Cessation of tobacco smoking
- Empiric treatment of CAP
 - 3rd generation cephalosporin (ceftriaxone, cefotaxime)

AND

 - Respiratory tract quinolone (levofloxacin 500-750 mg IV qd *or* azithromycin 500 mg IV qd)

AND

 - Doxycycline (100 mg IV bid)
- Corticosteroids
 - Solumedrol 80 mg IV q 8 hrs (or equivalent)
 - Begin taper over 2-4 weeks as symptoms resolve
- Pressure-control ventilation
- Evacuation from theater
