Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: King MS, Eisenberg R, Newman JH, et al. Constrictive bronchiolitis in soldiers returning from Iraq and Afghanistan. N Engl J Med 2011;365:222-30.

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SECTION 1. ACKNOWLEDGEMENTS

The Authors would like to recognize individuals who contributed to the care of the patients reported in this case series. Sallie Lewis, NP was the first Blanchfield Army Hospital provider to notice the trend of soldiers returning from service with unexplained shortness of breath. She coordinated the efforts of others, both at Blanchfield and at Vanderbilt to systematically evaluate those experiencing symptoms. Drs. Michael Dao and Victor Agnello from Blanchfield worked with Vanderbilt and Dr. Andrew Shorr from Walter Reed to establish a protocol to evaluate symptomatic soldiers.

The authors appreciate the commitment of Debbie Paulauskas RRT, Susan McDermott, RN and Christopher Shinault, RRT from Vanderbilt who coordinated the care of these patients. Their sustained commitment to this project will have long term benefits for all who serve.

SECTION 2. Patient Demographics.

Patient Identification Number	Age	Gender	Height (inches)	Height (meters)	Weight (lbs)	Weight (kgs)	BMI
1	23	F	68.0	1.73	207	94	31.5
2	26	M	76.0	1.93	295	134	36.0
3	25	M	72.0	1.83	200	91	27.2
4	37	M	71.0	1.80	172	78	24.0
5	38	M	72.5	1.84	216	98	29.0
6	27	M	67.0	1.70	184	84	28.9
7	34	M	68.5	1.74	190	86	28.5
8	28	M	70.5	1.79	219	100	31.0
9	42	M	75.0	1.91	269	122	33.7
10	44	M	70.5	1.79	177	80	25.1
11	42	M	66.5	1.69	173	79	27.6
12	35	M	72.0	1.83	246	112	33.4
13	26	M	72.0	1.83	234	106	31.8
14	28	M	72.0	1.83	192	87	26.1
15	37	M	72.0	1.83	177	80	24.1
16	41	M	70.0	1.78	254	115	36.5
17	31	M	67.5	1.71	159	72	24.6
18	38	M	69.5	1.77	211	96	30.8
19	27	M	69.5	1.77	207	94	30.2
20	32	M	72.0	1.83	213	97	28.9
21	23	M	71.5	1.82	173	79	23.8
22	33	M	66.0	1.68	174	79	28.1
23	35	M	70.0	1.78	228	104	32.8
24	26	M	69.0	1.75	186	84	27.5
25	28	M	67.0	1.70	163	74	25.6
26	39	M	72.5	1.84	250	114	33.5
27	28	M	72.0	1.83	190	86	25.8
28	42	F	63.0	1.60	124	57	22.1
29	28	M	72.0	1.83	220	100	29.9
30	36	M	68.0	1.73	148	67	22.6
31	36	M	67.0	1.70	189	86	29.7
32	37	M	68.0	1.73	210	95	32.0
33	29	F	65.0	1.65	160	73	26.7
34	36	M	73.0	1.85	225	102	29.7
35	40	M	69.0	1.75	210	95	31.1
36	35	M	69.0	1.75	200	91	29.6
37	35	M	70.5	1.79	216	98	30.6
38	42	M	73.0	1.85	223	101	29.5

BMI- Body Mass Index

SECTION 3. Chest Radiographs and High Resolution Computed Tomography Results.

Patient Identification Number	Chest Radiograph Interpretation	High Resolution Computed Tomography Interpretation
1	Normal	Mild air trapping
2	Normal	Normal
3	Normal	Normal
4	Normal	Mild air trapping
5	Normal	Normal
6	Normal	Normal
7	Normal	Normal
8	Normal	Normal
9	Normal	Mild air trapping
10	Normal	Small LUL density
11	Normal	Normal
12	Normal	Normal
13	Normal	Normal
14	Normal	Normal
15	Normal	N/A
16	Normal	Normal
17	Normal	Normal
18	Normal	Normal
19	Normal	Normal
20	Normal	Normal
21	Normal	Few bullae
22	Normal	Mild basilar scarring
23	Normal	Normal
24	Normal	Normal
25	Normal	Normal
26	Normal	Normal
27	Lingular nodules	Few lingular nodules
28	Normal	Normal
29	Normal	Subcentimeter nodules
30	Normal	Mild air trapping
31	Normal	Mild air trapping
32	Normal	Normal
33	Normal	Normal
34	Normal	Normal
35	Normal	Mild air trapping
36	Normal	Normal
37	Normal	Mild focal pleural thickening
38	Normal	Normal

SECTION 4. PULMONARY FUNCTION TESTING

Patient Identification Number	FEV_1 (L)	FEV_1 (% pred)	FVC (L)	FVC (% pred)	FEV_1/ FVC (%)	DL_{CO}	DL_{CO} (% pred)	TLC (L)	TLC (% pred)	BD resp
1	2.65	71	3.22	73	82	15.49	48	3.5	62	No
2	2.05	40	2.6	41	79	NA	NA	3.76	46	No
3	4.03	85	5.54	96	69	32.93	94	7.01	96	No
4	3.58	82	4.52	84	79	21.70	53	6.82	96	No
5	4.11	91	5.48	98	75	33.53	80	7.54	101	Yes
6	3.68	88	4.40	89	85	29.08	76	6.03	96	No
7	3.52	85	4.37	87	81	25.24	66	6.50	98	No
8	3.55	78	3.99	73	89	21.62	51	4.78	68	No
9	3.81	82	5.17	88	74	39.47	90	9.01	113	Yes
10	3.91	94	4.58	89	85	25.34	66	6.22	88	No
11	2.78	74	3.62	79	77	18.89	54	5.64	91	No
12	3.21	71	4.39	79	73	34.30	82	6.44	88	Yes
13	4.50	95	5.86	102	77	35.31	80	6.92	95	No
14	4.56	97	5.40	94	84	27.16	62	6.49	89	No
15	4.37	98	5.18	94	84	37.71	91	7.34	100	No
16	3.09	76	4.73	93	67	28.24	107	6.63	99	No
17	3.74	90	5.10	103	73	28.14	74	6.97	109	No
18	3.98	95	5.21	102	76	33.90	87	8.52	125	No
19	3.75	84	5.82	108	64	46.54	112	7.06	104	No
20	3.98	86	5.71	101	70	30.57	72	7.69	105	No
21	2.94	62	4.28	75	69	30.06	68	5.53	77	Yes
22	2.62	66	3.48	74	75	21.28	59	5.31	87	No
23	4.66	108	6.01	114	78	35.26	88	8.56	124	No
24	4.26	96	5.58	105	76	27.97	68	7.94	119	No
25	3.26	78	4.50	91	72	28.15	73	5.77	92	No
26	3.64	81	5.23	94	70	26.37	63	7.50	101	No
27	3.85	82	4.76	83	81	23.64	54	7.09	97	No
28	2.82	100	3.75	112	75	19.55	74	5.72	117	No
29	4.93	105	5.75	100	86	33.23	76	7.78	107	No
30	3.83	94	4.06	85	91	26.15	69	6.03	93	No
31	3.63	92	4.06	85	89	18.47	51	5.31	84	No
32	3.90	97	4.61	94	84	27.01	73	6.53	100	No
33	3.41	102	3.69	94	92	19.72	66	5.29	102	No
34	4.19	91	5.19	91	81	40.55	95	6.99	93	No
35	3.58	94	4.62	97	77	25.32	72	7.34	108	No
36	4.23	100	4.93	96	86	26.62	68	6.62	99	No
37	3.82	89	4.51	86	83	31.94	80	6.45	93	No
38	4.42	95	5.53	98	98	NA	NA	6.65	89	No

FEV_1 – forced expiratory volume in one second, FVC – forced vital capacity, TLC – total lung capacity, DL_{CO} – diffusing capacity of the lung for carbon monoxide

The criteria for diagnosing obstruction was an FEV_1/FVC ratio of < 70. The criteria for restriction was a TLC < 80% of predicted.[11, 12]

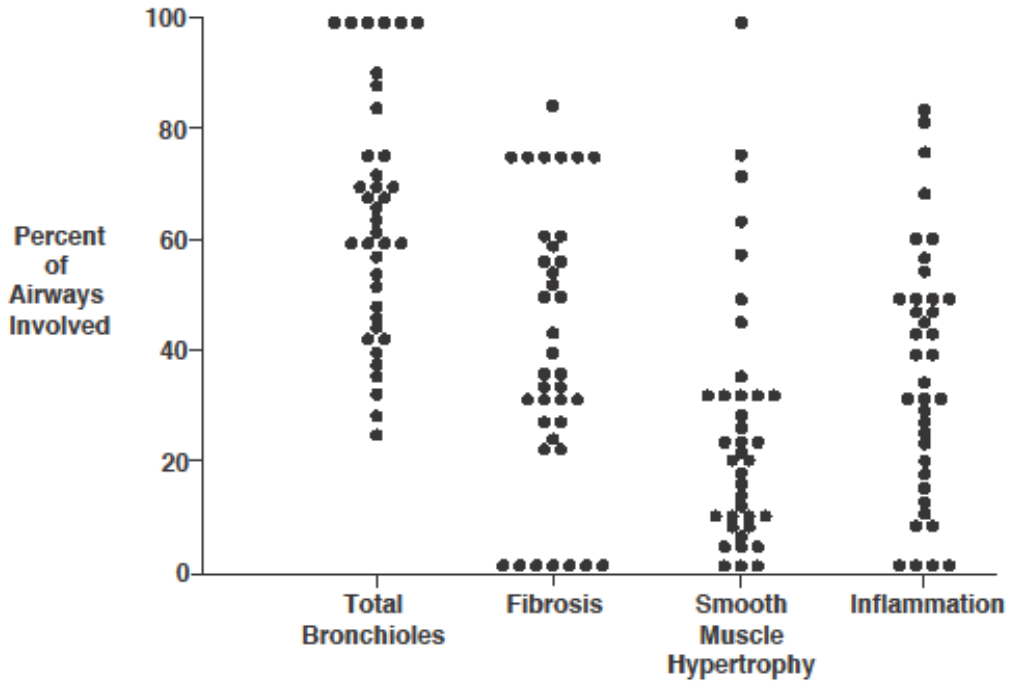
SECTION 5. CARDIO-PULMONARY EXERCISE TESTING

Patient Identification Number	VO_2 max (% pred)	VAT (%VO_2 max)	RER	Max HR (% pred)	RR (breaths/min)	VE/VCO_2	VE_{max}/MVV	MVV – VE (L/min)
1	60	NA	1.02	70.1	32	NA	74.8	21.7
2	NA	NA	NA	NA	NA	NA	NA	NA
3	NA	NA	NA	NA	NA	NA	NA	NA
4	68	31.5	1.25	76.5	36	32.0	59.7	59.2
5	85	44.6	1.11	96.7	33	29.9	57.1	72.3
6	86	36.0	1.04	87.6	42	28.2	67.3	49.4
7	79	33.4	1.18	91.9	41	30.6	64.3	51.0
8	80	37.9	1.18	78.6	47	32.5	86.5	19.3
9	104	55.7	1.17	94.4	33	27.2	65.7	53.6
10	91	45.5	1.17	106.8	36	37.4	65.6	55.1
11	NA	NA	NA	NA	NA	NA	NA	NA
12	88	49.0	1.12	90.3	39	27.0	68.5	41.4
13	90	48.1	1.13	86.6	35	24.6	59.8	74.2
14	75	45.4	1.05	80.2	22	23.8	36.4	119.0
15	95	39.8	1.11	100.5	37	27.5	57.7	75.9
16	114	50.3	1.02	78.8	36	29.5	85.0	19.0
17	64	37.1	1.07	74.6	30	29.6	40.9	90.6
18	80	37.3	1.00	86.3	25	32.7	50.1	81.4
19	81	50.5	1.96	93.8	44	33.6	65.7	52.8
20	NA	NA	NA	NA	NA	NA	NA	NA
21	NA	NA	NA	NA	NA	NA	NA	NA
22	76	44.5	1.08	90.9	47	35.6	80.1	21.4
23	99	48.7	1.01	85.9	49	25.4	58.6	79.2
24	63	39.5	1.22	88.7	21	24.9	45.9	94.5
25	65	30.3	1.33	99.5	37	25.0	74.7	33.9
26	118	54.0	1.11	83.4	34	28.4	83.2	25.0
27	67	37.8	1.33	91.7	41	24.9	48.8	80.9
28	NA	NA	NA	NA	NA	NA	NA	NA
29	NA	NA	NA	NA	NA	NA	NA	NA
30	74	45.9	1.24	95.1	32	27.2	61.6	60.3
31	99	41.0	0.95	82.1	27	25.8	58.1	57.7
32	94	58.6	1.23	96.2	40	25.1	64.8	56.3
33	110	77.0	1.00	85.9	34	28.9	57.4	59.5
34	94	42.7	1.11	87.0	29	25.8	51.8	82.8
35	83	55.2	1.11	87.2	22	24.6	49.1	68.4
36	NA	NA	NA	NA	NA	NA	NA	NA
37	79	47.1	1.02	61.2	28	25.8	49.2	69.0
38	91	42.0	1.12	88.2	23	26.9	57.0	70.3

VO_2 max – maximum oxygen consumption, VAT – ventilator anaerobic threshold, Max HR – maximum heart rate, RR – respiratory rate, VE – minute ventilation, VCO_2 – carbon dioxide production, MVV – predicted maximum minute ventilation (liters/min)

SECTION 6.

FIGURE 1. DISTRIBUTION OF INVOLVED AIRWAYS AND HISTOLOGIC FINDINGS



The mean number of bronchioles analyzed was 32.2 +/- 10.6 1 STD per subject. Each point on the graph represents the percent of abnormal airways in a single subject for each finding. The total number of airways assessed was 628, and the mean percent of abnormal airways was 64.6% +/-21.7 1 STD. The range of observed airways was 1-5 airways in 5 subjects, 6-20 airways in 13 subjects, and 20-72 in 20 subjects. . Because this is not a comparative study, statistical differences among subjects are not shown. Most airways revealed multiple lesions. See Table 4 for a breakdown of the abnormal findings.