

Lung Pathology in Patients with Post-deployment Constrictive Bronchiolitis

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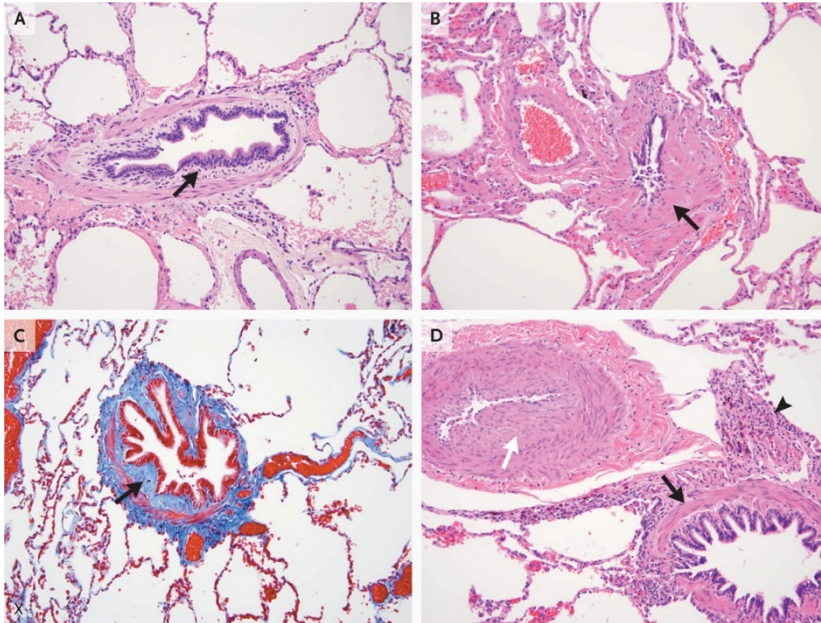
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Post-deployment Constrictive Bronchiolitis (CB)

- King et al. [*NEJM* 2011] evaluated 80 soldiers from Fort Campbell (Kentucky) with unexplained dyspnea.
- 49 underwent video-assisted thoracoscopic lung biopsy
 - 38 were diagnosed with CB
- Soldiers with CB reported exposure to:

• Sulfur-mine fire in 2003	28 (74%)
• Incinerated solid waste	24 (63%)
• Incinerated human waste	18 (47%)
• Dust storms	33 (87%)
• Combat smoke	17 (45%)

Lung pathology in soldiers with CB



King MS et al. *N Engl J Med* 2011;365:222-230.

Table 3. Pathological Features of Biopsy Samples Obtained from 38 Soldiers with Constrictive Bronchiolitis.

Variable	No. of Patients
Bronchiolar luminal constriction*	38
Predominant constrictive stroma	
Smooth muscle	7
Fibrous tissue	3
Mixed	28
Pigment deposition	37
Polarizable material within pigment	36
Peribronchiolar inflammation	34
Hypertensive-type arterial change	28
Respiratory bronchiolitis	27
Prominent bronchial-associated lymphoid tissue	19
Mucus plugging	13
Eosinophils in bronchiolar wall	7
Luminal granulation	2
Obliteration of bronchioles	0

Goals of current study

- Comprehensive morphometric analysis of small airways, blood vessels, and parenchyma in lungs of soldiers diagnosed with CB.
- Characterize inflammatory/immune phenotype.

Methods

- Lung tissue samples from:
 - CB patients who underwent surgical lung biopsy
 - Age-matched, non-diseased lungs declined for transplantation
 - Former smokers with COPD
- CB diagnosis made by clinical pathologist
- Inclusion requirements: ≥ 3 small airways/section, at least 2 sections/subject
- All small airways (< 2 mm in diameter) and adjacent arterioles on each lung section were evaluated
- Serial tissue section stained for H&E, PAS, picro-Sirius red, and Masson's trichrome
- Serial tissue sections immunostained for elastin, CD4, CD8, CD19, CD31 or neutrophil elastase
- Morphometry normalized to basement membrane length

Clinical characteristics

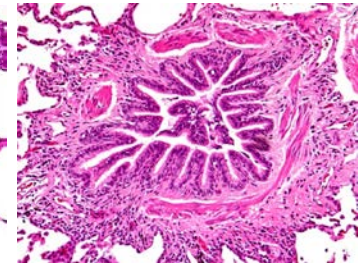
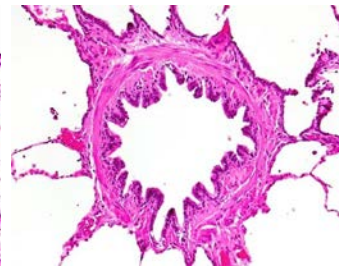
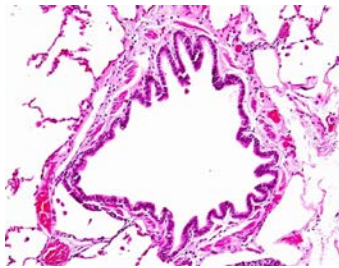
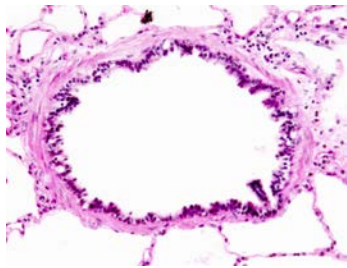
	Lifelong Non-smokers	Soldiers with Constrictive Bronchiolitis
Number of study participants	19	58
FEV ₁ (% of predicted)	N/A	90 (71-109)
FEV ₁ / FVC	N/A	78 (69-92)
Age (years)	37 (20-50)	35 (26-52)
Sex:		
Male	13	53
Female	6	5
Airways		
Number (per study participant)	8.0 ± 1.1	7.2 ± 0.7
Basement membrane length (mm)	1.5 ± 0.1	1.7 ± 0.1
Arterioles		
Number (per study participant)	16.7 ± 2.0	12.8 ± 1.2
Basement membrane length (mm)	0.8 ± 0.1	0.8 ± 0.1
Inter-alveolar septa		
Length (mm)	25.4 ± 1.6	18.9 ± 0.9

Widespread small airway pathology in CB patients

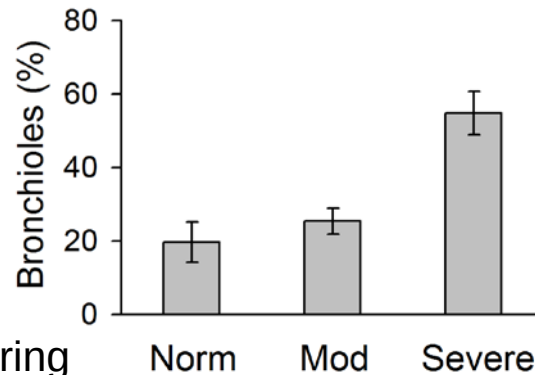
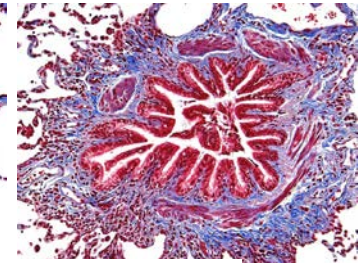
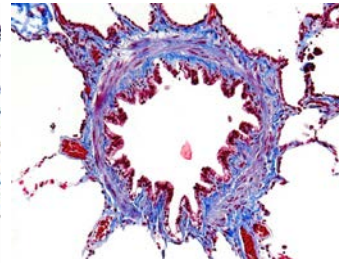
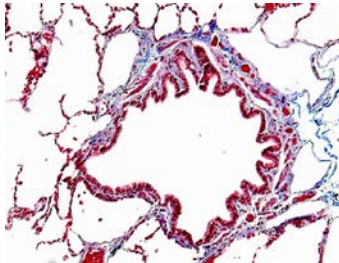
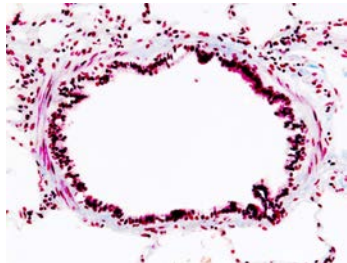
Non-diseased control

Constrictive bronchiolitis

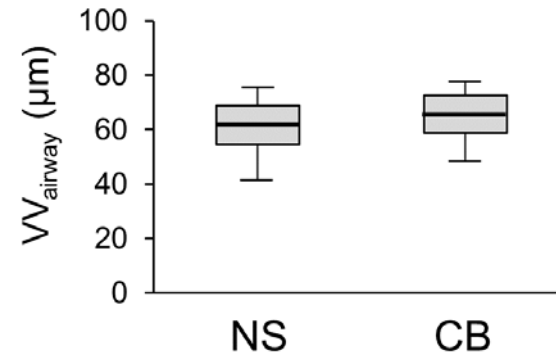
H&E



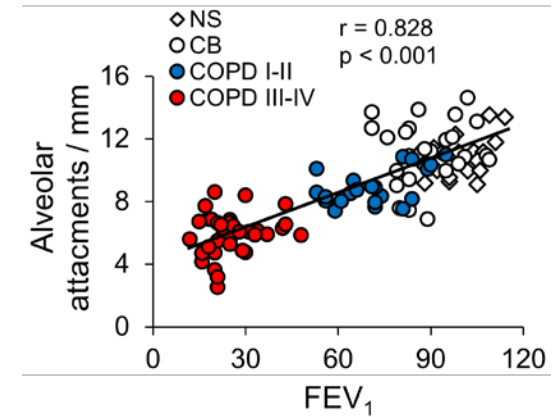
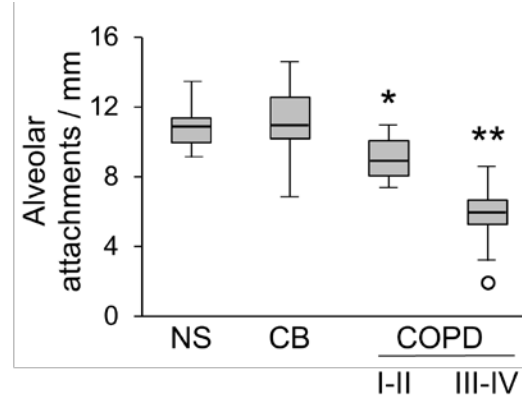
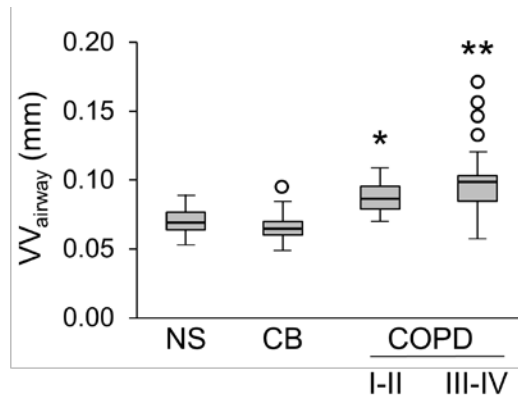
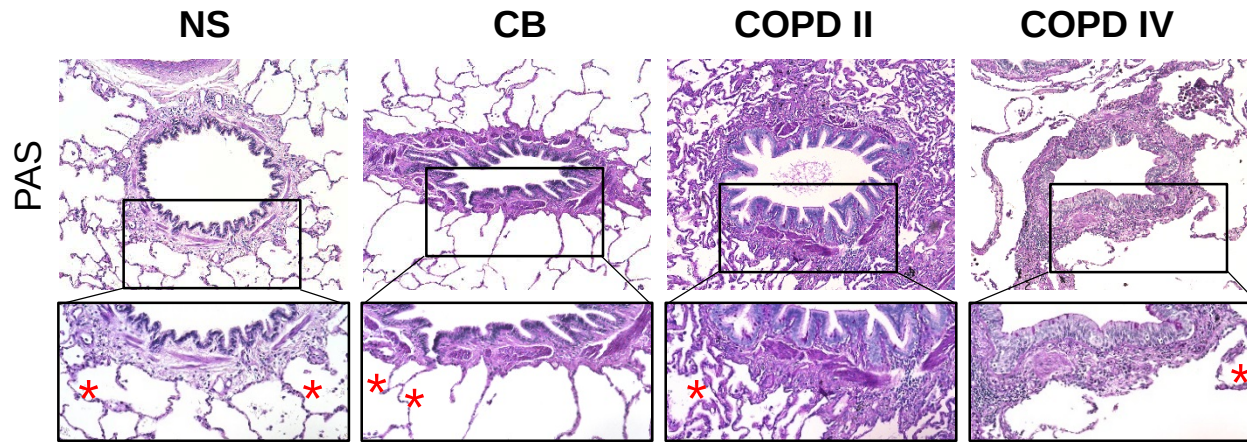
Masson's trichrome



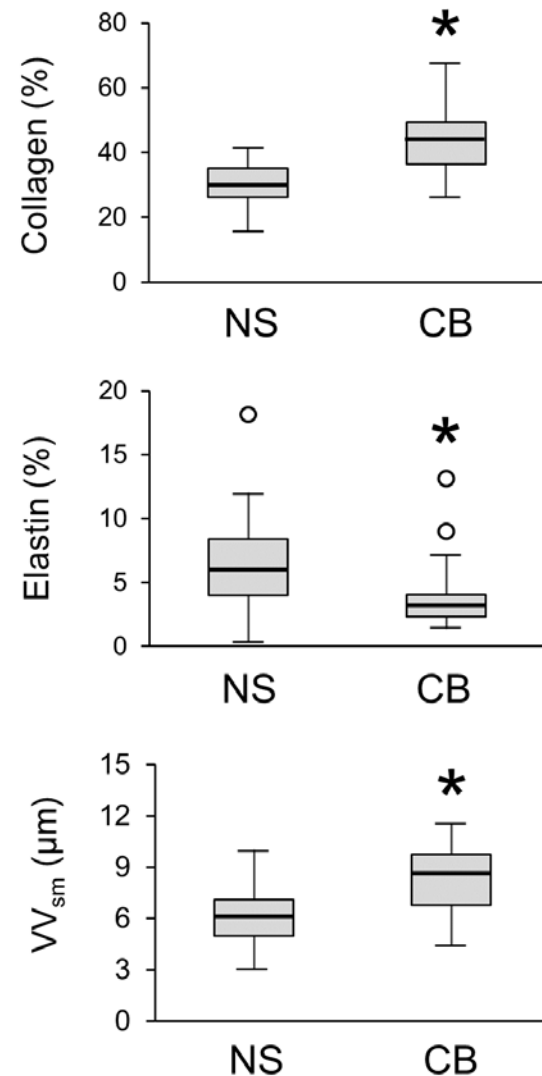
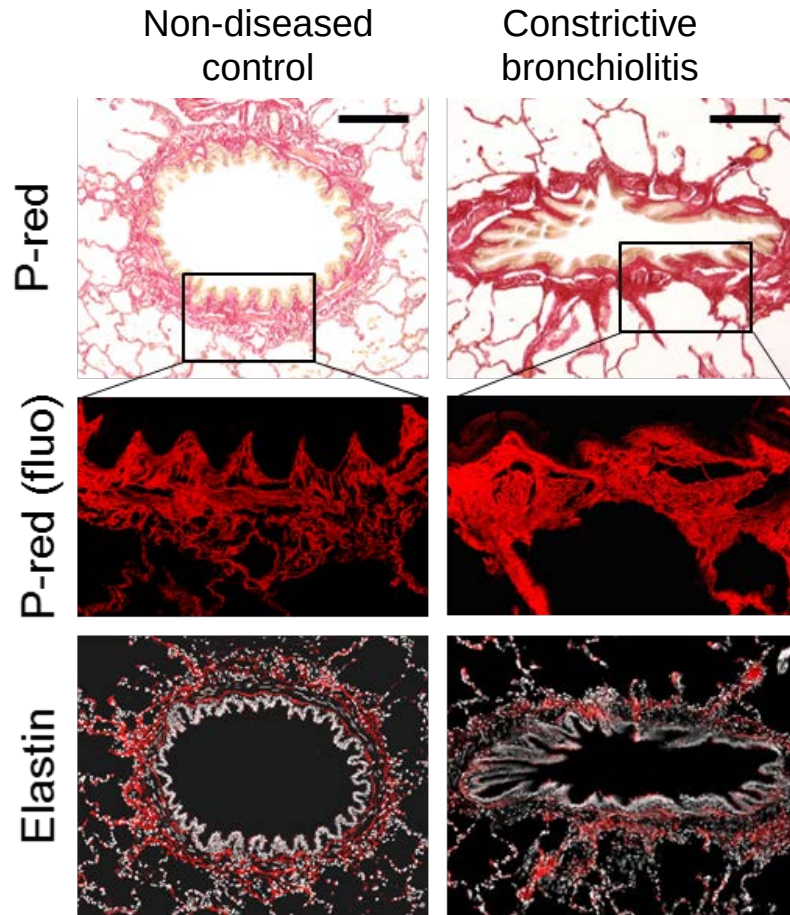
Airway Remodeling



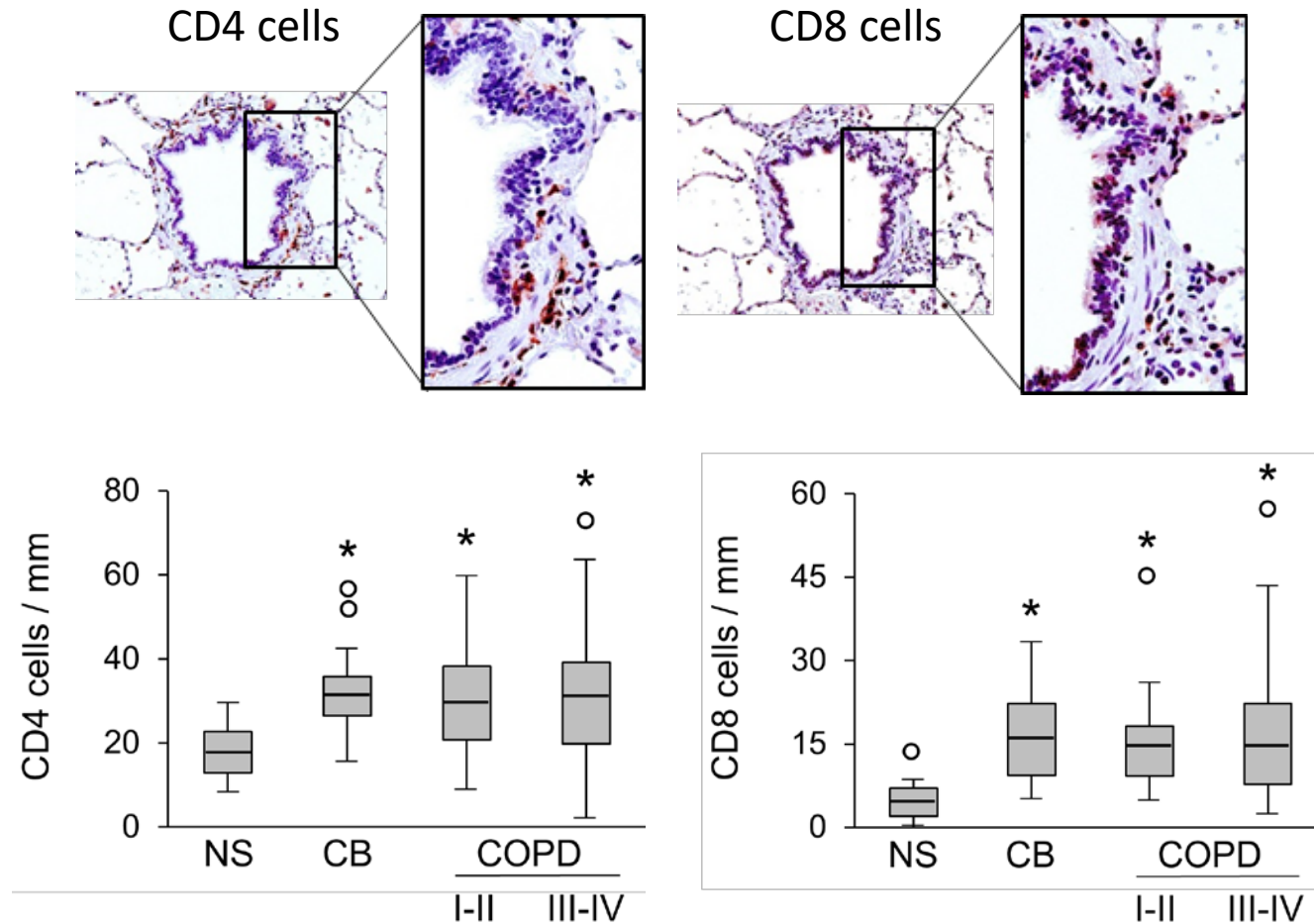
Contrast between airway remodeling in patients with CB and COPD



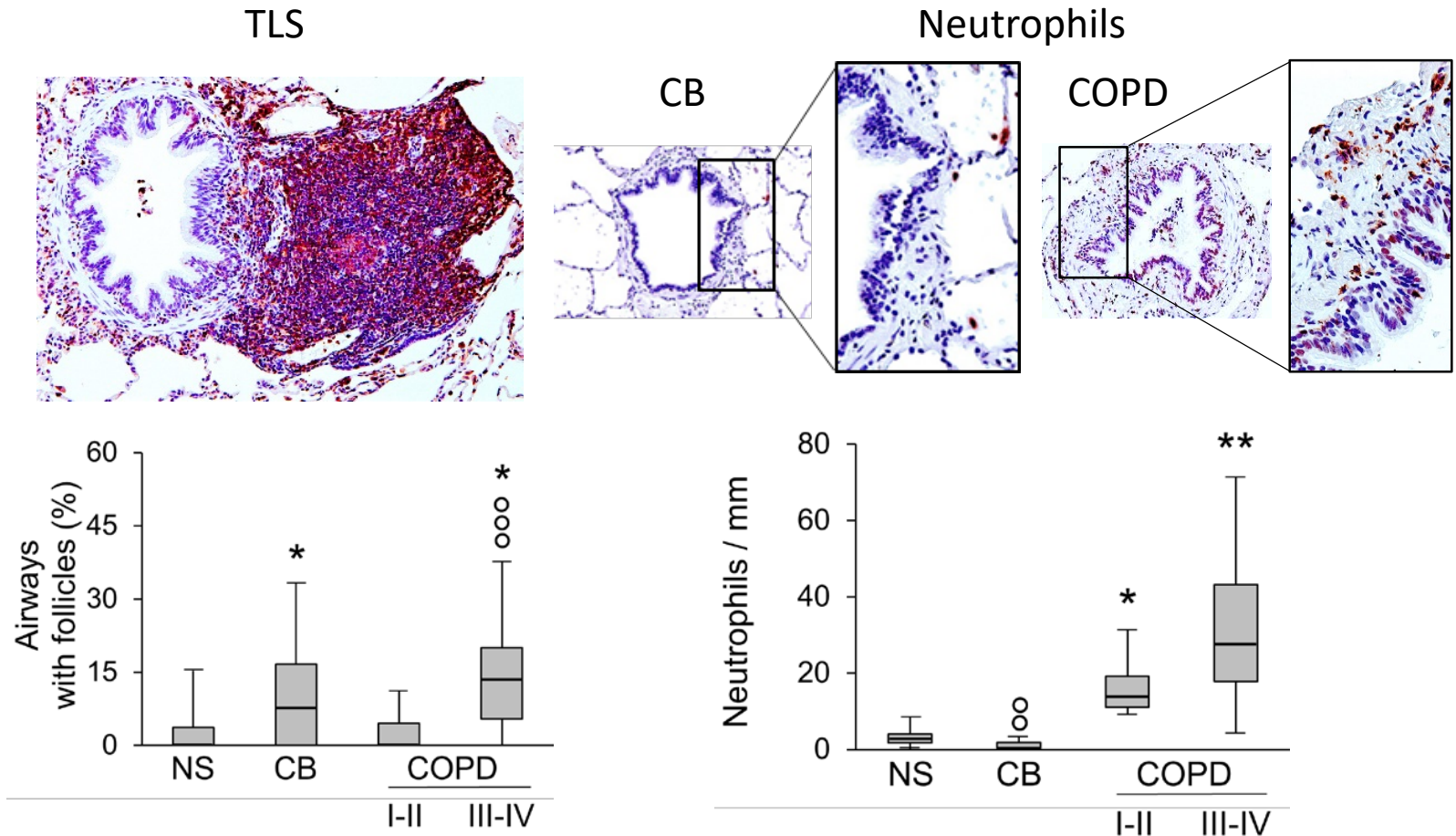
Increased collagen and smooth muscle hypertrophy in small airway walls from CB patients



Lymphocytic influx in small airways from CB and COPD patients

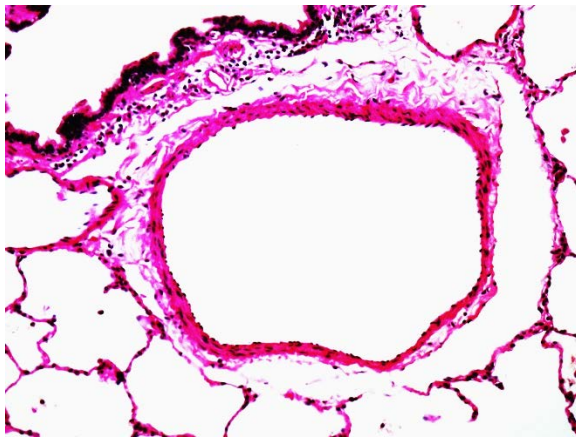


Tertiary lymphoid structures are common around small airways in CB and COPD, but neutrophils are limited to COPD

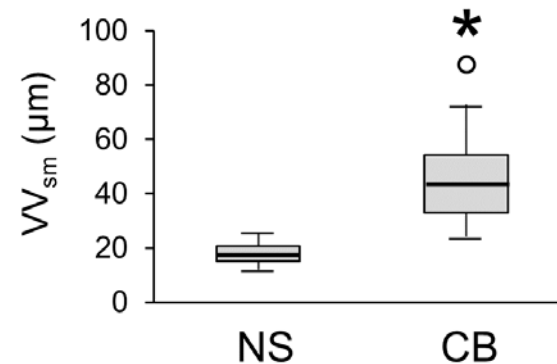
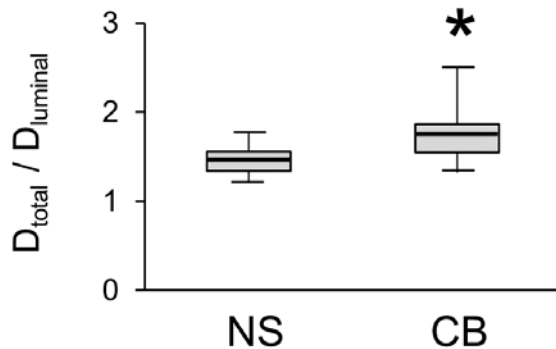
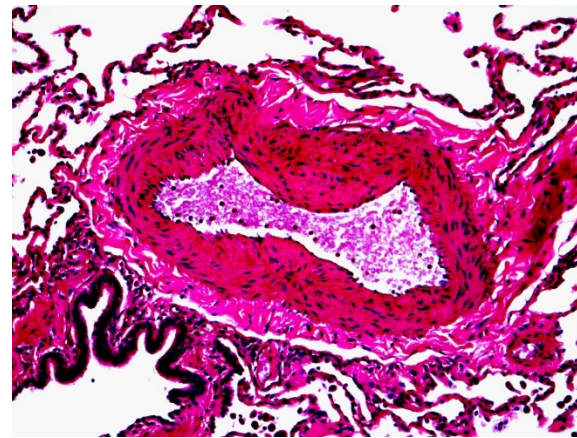


Vascular pathology in pulmonary arterioles from CB patients

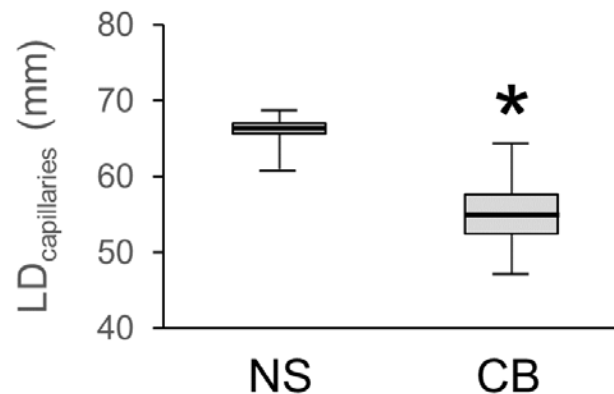
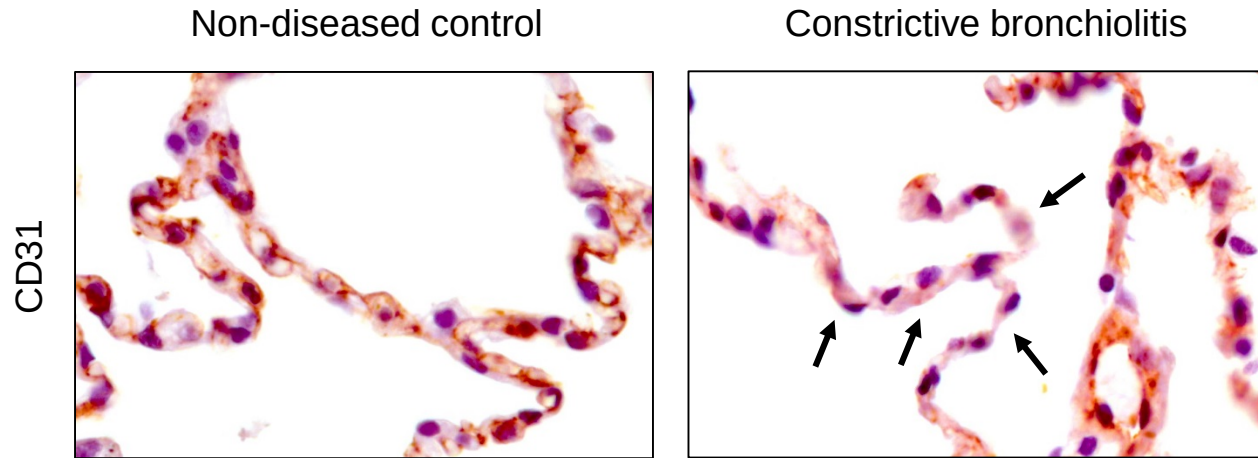
Non-diseased control



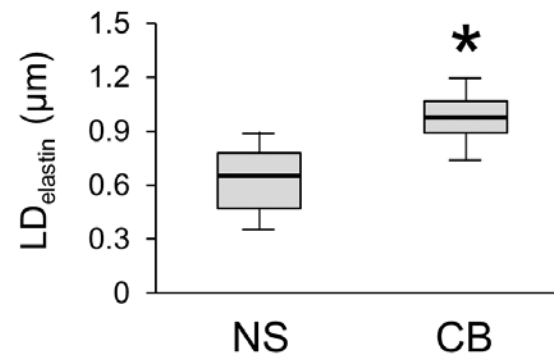
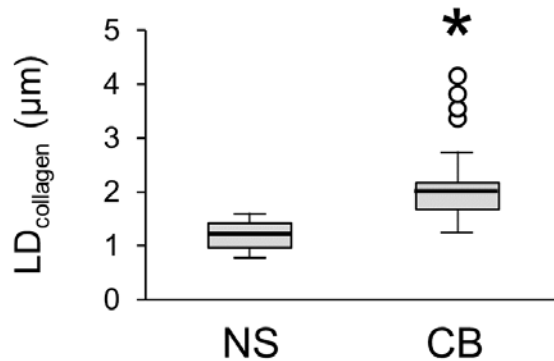
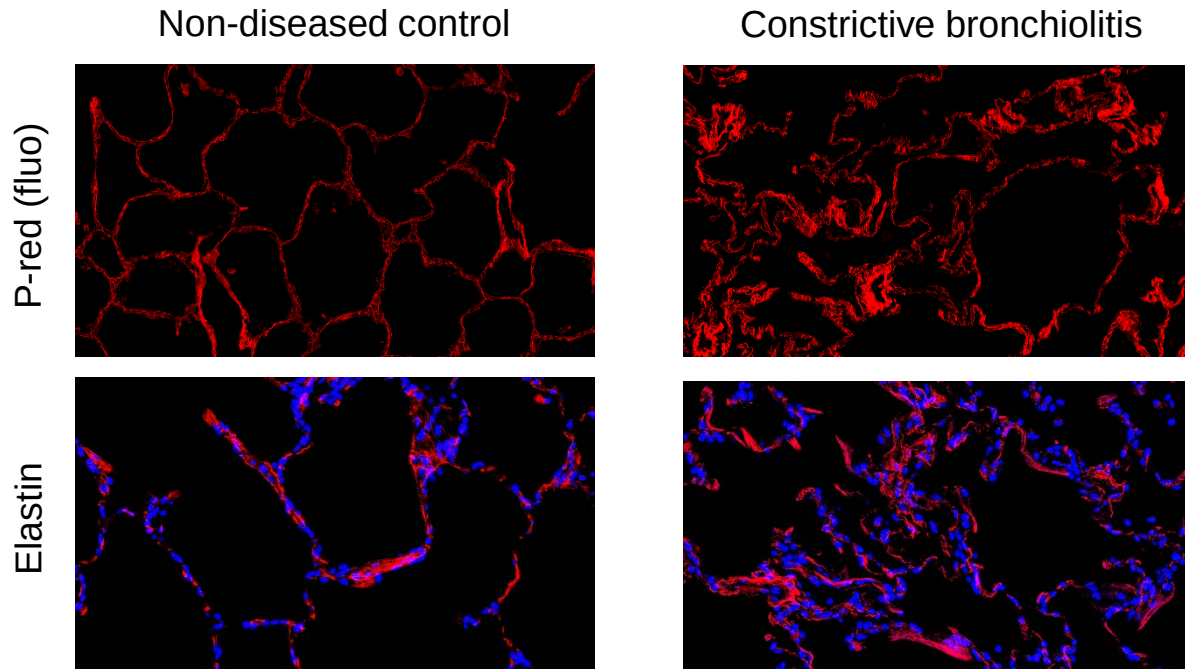
Constrictive bronchiolitis



Capillary loss in interalveolar septa from CB patients



Collagen and elastin accumulation in interalveolar septa of CB patients



Summary

- Soldiers with CB have widespread small airway pathology with increased collagen deposition and smooth muscle hypertrophy.
- Vascular pathology is present in post-deployment CB, including arterioles with medial hypertrophy and septal capillary loss.
- Linear deposits of collagen and elastin are present in interalveolar septa from lungs of CB patients.
- Lymphocyte influx and TLS are common in post-deployment CB.

Conclusions

- Post-deployment CB includes pathology in the airway, vascular, and alveolar compartments of the distal lungs.
- Post-deployment CB is associated with adaptive immune activation, suggesting the potential for disease progression.

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