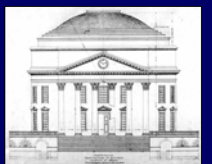




Compensatory Lung Growth is Not Uniform Among Lobes



Thomas S Maxey¹ Lucas G Fernandez¹, Timothy D. Le Cras², Peter Ellman¹, T Brett Reece¹, George Dimeling¹, Curtis Tribble¹, Irving Kron¹, and Victor E. Laubach¹

¹Division of Thoracic and Cardiovascular Surgery, Dept. of Surgery, University of Virginia Health System, Charlottesville, VA, USA

²Cincinnati Children's Hospital Medical Center, Division of Pulmonary Biology, Cincinnati, OH, USA

Background

- Pneumonectomy results in rapid, hyperplastic, compensatory growth of the remaining lung. The mechanisms mediating this regenerative growth are unknown, and the long-term goal of our research is to understand the mechanisms that trigger and regulate compensatory lung growth.
- Left pneumonectomy changes the distribution of pulmonary blood flow in that the entire cardiac output is diverted to the right lung, and blood flow to the remaining lung increases by 50% (in animals, the left lung constitutes approximately 35% of total lung mass). Increase in pulmonary blood flow following pneumonectomy may thus be an important mechanism in the initiation of compensatory lung growth.
- It is possible that differences in blood flow and/or ventilation between lobes could alter compensatory growth responses.

Hypothesis

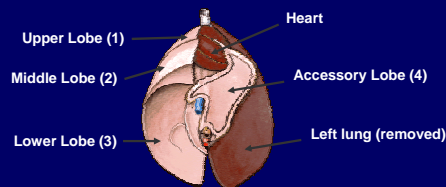
We hypothesized that compensatory lung growth is not distributed evenly in the lung but is instead lobe dependent.

Study

The four lobes of the right lung were studied in the following two groups of rats (n=8/group):

Pneum Group: Left pneumonectomy.

Sham Group: Sham left thoracotomy.



Methods

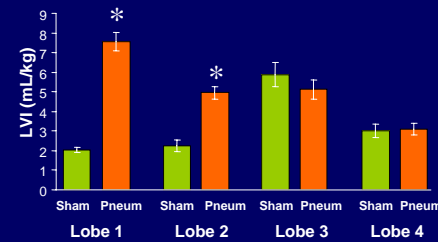
- Adult male Sprague-Dawley rats (300g) were anesthetized with ketamine and xylazine followed by tracheotomy and intubation, and ventilated with room air (n=8/group).
- Left pneumonectomy was performed through a small left anterior thoracotomy. The hilum was isolated and ligated with a silk suture. The chest was closed in layers and animals were recovered under normoxic conditions.
- Animals were recovered for 21 days after surgery and the right lungs were fixed by intratracheal administration of 10% buffered formalin at a constant pressure of 25 cm H₂O.
- Following fixation, individual lobes were isolated and lobe volumes measured by volume displacement technique.
- The four lobes of the right lung studied were:
 - Upper lobe
 - Middle lobe
 - Lower lobe
 - Accessory lobe (cardiac lobe)
- Lobes were paraffin embedded and morphometric measurements determined on lung sections using the point counting technique^{1, 2, 3}.

- Morphometric measurements included:
 - Total volume of respiratory region (TV_{vr})
 - Total volume respiratory airspace (TV_{vra})
 - Total volume respiratory tissue (TV_{vt})
 - Alveolar surface density (Sv)

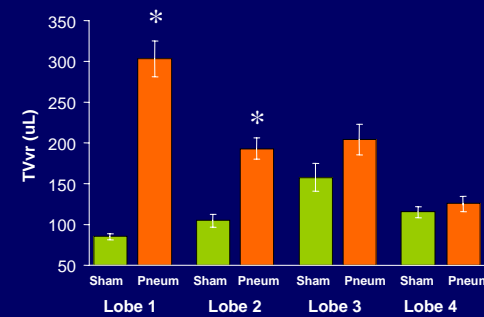
- For arteriograms, lungs were infused under constant pressure with a barium sulfate/gelatin solution through the pulmonary artery (74 mm Hg) prior to fixation and arteriogram.

Results

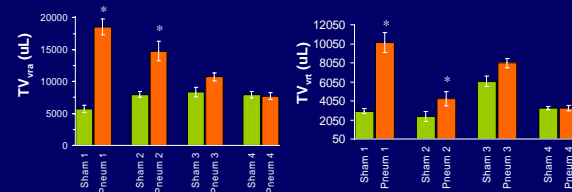
Lobe volume to body weight index (LVI) was significantly increased only in the upper two lobes (1 and 2) after pneumonectomy compared to sham.



Total volume of respiratory region (TV_{vr}) was significantly increased only in the upper two lobes (1 and 2) after pneumonectomy compared to sham.

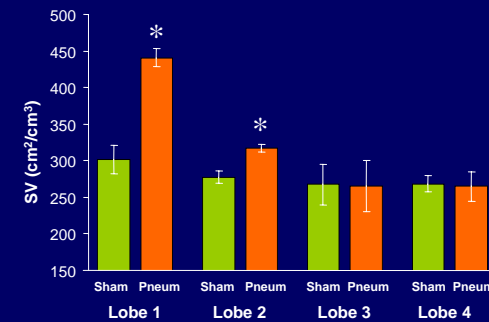


Total volume of respiratory airspace (TV_{vra}) and tissue (TV_{vt}) were significantly increased in the upper two lobes (1 and 2) after pneumonectomy compared to sham.

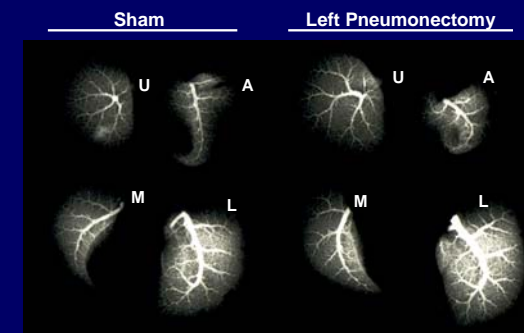


Results

Alveolar surface density (Sv) was significantly increased only in the upper two lobes (1 and 2) after pneumonectomy compared to sham.



Barium arteriogram of individual lobes from representative right lungs after sham or left pneumonectomy showing neo-vascularization mainly in the upper and middle lobes.



U = upper, M = middle, L = lower, A = accessory

*p<0.05 vs. Sham

Summary

- Left pneumonectomy results in compensatory growth in the right lung.
- Compensatory growth of the right lung was not distributed equally among the four lobes.
- Compensatory growth was observed mainly in the upper two lobes of the right lung as exemplified by increases in:
 - LVI
 - TV_{vr}
 - TV_{vra} and TV_{vt}
 - Sv
- Barium arteriograms reveal increased vascularization mainly in the upper two lobes after pneumonectomy. Vessels appear to be larger as well as more branched.
- Current studies are aimed at determining if these observations may be due to enhanced ventilation and/or perfusion in the upper two lobes compared to lobes 3 and 4. Analysis of neo-vascularization is also underway.

References

- Gil, J. 1990. *Models of lung disease*. New York: Marcel Dekker.
- Davies, P. 1991. Morphologic and morphometric techniques for the detection of drug- and toxin-induced changes in lung. *Pharmacol Ther* 50:321-336.
- Wandel, G., Berger, L.C., and Burri, P.H. 1983. Morphometric analysis of adult rat lung after bilobectomy. *Am. Rev. Respir. Dis.* 128:968-972.