

**PULMONARY PATHOLOGY JOURNAL CLUB**  
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Mohit Chawla et al. Chest 2008;134;1320-1324

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Benson A et al. Chest 2008; 134:1325–1331

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(case of Sweet syndrome involving lung)

Lawrence K et al. Chest 2008; 134:1340–1343

## **ARTICLES FOR DISCUSSION**

**1. Visceral Pleural Invasion: Pathologic Criteria and Use of Elastic Stains: Proposal for the 7th Edition of the TNM Classification for Lung Cancer** Travis WD et al on behalf of the International Staging Committee. J Thorac Oncol 2008; 3: 1384-1390.

Purpose: To define the anatomic extent of visceral pleural invasion (VPI) and to assess whether elastic stains are useful to determine VPI in lung cancer.

Methods: A Pub Med search for articles from 1970 to 2007 under search terms lung cancer and pleural invasion were reviewed for pathologic classification of extent of pleural invasion and use of elastic stains.

Results: 6 articles were identified that reported survival data using elastic stains to assess for VPI were reviewed. These articles defined P0 (T1) as lack of pleural invasion beyond the elastic layer, P1 (T2) as invasion beyond the elastic layer, P2 (T2) as invasion to the surface of the visceral pleura and P3 (T3) as invasion of the parietal pleura. In five studies, survival was shown to be significantly worse for VPI defined as P1 or P2 compared with P0.

Conclusions: The authors propose that the next TNM revision define VPI as invasion beyond the elastic layer (PL1) including invasion to the visceral pleural surface (PL2), and also recommend that elastic stains be used in cases when the distinction between PL0 and PL1 is not clear based on H&E.

**2. Immunohistochemical Expression of Estrogen and Progesterone Receptors in Primary Pulmonary Neuroendocrine Tumors** Sica G, et al. Arch Pathol Lab Med 2008; 132: 1889-1895.

Purpose: Assess estrogen and progesterone receptor expression in pulmonary neuroendocrine tumors.

Method: 71 neuroendocrine neoplasms including 42 TC, 7 AC, 14 SCLC, 2 LCNEC and 6 combined small cell carcinomas were evaluated for ER $\alpha$  (clone 6F11 Novocastra) and PR (clone 16 Novocastra). Breast and NSCLC cases were stained for comparison.

Results:

Focal to diffuse ER and PR nuclear positivity was frequent in pulmonary NE tumors:

typical carcinoid: ER 23/42, PR 11/42.

atypical carcinoid ER 6/7, PR 2/7.

small cell carcinoma ER 8/14, PR 7/14.

large cell neuroendocrine carcinoma ER 2/2, PR 0/2.

combined small cell carcinoma ER 4/6, PR 2/6.

ER and PR staining was also noted in endothelial cells.

Breast carcinomas expressed ER and PR more often than pulmonary NE tumors.

NSCLC had greater ER and similar PR immunoreactivity compared to pulmonary NE tumors.

### 3. Clinical Predictors and Histologic Appearance of Acute Exacerbations in Chronic Hypersensitivity Pneumonitis. Miyazaki Y et al. Chest 2008; 134:1265-1270.

Purpose: Evaluate the clinical and histological features of patients with chronic HP due to bird exposure who develop acute exacerbation.

Methods: Retrospective review of 100 consecutive patients with chronic bird fancier's lung (BFL) admitted to Tokyo Medical and Dental University Hospital from 1993 to 2006. Clinical, radiological and histological data collected from studies performed at the time of initial diagnosis of chronic BFL was compared between the 14 patients who developed acute exacerbation (AE) during the study period and those that did not. HRCTs and biopsies were reviewed. Roughly half of the patients in this study (55 of the 100) had open surgical lung biopsies at initial diagnosis, which included 7 of the 14 who developed AE. 12 of the 14 cases of AE were fatal, and autopsy results were available in 7 cases.

#### Results:

- AE developed more often in men than women (11 male, 3 female).
- AE was less likely to develop in non-smokers.
- Duration of illness was similar (AE 7.9 +/- 2.1 yrs vs non-AE group 6.4 +/- 1.8 yrs)
- PFTs tended to be worse in those who subsequently developed AE (the AE group).
- HRCTs showed less GGO and more severe fibrosis in those who subsequently developed AE.
- BAL fluid contained more neutrophils and less lymphocytes in the AE group.
- The 2-year frequency of AE among patients with chronic BFL having UIP-like lesions found on SLBx specimens was 11.5%.
- A UIP pattern on lung biopsy was significantly more common in the AE group:

Histologic Pattern	AE group ( n = 14)	Non -AE group (n=86)
UIP	7	10
F – NSIP	1	10
C – NSIP	0	6
OP	0	3

- UIP pattern with superimposed DAD in 6 of 7 autopsy cases, and UIP with OP seen in 1 of 7. One additional case had a surgical biopsy at time of AE, and this case showed UIP with OP (this pt was alive at the time of the report).

Conclusions: The authors conclude that low TLC and DLCO, low lymphocyte levels in BALF, and UIP pattern on histology may be risk factors for AE in pts with chronic BFL.

**4. Smoking-related changes in the background lung of specimens resected for lung cancer: a semiquantitative study with correlation to postoperative course.** Kawabata Y et al. *Histopathology* 2008; 53: 707-714.

Purpose: To assess background pathological changes in lung cancer resection specimens, and correlate them with smoking history and postoperative course.

Methods: Lobectomy and pneumonectomy specimens of 578 smokers and 230 non-smokers over an 8 year period were assessed macroscopically and microscopically for centrilobular emphysema (CLE), airspace enlargement with fibrosis (AEF) and UIP pattern fibrosis (UIP/P). Findings were graded and comparisons made between non-smokers, mild (25 or less cigarettes per day), moderate and heavy (over 50 cigarettes per day), as well as with post operative acute respiratory failure of unknown etiology.

AEF characterized by:

- 1) Fibrous interstitium with structural remodelling
- 2) Emphysematous change
- 3) Frequent bronchiolocentric location
- 4) Absence of fibroblast foci

Results:

- CLE, AEF, RB and UIP/P all showed increased frequency and degree with smoking history.
- CLE was found in 9.5 % of non-smokers, about 40% of mild smokers, and 57% to 60% of moderate to heavy smokers.
- AEF was found in 0.4% of non-smokers, 6.5% of mild smokers, and 17% to 21% of moderate to heavy smokers.
- CLE was predominantly in upper lobes, and AEF was predominantly in lower lobes.
- RB was identified in 2% of non-smokers, 15% of mild smokers, and about 23% of moderate to heavy smokers.
- UIP /P was found in 3% of non-smokers, 15% of mild smokers, and about 23% of moderate to heavy smokers. 49 patients had a pre-operative diagnosis of IPF (this is 37% of the total cases in which UIP /P was identified).
- The presence of UIP/P was associated with increased risk for post-op acute respiratory failure.

Conclusions: The authors conclude that AEF is an important smoking-related change in the lung that appears to correlate with the smoking history, and its distinction from UIP/P may be important.

**5. The Prognostic and Predictive Role of Histology in Advanced Non-small Cell Lung Cancer: A Literature Review. Hirsch FR et al. J Thorac Oncol 2008; 3: 1468-1481.**

Purpose: To identify and summarize studies in the English literature over the last 25 years that reported an association between the histologic subtype of advanced (unresectable) NSCLC and patient prognosis, and /or efficacy of specific chemotherapeutic agents.

Method: Literature search from 1982 to 2007.

Results: 408 publications were identified, of which 11 reported a prognostic association between histology and clinical outcomes, and 7 suggested that histologic subtype was predictive of outcomes in patients with advanced NSCLC treated with specific cytotoxic chemotherapy regimens. Fourteen publications reported histology was prognostic and/or predictive in patients treated with epidermal growth factor receptor inhibitors. Inadequate data collection, test methodology, or study design—including insufficient sample size, misclassified samples, and grouping of histologic subtypes for analysis—may have obscured the interpretation of the role of histology in many of the studies.

Conclusion of authors: Although differences in study design and analyses make definitive conclusions difficult, evidence suggests that histology may be prognostic or predictive of clinical efficacy outcomes. To determine which patients would benefit from specific treatments and to further understand the role of histology, future studies should focus on establishing a definitive histologic diagnosis, and should include an analysis of histologic subtypes and efficacy outcomes.

## **6. Validity of International Association for the Study of Lung Cancer Proposals for the Revision of N Descriptors in Lung Cancer**

Lee JG et al. J Thorac Oncol 2008; 3: 1421-14126.

Purpose: Assess the validity of the pending suggestions for N descriptors by the International Association for the Study of Lung Cancer.

Methods: Medical records from 1032 patients with resected NSCLC stage I–III were reviewed. Lymph node stations were grouped together into six “zones”: peripheral or hilar for N1 and upper or lower mediastinal, aortopulmonary, and subcarinal for N2. Survival was analyzed according to the proposed subdivisions single-zone N1 (N1a), multizone N1 (N1b), single-zone N2 (N2a), and multizone N2 (N2b).

Results: The 5-year survival rate was 63.8% for N0, 42.3% for N1a, 36.5% for N1b, 35.8% for N2a, and 17.4% for N2b. There were three distinct prognostic groups for N1 and N2 nodes: N1a, N1b or N2a, and N2b disease.

Conclusion: Amalgamating lymph node stations into zones and subdividing N descriptors corresponded to disease survival in this study. The authors disagree with the proposal of the IASLC staging project committee to make no changes to the N category in the current TMN system.