Pulmonary Pathology Journal Club

May 2026 articles

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Articles for discussion

1. Butnor KJ and Westom AM. Hilar fat invasion is a poorly defined and inconsistently interpreted lung carcinoma staging parameter. Am J Clin Pathol. 2026 May 5;165(5):aqag044.

Background: Hilar fat invasion raises the T category of otherwise pT1 lung carcinomas to pT2a. Pathologists were surveyed to better understand their awareness and interpretation of hilar fat invasion.

Methods: Pathologists interested in pulmonary pathology were invited to participate in an online survey of hilar fat invasion assessment.

Results: Of 80 respondents, 58% considered hilar fat any fat that is outside the lung but inside the pleural reflection, 32% considered it to be fat inside the pleural reflection near hilar lymph nodes around the main bronchus, and 10% were uncertain or had a different definition. When asked which pT designation is most appropriate for a lobectomy specimen with a pT1-sized invasive carcinoma that directly invades the fat around the lobar bronchus but does not involve the lobar bronchus margin, 69% indicated pT1c, 23% chose pT2a, and 8% were unsure/other. For a pneumonectomy specimen with a pT1-sized invasive carcinoma that directly invades the fat around both the lobar and main bronchus but does not extend beyond the pleural reflection or involve the main bronchus margin, 48% assigned pT2a, 39% chose pT1c, and 13% were unsure/other.

Take home message: There is a lack of consensus among pathologists as to what constitutes hilar fat invasion, resulting in considerable interobserver variability in pT categorization. Making hilar fat invasion a standard pT designation could improve awareness, and defining the anatomic boundaries of hilar fat could result in greater consistency in assigning a pT category to tumors that extend into fat outside the lung.

2. Moore et al. Surgical Pathology of Diffuse Parenchymal Lung Disease in Adults With IgA Vasculitis or IgA Nephropathy. Am J Surg Pathol . 2026 May 1;50(5):579-588.

Background: IgA vasculitis (IgAV) and IgA nephropathy (IgAN) are closely related disorders that usually present in childhood. Pulmonary involvement is rare and histopathologic features thereof in adults are poorly understood.

Methods: Institutional archives were searched for adults with IgAV or IgAN and diffuse parenchymal lung disease. Ten patients (6 men, median age 59 years) with lung tissue sampling were enrolled. Clinical history and pathology slides were reviewed.

Results: Histologically, 6 cases (60%) featured acute or subacute diffuse alveolar hemorrhage (DAH) accompanied by definite (40%) or probable (20%) capillaritis. Two cases (20%) featured resolved DAH only, manifesting as alveolar hemosiderosis without other changes. And 2 cases featured organizing pneumonia without DAH. Five patients had a chronic interstitial pneumonia in the background, including 3 with nonspecific interstitial pneumonia (NSIP) and 2 with unclassifiable fibrosis. Findings were similar in IgAV versus IgAN.

Take home message: As with other systemic rheumatologic disorders and vasculitic syndromes, some patients with IgAV or IgAN develop clinically significant DPLD. As in children, DAH and capillaritis are the most frequent pulmonary findings observed in adults with IgAV or IgAN. Histology may vary from acute DAH accompanied by acute fibrinous pneumonitis or frank DAD to old or quiescent DAH with alveolar hemosiderosis only, depending on disease activity and the timing of tissue sampling. Furthermore, pulmonary findings in adults are not limited to DAH and capillaritis, as patterns of organizing pneumonia, NSIP, and unclassifiable fibrosis can also be encountered without concomitant DAH. Pulmonary manifestations of IgAV and IgAN appear to be similar.

3. Willner J et al. Analysis of SCLC subtype markers (ASCL1, NEUROD1, POU2F3, YAP1), DLL3, OTP, and TTF1 in 300 lung carcinoids and enteropancreatic neuroendocrine tumours. Histopathology. 2026 May;88(6):1184-1196.

Background: ASCL1, NEUROD1, POU2F3 and YAP1 are recently described markers of transcriptional subtypes in small cell lung carcinoma (SCLC), while DLL3, regulated by ASCL1, is a target of novel therapeutic agents in various neuroendocrine neoplasms. The expression of these markers in lung carcinoids is not well established**.**

Methods: The group examined these markers in 109 lung carcinoids and compared their expression with that in 191 enteropancreatic neuroendocrine tumours (EP-NETs) and with lung carcinoid markers (OTP, TTF1).

Results: ASCL1, NEUROD1, OTP and TTF1 were positive in 56%, 0%, 84% and 35% of lung carcinoids, respectively. Of the OTP-negative lung carcinoids (n = 18), 4 (22%) were ASCL1-positive, of which one was TTF1-positive. In contrast, 59% of EP-NETs were NEUROD1-positive, whereas only rare tumours focally expressed ASCL1 (1.1%) and OTP (0.5%) and none expressed TTF1. DLL3 was positive in 57 (52%) lung carcinoids versus 5 (2.6%) EP-NETs. All lung carcinoids and EP-NETs were completely negative for POU2F3 and YAP1.

Take home message: Unlike SCLC, lung carcinoids and EP-NETs completely lack the expression of POU2F3 and YAP1, which offers diagnostic applications. Our findings also

nominate ASCL1 and NEUROD1 as site of origin markers for lung versus digestive NETs/carcinoids, respectively. Finally, the divergent expression of DLL3 in lung carcinoids and EP-NETs has therapeutic implications.

4. Wang K. et al. Risk stratification in stage I invasive non-mucinous lung adenocarcinoma based on high-risk histopathologic features. Lung Cancer. 2026 May:215:109388.

Background: High-risk histopathologic features (HRHFs) are recognized adverse markers in stage I lung adenocarcinoma (LUAD), but there is no simple way to integrate them into routine postoperative risk assessment. This group aimed to develop and validate a pathology-only risk score based on four prespecified HRHFs.

Methods: Consecutive patients with pathologic stage I invasive non-mucinous LUAD who underwent R0 resection at a tertiary center (training cohort, n = 373) and two external hospitals (validation cohort, n = 257) were retrospectively analyzed. IASLC Grade 3, spread through air spaces (STAS), visceral pleural invasion (VPI) and lymphovascular invasion (LVI) were entered together into a multivariable Cox model for disease-free survival (DFS). Regression coefficients were translated into a points-based HRHF score (2 points for Grade 3; 1 point each for STAS, VPI and LVI; range 0–5), then grouped into low (0), intermediate (1–2) and high (≥3) risk strata. Discrimination was assessed in the training and combined external cohorts.

Results: All four HRHFs showed adverse associations with DFS and remained in the multivariable model. The pathology-only predictor achieved 5-year time-dependent AUCs of 0.75 in the training and 0.73 in the validation cohort. The three-level HRHF score preserved most of this performance and produced clearly separated 5-year DFS across strata (training: 98.6%, 90.9%, 79.3%; validation: 96.5%, 91.8%, 71.7% for low, intermediate and high risk, respectively).

Take Home: This multicenter study shows that four routinely reported high-risk histologic features —IASLC Grade 3, STAS, visceral pleural invasion and LVI—can be combined into a simple pathology-based score that quantifies residual risk within pathologic stage I invasive non-mucinous LUAD.

Articles for notation

Neoplastic

1. Li J et al. The Utility of CDX2 and CK20 Immunohistochemical Reactivity to Distinguish Adenocarcinomas of the Lung From Their Benign Mimics. Arch Pathol Lab Med. 2025 Dec 30;150(5):360-364.

Take Home: CDX2 and CK20 is not expressed in benign reactive processes in the lung making list a potential way to distinguish them from adenocarcinoma.

2. Jin H. et al. PD-L1 expression is associated with inferior outcomes independent of EGFR subtype in advanced non-small cell lung cancer with uncommon EGFR mutations treated with first-line second-generation EGFR-tyrosine kinase inhibitors. Cancer. 2026 May 15;132(10):e70460. doi: 10.1002/cncr.70460.

Take Home: First-line second-generation EGFR-TKI monotherapy showed no statistically significant differences in efficacy across uncommon EGFR mutation subtypes in advanced NSCLC. In contrast, PD-L1 expression—particularly in primary lung tumors—was associated with shorter progression-free survival and demonstrated greater prognostic relevance than EGFR subtype, with effects varying by tissue sampling site.

3. Farhat EB et al. High prevalence of TSC2 mutations in lung tissue samples from patients with sporadic lymphangioleiomyomatosis. Eur Respir J. 2026 May 7;67(5):2502321.

Take Home: The findings strongly support the conclusion that *TSC2* mutations are the main pathogenic driver of sporadic LAM.

4. Churg A et al. Glutamine fructose 6-phosphate transaminase-2 as a marker of mesothelial proliferations. Histopathology. 2026 May;88(6):1278-1281.

Take Home: GFPT2 is not useful for separating benign from malignant mesothelial proliferations because it usually produces strong diffuse staining in reactive processes. A further issue is that it variably stains fibroblasts, producing another confounding factor with spindle cell reactions. GFPT2 is useful in separating epithelioid mesotheliomas from adenocarcinomas of lung.

5. Sharma R et al. OA01.05: A Novel Deep Learning Model for Automated Classification of Thymic Epithelial Tumors. Journal of Thoracic Oncology Volume 21, Issue 5, Supplement 1, May 2026, 103744 (abstract supplement, no pubmed ID)

Take Home: The authors report to have produced a deep learning model trained on 119 cases that is able to reliably distinguish thymic epithelial tumor subtypes, with particularly strong performance and identified thymic carcinoma.

6. **Delva F et al. Coexposure to asbestos, mineral wool, crystalline silica and refractory ceramic fibres and risk of lung cancer and mesothelioma. Thorax. 2026 Apr 16;81(5):430-438.**

Take Home: Crystalline silica is not known to induce mesothelioma but coexposure to asbestos could increase the effect of asbestos on the mesothelial cells.

Non neoplastic

1. Gaffney AW et al. Implications of year 1 Trump Administration policies for Americans' lung health. Am J Respir Crit Care Med. 2026 May 1;212(5):900-910.

Take Home: Lung disease is a leading cause of suffering and death. Policies pursued or enacted during the Trump Administration's first year will likely increase pulmonary morbidity and mortality, and widen already growing inequalities in lung health and care. The pulmonary and critical care medicine community should respond vigorously to this crisis.

Reviews, editorial, letters, and case reports

1. Mujcin M et al. Am J Clin Pathol. Primary Paget-like intraepithelial glandular lesion of the bronchus: report of a first case. 2026 May 5;165(5):aqag048.

Take Home: Description of a primary Paget-like intraepithelial glandular neoplasia originating in the bronchial epithelium challenging the existing hypotheses concerning the cellular origin of extramammary Paget disease, which include Toker cells, pluripotent keratinocyte stem cells, and apocrine gland ducts, none of which are native to the bronchial epithelium.

2. **Mukhopadhyay S. et al. Radiation injury to the lung caused by yttrium-90 resin microspheres (SIR-Spheres) diagnosed by transbronchial lung biopsy. Am J Clin Pathol. 2026 May 5;165(5):aqag056.**

Take Home: Case report of 90Y-related radiation lung injury in a patient in whom this diagnosis was not previously suspected.

3. **Goodfellow AM. Et al. Endobronchial cryptococcoma. Am J Respir Crit Care Med. 2026 May 1;212(5):1020-1021.**

Take Home: Case report of an endobronchial cryptococcoma thought to be malignancy.

4. **Rajan S et al. Malignancies that are ILDs. Am J Respir Crit Care Med. 2026 May 1;212(5):1060.**

Take Home: Commentary on all the non-neoplastic diagnoses that may be misinterpreted as malignancy, recommeded adding lepidic pattern predominant adenocarcinoma and lympoma.

5. Johannson KA et al. Response to Rajan et al.: Malignancies that are ILDs. Am J Respir Crit Care Med. 2026 May 1;212(5):1061. doi: 10.1093/ajrccm/aamag057.

Take Home: Rebuttal that lepidic pattern predominant adenocarcinoma and lymphoma should not be categorized as ILDs.

6. Stoler MH and Mills SE. Mark R. Wick, MD. Am J Surg Pathol. 2026 May 1;50(5):467-468.

Take Home: In Memoriam for Dr. Wick.

7. Patel et al. The American Cancer Society National Lung Cancer Roundtable strategic plan: Challenges in clinical guideline recommendations for biomarker testing in lung cancer. Cancer. 2026 May 15;132(10):e70384. doi: 10.1002/cncr.70384.

Take Home: This article reviews the clinical importance of biomarker testing in NSCLC, compares major guidelines, and highlights the challenges and implications of guideline variability in formulating recommendations on biomarker testing for patients with NSCLC.

8. **Wisnivesky JP. Beyond Tobacco: Identifying Lung Cancer Risk Among Individuals Who Have Never Smoked. Chest. 2026 May;169(5):1174-1175.**

Take Home: Lung cancer in individuals who have never smoked represents a distinct and growing public health challenge. Factors including chronic pulmonary diseases characterized by persistent inflammation, such as COPD, pulmonary fibrosis, previous tuberculosis, occupational exposures, environmental exposures, and secondhand smoke exposures as well as family history as an independent risk factor were identified.

9. **Narayan SC. An Unusual Cause of Cavitary Lung Lesions. Chest. 2026 May;169(5):e151-e155.**

Take Home: A case report of Crohns Disease with necrobiotic nodules in the lungs.

10. **Wahab A et al. A 62-Year-Old Woman With Progressive Dyspnea, Interlobular Septal Thickening, and Ground-Glass Opacities. Chest. 2026 May;169(5):e157-e163.**

Take Home: A case report of Erdheim-Chester disease in the lung.

11. **Curioni AV et al. Reading the monocyte code in idiopathic pulmonary fibrosis. Eur Respir J. 2026 May 7;67(5):2600349.**

Take Home: Monocyte signatures may help to improve patient stratification based on various immune profiles.

12. **Snoeck H-W. Advances in our understanding of distal progenitors in idiopathic pulmonary fibrosis: implications for novel therapeutics. Eur Respir J. 2026 May 21;67(5):2502083.**

Take Home: The diversity of genetic and environmental risk factors underlying IPF raises the question whether mechanisms of epithelial dysfunction shared across all etiologies for IPF exist. Deeper understanding of such mechanisms could lead to causative, disease-

modifying treatments, but first requires insight into the identity of the epithelial drivers of IPF. Two schools of thought exist - one focuses on type 2 alveolar epithelial (AT2) cells, the surfactant-producing cells in the alveoli that can also function as alveolar stem cells. The second school of thought sees a contribution of the distal airways to IPF pathogenesis. This article summarises the arguments in favour of each proposition, discusses the limitations of mouse models, which have supported a role for AT2 cells, and argues, based on studies in human lungs and organoid models, that the epithelium of the most distal airway branches, which are absent in rodents, may play a major role in IPF pathogenesis.

13. **Drevet G et al. Moving Beyond Morphology: Toward a Morpho-Molecular Classification of Pleural Mesothelioma. J Thorac Oncol. 2026 May;21(5):103551.**

Take Home: The authors discuss the potential for a new morpho-molecular classification based on molecular findings to overcome the current clinical challenges. Future directions for the field are also proposed, including the potential for emerging technologies such as single-cell, spatial omics, and artificial intelligence to fill in the gaps of bulk studies and unveil clinically relevant information about pleural mesothelioma tumor heterogeneity.

14. **Ardeshir-Larinani F. Challenges and Controversies in the Diagnosis and Management of Thymic Epithelial Tumors from the Thymic Tumor Subcommittee of the International Association for the Study of Lung Cancer Rare Tumors Committee. J Thorac Oncol. 2026 May;21(5):103611.**

Take Home: This review addresses current challenges across the diagnosis, management, and treatment of thymic epithelial tumors (TETs). The authors outline diagnostic difficulties, including distinguishing TETs from histologic mimickers, and highlight the utility of immunohistochemical and molecular markers. Surgical considerations for early-stage disease are explored, debating thymomectomy versus complete thymectomy and optimal minimally invasive approaches, while also discussing the role of lymph node dissection and adjuvant therapy. Furthermore, this review delves into the evolving roles of immunotherapy and targeted therapy in TETs, acknowledging their potential while addressing challenges such as high rates of autoimmune disease recurrence and adverse events. The promising, albeit largely retrospective, applications of artificial intelligence in TETs, spanning diagnosis, target discovery, and prognostic modeling, are also explored as a critical area for future integration into clinical practice.

15. **Fernandez GN. et al. Pulmonary artery angiosarcoma. Thorax. 2026 Apr 16;81(5):495-496.**

Take Home: Pulmonary artery angiosarcoma case report in a 35-year old woman.