PULMONARY PATHOLOGY JOURNAL CLUB
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Non-neoplastic diseases


**Discussion articles**

Kozu Y et al. The usefulness of mutation-specific antibodies in detecting epidermal growth factor receptor mutations and in predicting response to tyrosine kinase inhibitor therapy in lung adenocarcinoma. Lung Cancer 73: 45-50.

- **Purpose:** To evaluate the sensitivity and specificity of two mutation-specific immunohistochemical stains for detecting the presence of the two most common EGFR mutations and to assess response rates to EGFR-TKIs in patients positive by molecular compared to immunohistochemical methods.

- **Methods:** 577 patients undergoing surgical resection regardless of histologic type
  - Used HRMA (high resolution melting analysis) to detect both deletions in exon 19 (DEL) and the L858R point mutation in codon 21 (L858R)
  - Constructed TMAs and stained with monoclonal antibodies against DEL and L858R
    - Scored from 0 (negative) to 3 (reactivity equal to or stronger than positive control) and also gave percentage of positive cells
  - 116 patients received EGFR-TKI therapy—categorized as complete response, partial response, stable disease, and progressive disease

- **Results:**
  - Molecular results: DEL seen in 135 (23%) and L858R in 172 (30%)
  - IHC results: DEL seen in 59 (10%) and L858R in 139 (24%)

<table>
<thead>
<tr>
<th>IHC-based EGFR mutation of DEL</th>
<th>Molecular-based EGFR mutation of DEL</th>
<th>Responder (CR + PR, n = 64)</th>
<th>Non-responder (SD + PD, n = 50)</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>Staining score &gt; 10 (+)</td>
<td>(+)</td>
<td>50</td>
<td>5</td>
<td>0.001</td>
</tr>
<tr>
<td>Staining score &gt; 10 (-)</td>
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<td>32</td>
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<tr>
<td>Sensitivity 42.2% specificity 99.5%</td>
<td>&gt;50% of immunopositive tumor cells</td>
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<tr>
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<td>15</td>
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<td>Immunoexpressive tumor cells &gt;50%</td>
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<td>Immunoexpressive tumor cells &lt;50%</td>
<td>(-)</td>
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- Sensitivity/specificity of DEL IHC was 42.2% and 99.5%
- Sensitivity/specificity of L858R was 75.6% and 97.8%
- Overall sensitivity specificity of IHC was 60.9% and 98.7%

  - TKI response:
    - Of the 77 molecular + patients, 59 (77%) were responders
    - Of the 55 IHC+ patients, 40 (73%) were responders
      - Of the 59 IHC- patients, 24 (41%) were responders

- **Take-home messages:** Overall the sensitivity of mutation specific IHC was not great in this study, especially as compared to some groups’ previously reported sensitivities (from 78-92%)—authors claim this is because their molecular method is more sensitivity than direct sequencing, therefore decreasing sensitivity of IHC. However, seems that looking at the high number of EGFR-TKI responders who were IHC negative would refute that. To screen or not to screen using EGFR IHC?

- **Purpose:** To evaluate the number of lung cancer patients who have lung carcinoma cells present in urine cytology despite having no obvious urinary tract metastases, and to correlate this with clinical and pathologic findings.

- **Methods:** 150 consecutive patients with lung cancer of all histologic types—only inclusion criteria were diagnosis of lung cancer and willingness to provide a urine sample
  - Controls = 15 patients each with metastatic colorectal, breast, and non-Hodgkin lymphoma
  - Obtained urine samples from 3 consecutive days, which were evaluated using Thin-Prep
    - Positive samples were stained for CK7, CK20, and TTF-1 if possible
  - Chemokine profile of original tumor sample
  - All patients underwent detailed imaging of the abdomen and pelvis…and 4 patients agreed to undergo cystoscopy with biopsy
  - Also prepared an animal model by injecting mice with a cancer cell line subq, then taking urine samples and sacrificing the animals to examine their GU tracts

- **Results:** 102 male : 48 female, median age 63 yrs (range 29-84 yrs)
  - 38 patients were stage I-III, 84 were metastatic/stage IV
  - 122 NSCLC and 28 SCLC
  - Atypical urothelial cells present in 60 (40%)  
    - Of NSCLC: positive urine cytology in 13 (11%)—stains + for lung markers in all of those that could be stained, the remainder were morphologically identical to original lung tumor
    - All patients had metastatic/stage IV disease; no + urine cytology in any stage I-III patients
    - 5 adenoca, 5 SqCC, 2 “undifferentiated”, 1 non-classifiable
    - Of SCLC: positive urine cytology in 2 (7%)  
    - All had negative imaging exams—no macroscopic metastases
  - + urine cytology correlated to stage IV disease and high tumor burden, but did not correlate to chemo response or prognosis
  - Cases with positive urine cytology correlated with expression of chemokines CXCR4 and CCL21 in original tumor
  - In the mouse model, tumor cells were found in urine samples, but not in the tissue taken from sacrificed animals
  - No positive urines in the control population

- **Take-home points:** It seems that lung cancer may show some sort of “tropism” to the urothelium, although the mechanism of how cells get into urine without showing up in tissue is unknown—structural damage to renal tubules? Disruption of capillary/glomerular barrier? Cytokine driven? How many of these patients would have had positive bladder biopsies (if they had agreed to undergo cystoscopy)? Either way, it does not seem to correlate with prognosis or response to therapy, therefore unlikely to come into clinical use as any sort of diagnostic test.
Sakai Y et al. Significance of microscopic invasion into hilar peribronchovascular soft tissue in resection specimens of primary non-small cell lung cancer. Lung Cancer, 73: 89-95

- **Purpose:** To correlate the characteristics and prognostic significance of microscopic invasion into peribronchovascular soft tissue (referred to as SHEATH) as well as the significance of a positive margin of resection in the SHEATH tissue.

- **Methods:** 592 consecutive patients undergoing lobectomy, sleeve lobectomy, or pneumonectomy without preoperative chemo/radiation (excluded BAC/AIS, salivary gland tumors, carcinoids, and small cell)
  - All specimens insuflated, submitted for “routine histologic examination”—not detailed how extensive hilar/mediastinal sampling was
  - SHEATH involvement defined as microscopic invasion into hilar peribronchovascular soft tissue either at the mediastinal side across the lung along the lung surface around hilum, outside the outer rim of bronchial cartilage, or inside the mesopneumonperitoneum

- **Results:** Among all patients, SqCC associated more often with male gender, central location, larger operations; no TNM stage difference between SqCC and non-SqCC
  - SHEATH+ tumors were more likely to be central, to have N1-3 nodal disease, to have vascular invasion, and to be more advanced TNM stage
    - No association with histologic type
  - In multivariate analysis, age, gender, lobe, histology, lymphatic invasion, and TNM stage were associated with prognosis; SHEATH+ was NOT
• **Take-home points:** Paper included in its discussion comments on bronchial margin positivity in SHEATH positive tumors, however this data was not presented in the results section. However, they do suggest that since SHEATH positive tumors are associated with nodal disease and lymphovascular invasion, frozen sections of the bronchial margins may not be indicated in those cases. Also, as SHEATH+ tumors are not associated with worse prognosis, the TNM staging should not need to be changed.

- **Purpose:** To evaluate the significance of histology as a predictor of recurrence after resection in patients with early stage non-small cell lung cancer.

- **Methods:** 1,870 consecutive patients in stage I and II with adenocarcinoma or squamous cell carcinoma (SCC) who underwent complete tumor resection with systematic lymph node dissection between August 1992 and December 2007 were included. Clinicopathologic information was obtained for each of the study subjects. Additionally, pathologic evaluation was conducted and numerous parameters were measured. Included parameters included histology subtype based on World Health Organization (WHO) criteria. Other measured parameters were lymphatic invasion, intravascular tumoral invasion, visceral pleural invasion. Pathologic staging was conducted based on TNM classification of the International Union Against Cancer. There were 1,415 patients with adenocarcinoma and 455 with SCC.

- **Results:** See below

- Recurrence-free probability curves according to histology in each stage. A, Recurrence-free probability curves in stage IA. B, Recurrence-free probability curves in stage IB. C, Recurrence-free probability curves in stage II.

- Overall survival rate and recurrence-free probability of patients with SCC were significantly lower than those of patients with adenocarcinoma among patients with stage IA tumors. In stage II, significantly lower recurrence-free probability was observed in adenocarcinoma, whereas no significant difference was observed in overall survival rate.

- The best measure is recurrence free probability. Other measures were studied including survival. However, those with SCC may have many other smoking related co-morbidities, which may affect survival.
Conclusions: When stratified by substage, histology showed a different impact on postoperative recurrence. Recurrence-free probability is significantly lower for SCC in stage IA. Recurrence-free probability is significantly lower for adenocarcinoma in stage II.
Articles for notation

Neoplastic diseases

- Purpose: Case study of a gentleman with ALK (Anaplastic lymphoma kinase) positive adenocarcinoma of the lung. Findings included multiple lung nodules and masses of enlarged subcarinal and paraesophageal lymph nodes. ALK positive tumors are more commonly seen in light or never smokers with a median age of presentation of 50. There are nice figures showing the FISH for ALK as well as signet ring morphology described in these tumors. There is then further discussion on typical presentation and available novel therapies. Overall a very nice review of one of the most up-and-coming topics in lung neoplasia.

- Purpose: To assess the diagnostic accuracy of classification of lung adenocarcinoma and SCC on small cytologic and biopsy specimens based on cytomorphologic studies alone or in combination with ancillary studies.
- Methods: 448 diagnostic preoperative cytologic specimens including transthoracic CT guided FNA specimens, bronchial brushings, and bronchial washings of primary lung adenocarcinomas (263 cases) and SCC (185 cases) from patients who later underwent surgical resection of the tumors were included in the study. Histologic diagnoses based on the cytologic specimens were compared with those of the corresponding surgical resection specimens. A variety of immunohistochemical and histochemical markers were studied.
- Results: Of 263 adenocarcinomas, the cytologic diagnosis was made on cytomorphology alone in 107 cases (40.7%). Of 185 SCC’s the cytologic diagnosis was made based on cytomorphology alone in 139 cases (75.1%). Use of immunohistochemical/histochemical studies significantly reduced the number of adenocarcinomas classified as NSCLC. Immunohistochemical studies did not increase the diagnostic accuracy of SCC. A significant improvement in diagnostic accuracy was made with adenocarcinoma.
- Conclusion: Use of immunohistochemical studies on cytologic cell blocks may improve classification of NSCLC. (Of note—we’ve had great success here at U of M performing immuns on direct smears, no need to wait for cell blocks or risk not having a good cell block)

- Purpose: Here the authors review drug induced pulmonary toxicity (DIPT) related to treatment for non-small cell lung cancer. The review is comprehensive and covers quite well the range of clinical, radiographic and histologic findings that may be encountered in these conditions. Although, the review does not focus on histology, it does describe potential findings in a nicely configured table. Histology of DIPT can encompass a very wide range of appearances. In this review they are described as NSIP-like, AIP-like, HP-like, BOOP-like, alveolar hemorrhage and noncardiogenic pulmonary edema. This is merely a descriptive table and does not include all potential appearances. A range of potential anti-neoplastic
agents are described and includes everything from platinum agents up to and including newer tyrosine kinase inhibitors and bevacizumab.


- **Purpose:** To study the clinicopathologic features of pulmonary adenocarcinomas with a high proportion of goblet cells.
- **Methods:** A series of 2228 surgically resected lung adenocarcinomas were reviewed. Tumors were considered “primary lung adenocarcinoma composed predominantly of goblet cells (APGC)” if they had >90% goblet cells present.
- **Results:** A total of 46 (2.1%) cases met criteria for APGC
  - No male/female predominance, median age 65 years (range 40-84 yrs)
  - Low pathologic stage (most stage I), low association with pleural invasion, lymphatic invasion, stromal invasion, and lymph node metastases.
  - Two local recurrences and one death due to disease in these cases.
- **Take-home points:** Sounds like they are describing mucinous BAC/AIS, so I think a lot of this data is already known regarding BAC/AIS. The authors maintain that this is a separate entity, but personally I’m not quite sure how.

Wilbertz T et al. SOX2 gene amplification and protein overexpression are associated with better outcome in squamous lung cancer. Mod Pathol; 24: 944-953.

- **Purpose:** To assess the amplification of the SOX2 gene in lung squamous and adenocarcinoma and to correlate this with expression (as measured through immunohistochemistry) and clinicopathologic data.
- **Methods:** Two cohorts were studied—one from Zurich and one from New York—totalling 891 patients. Tissue microarrays were created from these tumors, which were then assessed for SOX2 amplification via FISH and overexpression via immunohistochemistry. In the FISH portion, low-level amplification was defined as 2-9 SOX2 target signals per reference signal in at least 30% of cells; high-level amplification was >10 SOX signals per reference. IHC was assessed quantitatively using image analysis software.
- **Results:** Overall, 8% of SCC showed high-level overexpression, 65-68% showed low-level, and 24-27% showed no overexpression. In adenocarcinomas, 6% showed low-level overexpression, and 94-95% showed no overexpression. High amplification was associated with lower tumor grad. Smaller tumors and tumors with low T stage showed higher SOX2 amplification; increased expression was also associated with lower stage, lack of angiolymphatic invasion, and lack of metastases. High-level overexpression was associated with better survival, though in Cox regression models considering all prognostic factors, neither amplification nor overexpression was an independent prognostic indicator.
- **Take-home points:** SOX2 gene amplification may be a marker for biologic behavior within squamous cell carcinomas, with higher levels associated with better prognostic indicators in squamous cell carcinoma. However, it is rarely expressed in adenocarcinoma.

**Purpose:** To evaluate the use of an immunohistochemical stain, LC3A, which is associated with autophagocytosis in tumor cells, as a prognostic marker in lung carcinomas.

**Methods:** 115 tumors (64 SCC, 24 adca, 18 large cell, 9 “other”) analyzed.
- Stained with LC3A antibody, with pattern of staining and percentage of stained cells analyzed
- Tumors with >70th percentile staining were considered “high”
- “SLS” counts = stone-like structures—a structure surrounded by staining within cytoplasm

**Results:** 23/115 had high cytoplasmic staining; 34/115 had high juxtaglomerular staining—no important prognostic associations with staining pattern (though high juxtaglomerular associated with large cell and poor differentiation)
- High SLS associated with SCC, tumor necrosis
- SLS count strongest predictor of death

**Take-home points:** Counts of SLS, a particular staining pattern of LC3A, is associated with things that are considered poor prognostic indicators (such as poor differentiation).


**Purpose:** To correlate the expression of a particular microRNA (miR-126—promotes angiogenesis) with outcomes in lung carcinoma and with vascular endothelial growth factor (VEGF) expression

**Methods:** 371 patients—all histologic subtypes—made into TMAs; miR-126 analyzed through FISH; VEGF analyzed through immunohistochemistry
- Images taken with a digital imaging system, then analyzed manually for cytoplasmic staining (0 = negative; 1 = weak; 2 = intermediate; 3 = strong)

**Results:** miR-126 expressed in most neoplastic tumor cells, also in some surrounding normal tissue
- No significant association with miR-126 and any clinicopathologic variable except for histology (more associated with SCC and large cell)
- Weak correlation between miR-126 and VEGF expression
- In SCC but not adca, high miR-126 expression was a poor prognostic indicator
- In node positive pts but not node negative, high miR-126 expression was a poor prognostic indicator
- miR-126 was an independent prognostic factor

**Take-home points:** High miR-126 expression is an independent negative prognostic indicator in lung carcinoma—especially in squamous cell carcinoma and node positive patients. Coexpression of VEGF and miR-126 also a strong negative prognostic indicator.


**Purpose:** Case series reporting thymic carcinomas associated with multilocular thymic cysts.

**Methods:** The authors reviewed their series of 57 primary thymic carcinomas to identify cases associated with multilocular thymic cysts (MTC). They also performed several immunohistochemical stains (panCK, CK5/6, CK7, p63, TTF-1, CD5), although these results were not reported in the results section.
• **Results:** The authors identified 7 thymic carcinomas associated with MTCs, representing 12% of their thymic carcinomas. Four were grossly solid with a cystic component, three were solid only. Histologically, four were squamous cell carcinomas, and one each were sarcomatoid carcinoma, papillary carcinoma, and basaloid carcinoma. All were lobulated with a sclerotic stromal background. Two were classified as combined thymoma/thymic carcinomas. All cases, even those that were grossly solid, showed typical features of MTC.

• **Take-home message:** These cases expand the histologic spectrum of thymic carcinoma which has been associated with MTC to include sarcomatoid and papillary carcinomas. These may represent either malignant degeneration of the cyst lining or a cystic change as a hyperplastic response to tumor. In this series, tumors associated with MTC may be more common than previously recognized, and these patients had a better outcome than thymic carcinomas not associated with MTC.

Hashimoto K et al. Tumor-to-tumor metastasis: lung adenocarcinoma metastasizing to a follicular variant of papillary thyroid carcinoma. Path International; 61:435-441.

• **Purpose:** An interesting case report of a difficult process to diagnose—one tumor metastasizing to another (lung adenocarcinoma to a papillary thyroid carcinoma (FVPTC) in this case).

• **Case/results:** A 60-year-old woman presents with a thyroid nodule as well as multiple lung nodules. The thyroid nodule showed both FVPTC as well as a poorly differentiated component, which was histologically identical to one of the lung masses as sampled by tbbx. Both components were positive for TTF-1, CK7, and CK19; thyroglobulin was only positive in the FVPTC component and CEA only in the adenoc. An EGFR mutation was found in the adeno component not the FVPTC, serving both as a basis for therapy and a useful diagnostic tool (EGFR mutations being rare in FVPTC).

• **Take-home points:** Tumor-to-tumor metastases can present an interesting diagnostic difficulty—especially with tumors that have overlapping immunohistochemical features (ie TTF-1 staining). Molecular testing can be a useful adjunct in sorting out which came first.


• **Purpose:** Case report of an 85-year-old man presenting with right shoulder pain. Imaging showed only pleural effusions, without pleural thickening or masses. Biopsy showed epithelioid hemangioendothelioma (EHE); the patient later developed extensive pleural thickening and died.

• **Take-home message:** Nice review of some of the clinical and pathologic features of EHE (despite horrifying grammar and spelling in the paper). Important to note that EHE can occur in older individuals, grossly it often forms pleural plaques that can extend through fissures and interlobular septae. Also has a good microscopic description, including immunostaining profiles of reported cases. Patients have a poor prognosis, as this patient did.


• **Purpose:** Case report of a 72-year-old woman presenting with hemopsysis, chest pain, found to have multiple bilateral nodules surrounded by ground glass opacities. Biopsy demonstrated
epithelioid angiosarcoma. The patient had no evidence of primary disease elsewhere, therefore she was considered to have primary pulmonary angiosarcoma (PPA).

- **Take-home message:** Nice review of the histologic features, radiographic features, and clinical presentation of angiosarcomas in the lung. PPA arises from arterial or venous pulmonary vessels, and as such symptoms are usually related to vascular injury. Pleural effusion is also a common presenting symptom (seen in ¼ of reported cases). Radiographically, CT often shows central areas of soft tissue surrounded by a halo of ground glass, representing bleeding into surrounding alveolar parenchyma. Important to note, there are no histologic features that can help in the determination of primary versus metastatic angiosarcoma, and the diagnosis of PPA requires the exclusion of a primary tumor elsewhere. As this is such an uncommon primary tumor in the lung, the paper provides a nice chart comparing and contrasting features of PPA versus metastatic angiosarcoma.


- **Purpose:** An overview of currently published cases of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH), including the addition of one case previously not reported in the literature.
- **Methods/results:** Literature search found a total of 25 reported cases (including the previously unreported case).
  - Female predominance (92% women); mean age 58 years (range 36-76 yrs)
  - Most patients have symptoms—including cough, wheezing, and dyspnea
  - PFT’s = most often obstructive defects
  - 68% have associated tumorlets; 40% have associated carcinoids
  - No deaths due to pulmonary complications; two patients experienced clinical decline, including one who required lung transplant
  - Histology = neuroendocrine proliferation within epithelium of large and small airways; can also be associated with constrictive bronchiolitis
- **Take-home points:** An excellent review of the clinical and pathologic features of DIPNECH, which may in fact represent a preneoplastic condition. It has a good prognosis, without any deaths due to disease reported. Currently, the only therapies available are steroids (oral and inhaled), bronchodilators, or transplant in one reported case, although decline in function is rare.


- **Purpose:** Discusses the major genetic and epigenetic changes in lung carcinoma. Many areas are explored and includes loss of heterozygosity (LOH). Additionally, discussion focused on p53 mutations with note that mutations are more commonly seen in smokers. Studies have tried to predict survival with p53 status, but there is controversy within the literature on this topic. A lengthy discussion is present for EGFR. The most common mutations are those involving exon 19 and a point mutation of exon 21 (L858R). EGFR mutations are more commonly seen in adenocarcinomas and those of Asian descent, women, and never or light smokers. There is further discussion of therapy and the role of tyrosine kinase inhibitors with EGFR mutations. A large segment of the paper is also dedicated to the
role of k-ras. k-ras is involved in cellular proliferation with transduction of signals across cellular membranes. Unlike EGFR mutations, most k-ras mutations occur in smokers. It is important to note that mutations in k-ras and EGFR are mutually exclusive. The anaplastic lymphoma kinase (ALK) gene has been found to be rearranged with EML4, with a noted EML4-ALK fusion. This may effect areas of cell survival and transformation. Molecular therapies are available for ALK mutations. ALK mutation is known to be mutually exclusive with k-ras and EGFR mutations. Discussion of epigenetic changes included methylation, which influences gene regulation. Also discussed is histone modification and microRNAs. These may serve as potential therapeutic targets in lung cancer.


- **Purpose:** A trio of correspondances related to the specificity of TTF-1 staining in various tumors. The first two are regarding an article published in April regarding the finding of TTF-1 positivity in some gynecologic malignancies, and its association with better outcomes. The point was raised that this could be nonspecific staining due to antigen retrieval techniques; however, original authors also responded by testing their TTF-1 positive tumors for TTF-1 mRNA, which was present. The third correspondence reports three cases of TTF-1 positive invasive ductal breast carcinomas, which has also previously been reported.

- **Take-home message:** TTF-1 should be used with caution in determining site of origin for a tumor, however, I think this is something we all already practice. And it’s probably only a matter of time before these sorts of papers demonstrate napsin A staining in every other organ system as well.


- **Purpose:** A letter to the editor regarding the diagnosis of so-called fetal lung interstitial tumor (FLIT), previously reported in an earlier paper, which the authors of the letter maintain may represent a cystic pleuropulmonary blastoma—which must be ruled out with FISH testing. The response from the original authors suggests that this may just be a case of FLIT that happened to have trisomy 8.

- **Take-home message:** Hopefully both of these entities are exceedingly rare, and I never have to diagnose one. However, if I do, I should get FISH testing to make sure I know which one it is.

**Non-neoplastic diseases**


- **Purpose:** A descriptive case series of 80 soldiers from Kentucky with inhalational exposures during service that were evaluated for dyspnea on exertion.
Methods: The soldiers underwent extensive evaluation including clinical, radiologic and physiologic studies. Additionally, 49 of the 80 underwent thoracoscopic lung biopsy. Each of the lung biopsies was reviewed by two lung pathologists. Data obtained from the soldiers was compared to historical military control subjects.

Results: Of the 49 soldiers who underwent lung biopsy, 38 were diagnostic of constrictive bronchiolitis. In the other 11 cases, diagnoses that could explain the dyspnea were established. Table from article lists the entirety of pathologic findings. Of note, 37 of the 38 constrictive bronchiolitis specimens demonstrated deposition of grayish-black peribronchiolar pigment, with 36 showing polarizable material within the pigment.

Conclusion: A high prevalence of constrictive bronchiolitis was found in 80 evaluated soldiers. Constrictive bronchiolitis should be considered among returning veterans who report exercise limitations.


Purpose: An overall review of lung transplantation in its current state. This paper goes over many useful aspects of lung transplantation, including indications for transplant, contraindications to transplantation, methods of listing patients, allocation of available lungs, donor standards, and complications/outcomes of transplantation (including infection, rejection, and graft dysfunction).

Take-home message: This is an excellent review if you need a good overview of most aspects of lung transplantation. Although it does not address the histology of the ISHLT rejection grading system, there is a ton of good information about outcomes that could come in very handy.


Purpose: This article reviews current developments in Alveolar Capillary Dysplasia with misalignment of the pulmonary veins (ACD/MPV). This is a rare, lethal, neonatal developmental lung disorder. The initial clinical presentation is often that of hypoxemia with pulmonary hypertension. Histologic evaluation is the current gold standard for diagnosis. Histologic features may include immature lobular development, decreased number of pulmonary capillaries located away from the alveolar epithelium, thickened alveolar septae, medial hypertrophy of small pulmonary arteries and muscularization of distal arterioles, malposition of pulmonary vein branches adjacent to pulmonary arteries (same adventitial sheath) and lymphangiectasis (30%). The diagnosis may be missed by pathologists unfamiliar with the disorder. Additionally, the FOXF1 gene has been identified as being responsible for ACD/MPV in 40% of cases. Other genes and potential causes are being investigated.


Purpose: To assess quality of life in patients undergoing screening images for lung cancer—which will probably become more important as new screening recommendations are released

Methods: Quality of life questionnaires generic quality of life, anxiety, and lung cancer-specific distress were given to a sample taken from 1466 patients undergoing screening CT.
Questionnaires were given before scan, 2 months following first scan, and 2 years after scan. The possible outcomes from CT were:
  o Positive
  o Negative
  o Indeterminate

- **Results:** No statistically significant differences in quality of life were found, even in patients who received an indeterminate result and had to undergo additional screening.
- **Take-home points:** Even indeterminate radiology results don’t seem to negatively impact quality of life or anxiety levels—at least in the Dutch (I wonder what results here would show). Nothing was studied regarding cost of medical care, however.