Basics of diagnosis in respiratory disease -Bronchoscopy-

Division of Pulmonology, Department of Internal Medicine,
INJE Haeundae Paik Hospital

Jin-han Park

Contents

BTS: **British Thoracic Society** guideline for diagnostic flexible bronchoscopy in adults 2013

JICS: Guidelines for Diagnostic Flexible Bronchoscopy in Adults: **Joint Indian Chest Society**/National College of Chest Physicians (I)/Indian Association for Bronchology Recommendations 2019

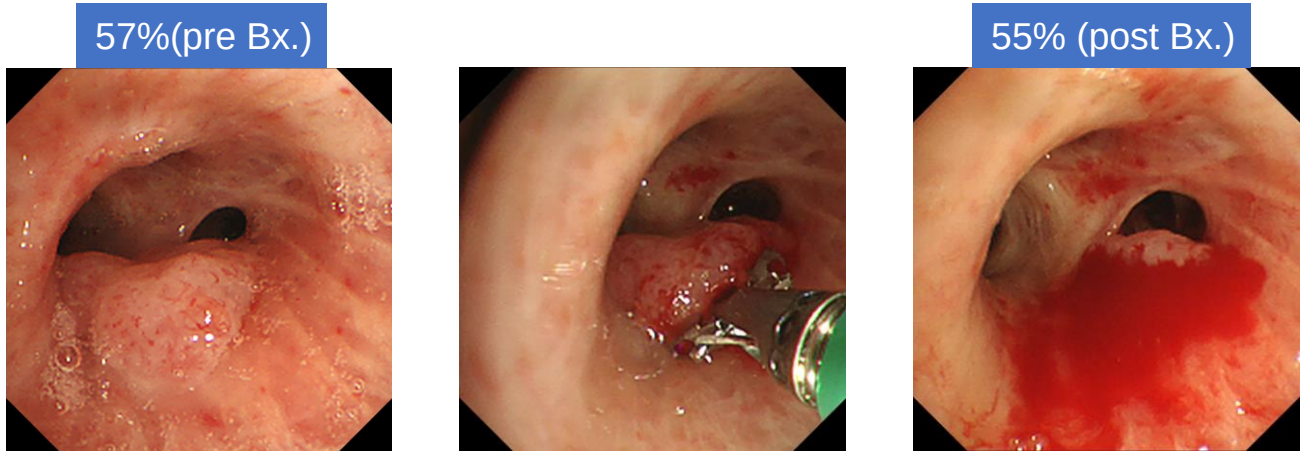
ATS : An Official **American Thoracic Society** Clinical Practice Guideline: The Clinical Utility of Bronchoalveolar Lavage Cellular Analysis in Interstitial Lung Disease 2012

Technical aspect

Bronchial washing(BW)
Bronchoalveolar lavage(BAL)

Bronchial washing

- Secretions are aspirated from **large airways** directly or following the instillation of 5 to 50 mL saline
  - 5-15ml for basic microbiology
  - 10ml for cytology
- High potential for **respiratory flora contamination**



- Lidocaine < 3ml prior to collection will **reduce bactericidal effect**
- **Before biopsy** to avoid RBCs obscure cytologic interpretation Diagnostic yield

Bronchoalveolar lavage (BAL)

- Secretions(Cellular and acellular components) that coat the **distal bronchioles and alveolar epithelium**
  - Less microbial contamination from the upper aero-digestive tract
  - 100 mL samples approximately one million alveoli (1.5 to 3% of the lung)

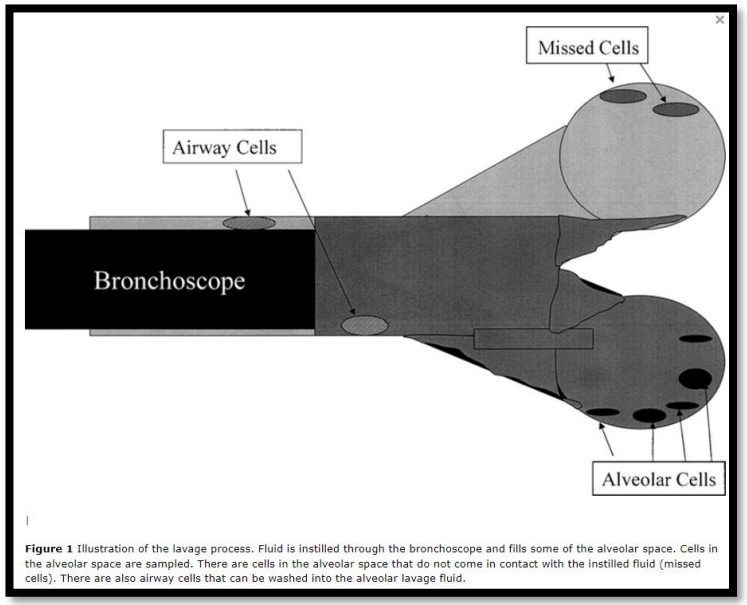


Figure 1 Illustration of the lavage process. Fluid is instilled through the bronchoscope and fills some of the alveolar space. Cells in the alveolar space are sampled. There are cells in the alveolar space that do not come in contact with the instilled fluid (missed cells). There are also airway cells that can be washed into the alveolar lavage fluid.

- Analysis details
  - Cell counting and differentiation
  - Microbiologic analysis (opportunistic infections in immunocompromised hosts)
  - Cytologic analysis

- Usefulness of BAL cell profiles
  - BAL analysis is seldom diagnostic, ongoing **debate** and **controversy** because its findings are hampered by **poor sensitivity and specificity**
  - May provide strong **support** or clues for a diagnosis or help narrow the **differential diagnosis**

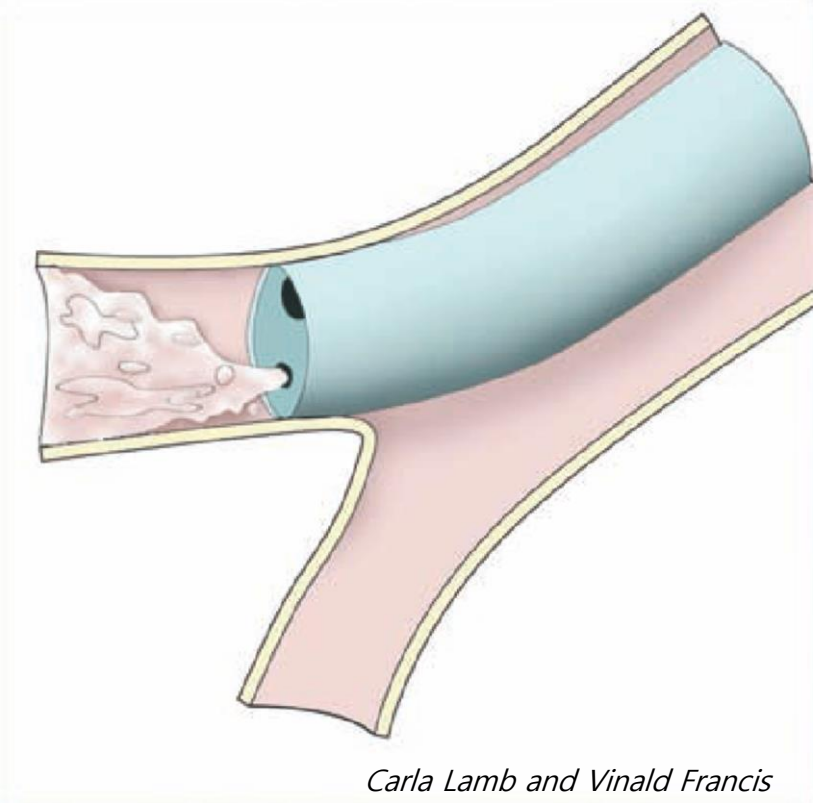
Semin Respir Crit Care Med 2007; 28(5): 475-485 J Thorac Dis. 2020 Sep; 12(9): 4991-5019

Technique of BAL

- Wedge position in the 3rd to 4th ,subsegmental bronchi
  - Snug wedge position, Saline instilled does not escape
  - Not advancing too far in order to avoid trauma to the bronchial mucosa
  - Leakage of lavage fluid →leading to cough
  - Slight airway collapse when gentle suction

- BAL is planned for cellular analysis, it should be the **1st procedure**
  - Prior to BW, brush and biopsy

    → not to obscure the cellular contents with trauma-induced RBCs
  - Avoid suctioning while passing central airway prior to BAL
  - Flushing sterile saline prior to specimen collection
  - Lidocaine (<3ml) in the working channel



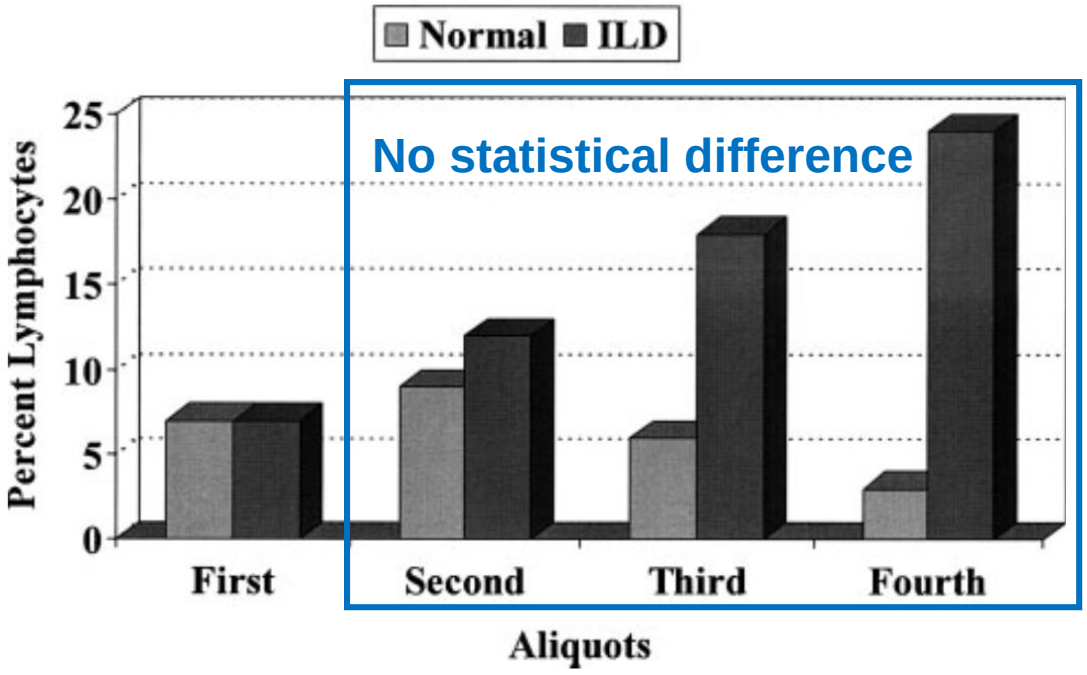
Carla Lamb and Vinald Francis

Technique of BAL, details

	JICS 2019	ATS 2012
Instilled volume	≥100ml, <200ml	≥100ml, ≤300ml
Optimal sampling retrieves	≥ 10%	≥30% (minimal ≥ 5%)
BAL cell differential counts (cellular analysis)		minimal volume of 5 ml, optimal volume is 10–20 ml
HRCT	Prior to BAL	within 6 weeks prior to BAL
Optimal site (difuse)	**RML, lingular** (PCP or CMV with Diffuse lung involvement, bilaterally , >one lobe, including upper lobe, *Baughman R chest 1993, 1994*)	**RML, lingular** (Supine, the anatomy favors maximal recovery of fluid and cells from these sites)
Optimal site (focal/patchy)	**GGO**, tree-in-bud lesions, or focal consolidation is associated with higher diagnostic yield	Alveolar **GGO**, more prominent nodular profusion , fine reticulation
Suction	Manual suction or wall suction, Less than 100 mmHg (Tubing should be added to the handheld syringe)	Retrieved using a negative suction pressure less than 100 mmHg
Platelet	Minimal 20,000/mm3 <20,000 per mm^3 if clinically indicated	
Anti-coagulation	can be performed	

50 mL syringes obtains more fluid with less oxygen desaturation > 20 ml syringe (n=30, *J Bronchol 1995;2:107–12*)

Instilled volume ≥100ml



- Percent lymphocytes is significantly higher after the 2nd aliquot (a total of 120 ml)

- First 20 mL aliquot contain more epithelial cells and lactoferrin (airway secretions)

→ “bronchial” lavage ???

→ Small volume returns

→ Not necessarily true BAL samples

Semin Respir Crit Care Med 2007; 28(5): 475-485

Instilled volume 100ml vs. 250ml

J Appl Physiol (1985). 1989 Oct;67(4):1443-6. doi: 10.1152/jappl.1989.67.4.1443.

Bronchoalveolar lavage in interstitial lung disease: effect of volume of fluid infused

R A Helmers [1], C S Dayton, C Floerchinger, G W Hunninghake

Affiliations + expand

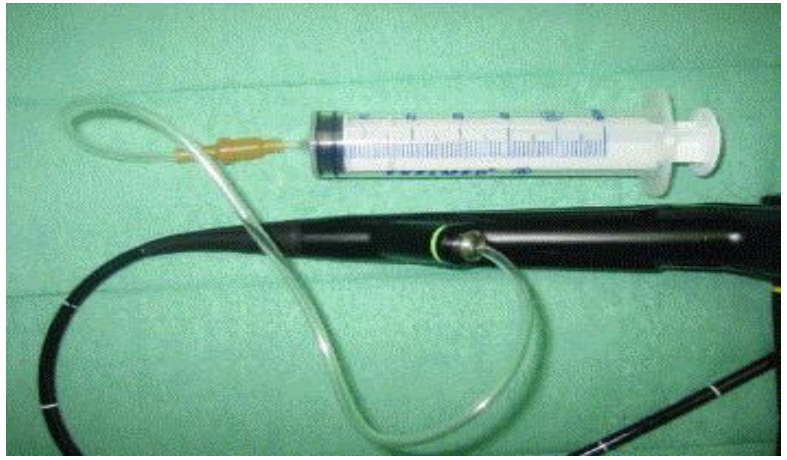
PMID: 2793747 DOI: 10.1152/jappl.1989.67.4.1443

100-300ml

Abstract

To evaluate the effect of varying infusate volume on the results of bronchoalveolar lavage (BAL) in patients with interstitial lung disease, 55 patients underwent 58 BAL during which both a 100- and 250-ml lavage was performed in the same lobe of the lung. Although the percent of the fluid that was returned and the total numbers of cells were greater in the 250- vs. the 100-ml lavage, there were no significant differences in cell differentials or numbers of cells per milliliter between the 100- and 250-ml BAL. We conclude that infusate volume does not affect cell differentials or numbers of cells per milliliter of bronchoalveolar lavage fluid in patients with interstitial lung disease.

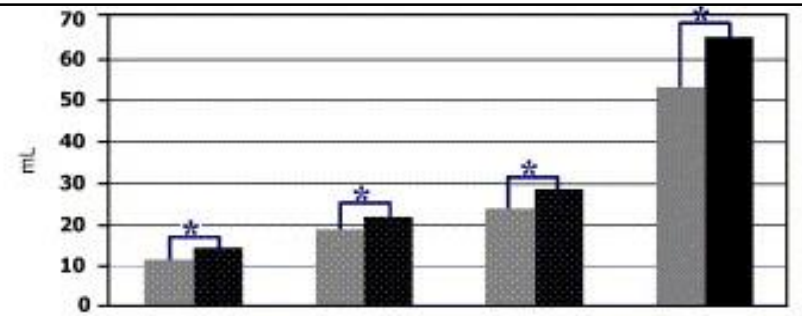
Tubing suction



Attaching a plastic tube

between the syringe and the working channel

35.2% without tubing and **43.2%** with tubing



50 mL syringe	1st syringe	2nd syringe	3th syringe	TOTAL (150 mL)
WITHOUT tubing	11.1 mL	18.2 mL	23.5 mL	52.8 mL
WITH tubing	13.9 mL	21.4 mL	28.2 mL	64.8 mL

Table 2 Diagnoses and complications.

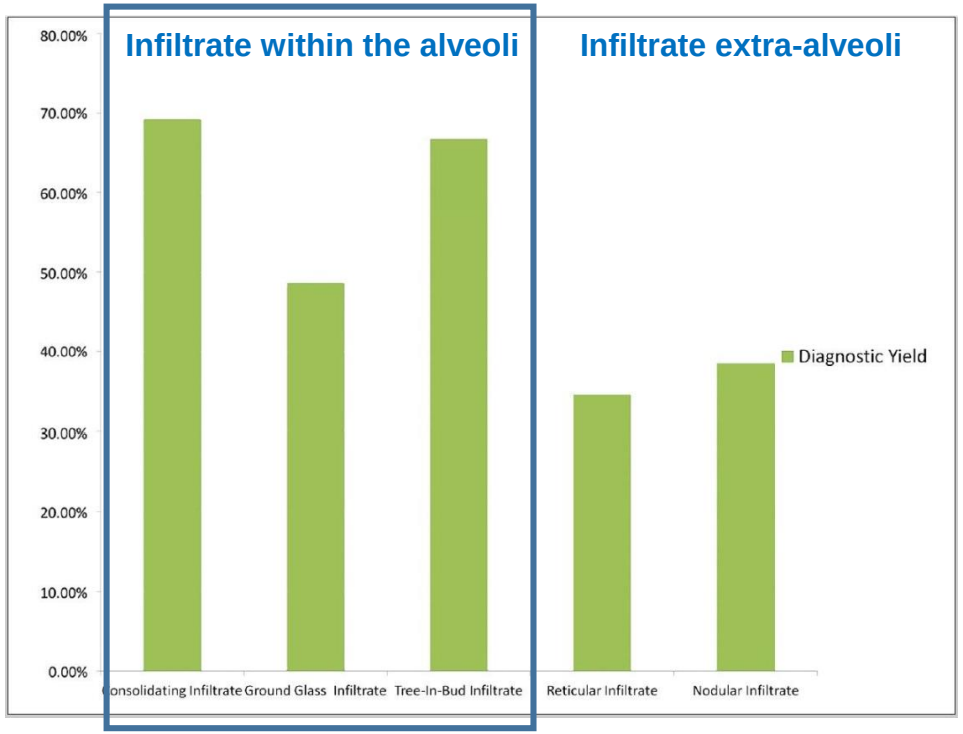
	Without tubing $n = 155$	With tubing $n = 140$	P
Diagnoses			
Tuberculosis	8 (5.2%)	12 (8.5%)	
Pneumonia *(viral, Pseudomonas aeruginosa)*	4 (2.6%)	3 (2.1%)	
Pneumocystis carinii pneumonia	13 (8.3%)	8 (5.7%)	
Pulmonary hemorrhage	1 (0.6%)	4 (2.8%)	
Aspergillosis	2 (1.2%)	1 (0.7%)	
Adenocarcinoma	4 (2.6%)	3 (2.1%)	
Other	0	2 (1.4%)	
Alveolitis	33 (21.3%)	50 (35.7%)	
TOTAL	65 (41.9%)	83 (59.3%)	0.002
Complications			
Acute respiratory failure	1 (0.6%)	0	
Bleeding (>30 mL)	1 (0.6%)	0	
Bronchospasm	1 (0.6%)	0	
Dizziness and nausea	1 (0.6%)	0	
Hypertension and diplopia	0	1 (0.7%)	
Oxygen desaturation (<90%)	9 (5.8%)	1 (0.7%)	
TOTAL	13 (8.3%)	2 (1.4%)	0.02

Other included 1 metastasis of breast cancer and 1 eosinophilic granuloma.
Alveolitis was defined as any abnormal population cell count (lymphocytes ⩾15%, neutrophils ⩾5%, eosinophils ⩾2%) without a specific diagnoses.

Respiratory Medicine (2006) 100, 529–535

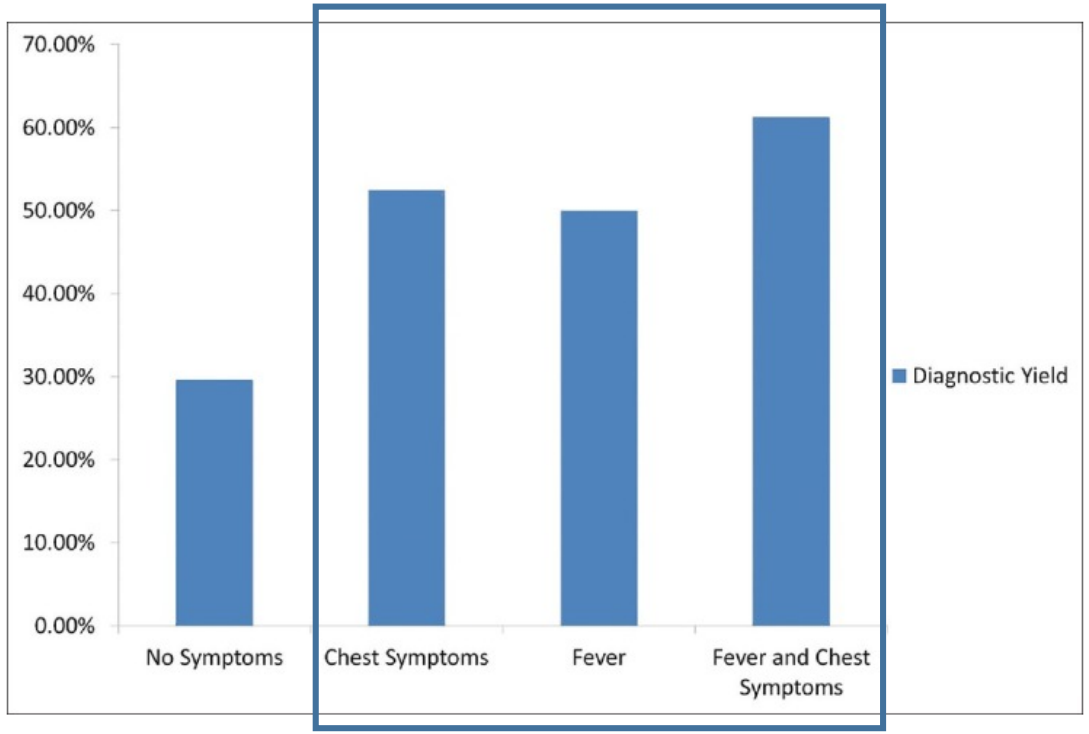
Optimal site - immunocompromised patients

Consolidation/ GGO/ tree-in bud vs. reticular/ nodular



61.2% vs. 36.5% , *P* = 0.0058

- N=133 (female 57, male 76)



61.3% vs. 29.6%, *P* = 0.0066

Ann Thorac Med. 2013;8(3):153

Lavage fluid recovery

- Increases with larger volumes instilled
- Decreases with increasing **age, smoking history or COPD** (Healthy nonsmokers 50-80%, smoker 20-30%)
- First aliquot (<20 percent) vs. **subsequent aliquots (40-70%)**
- Terminated if the **instilled volume exceeds recovery > 100 mL** or patient distress (eg, excessive coughing) or falling oxygen saturation

- Storage of Fluid
  - Minimize delay between BAL fluid retrieval and delivery to the laboratory (<1 hour)
  - Cells stored at 4℃ can be analyzed up to 24 hours after the procedure (without significant changes in the count and differentials)
  - Delivery time > 1 hour, specimens should be centrifuged and then re-suspended in a nutrient-supplemented medium

Clin Respir J. 2022 Feb; 16(2): 142–151.

Potential complications of BAL

- Fever (2%)
- Pneumonitis (0.4%)
- Pneumonia
- Hypoxemia
- Repiratory failure
- Hemorrhage (0.7%)
- Bronchospasm (0.7%)
- Rarely pneumothorax

- >200ml are associated with
  - Higher rates of adverse events

    (fever, hypoxemia, cough, and dyspnea) (JCTO)

- Safely performed in acutely ill patients (e.g.,ARDS) (ATS)

- Rarely been reported to precipitate AE or progression of ILD (ATS)

Analysis

Bronchoalveolar lavage

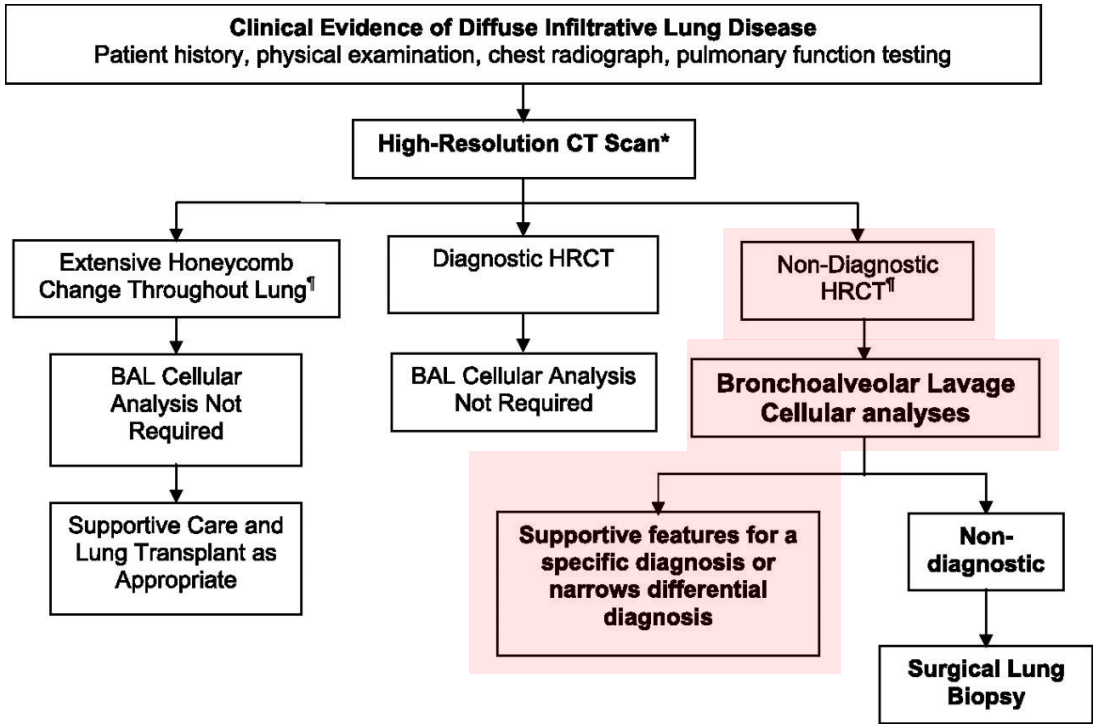
1.Cell counting and differentiation

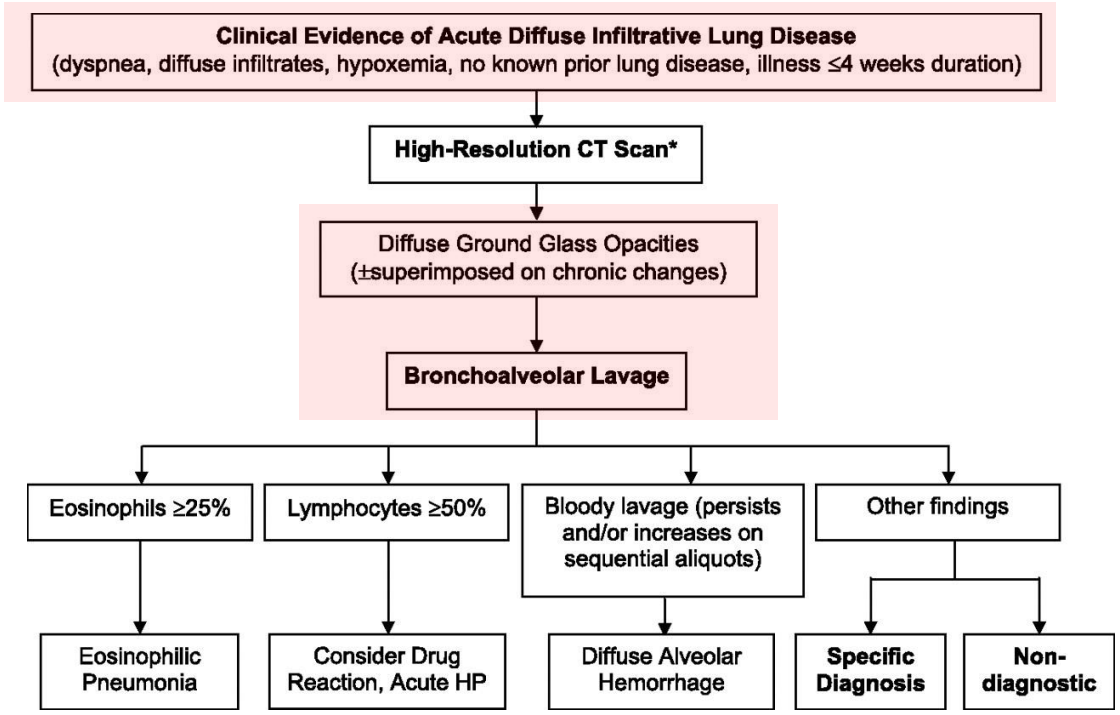
2.Microbiologic analysis

3.Cytologic analysis

Cell counting and differentiation

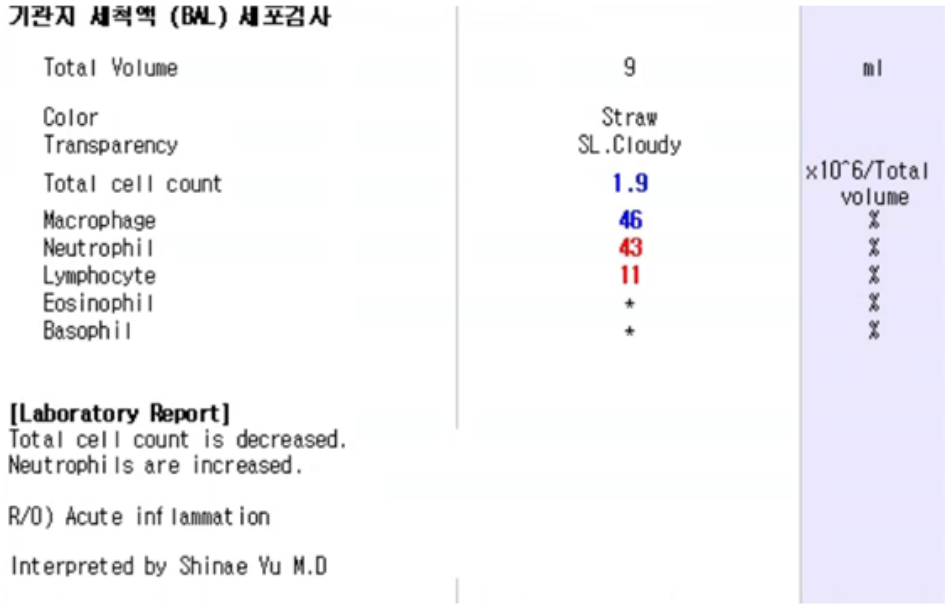
Algorithm for the clinical utility of BAL cellular analysis





Am J Respir Crit Care Med 2012 1851004-1014

Cell counting



기관지 세척액 (BAL) 세포검사

Total Volume	9	ml
Color	Straw	
Transparency	SL.Cloudy	
Total cell count	1.9	x10^6/Total volume
Macrophage	46	%
Neutrophil	43	%
Lymphocyte	11	%
Eosinophil	*	%
Basophil	*	%

[Laboratory Report]
Total cell count is decreased.
Neutrophils are increased.

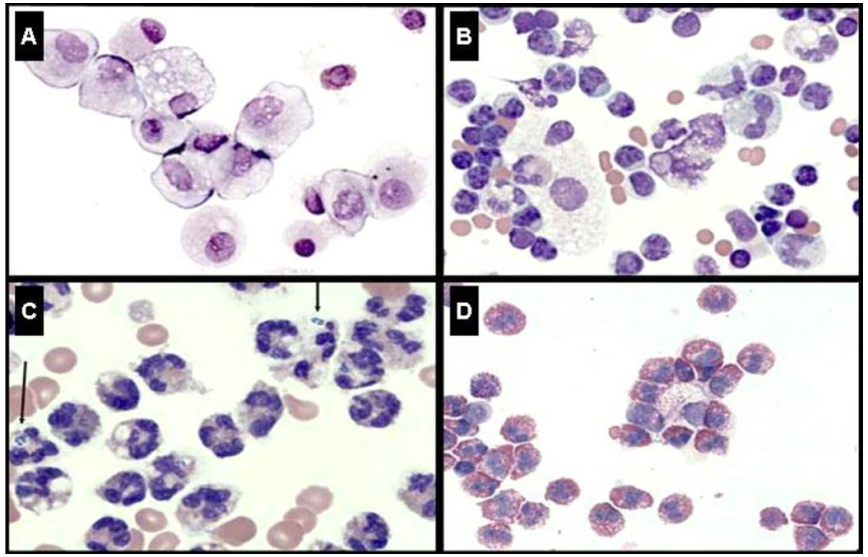
R/O) Acute inflammation

Interpreted by Shinae Yu M.D

- Total cell count
  - Total number of cells
  - Concentration of cells per mL
- Differential cell counts
  - Random fields of 200 to 500 cells
- Unsatisfactory specimens (No clear criteria exist)
  - < Two million total cells
  - < 10 alveolar macrophages per HPF
  - Contain
    - Excessive airway epithelial cells (>5%)
    - Excessive RBCs
    - Mucopurulent exudate
    - Degenerative changes or artifact

Normal BAL cellular patterns

	Non smoker	Smoker (increased cellularity)
Alveolar macrophages	>85%	increased pigmented macrophages
Lymphocytes (CD4+/CD8+ = 0.9–2.5)	10-15% (5-10%)	decreased
Neutrophils	≤3%	
Eosinophils	≤1%	
Epithelial cells (upper airway contamination)	≤5%	



(*A*) Predominance of alveolar macrophages in BAL from a normal subject

(*B*) BAL lymphocytosis

(*C*) BAL neutrophil predominance with intracellular bacteria (*arrows*)

(*D*) BAL eosinophilia

Am J Respir Crit Care Med 2012

Lymphocytic cellular pattern

- **>15% lymphocytes**
  - **Sarcoidosis**
  - **Hypersensitivity pneumonitis (HP)**
  - **Nonspecific interstitial pneumonia (NSIP)**
  - **Cryptogenic organizing pneumonia (COP)**
  - **Drug-induced pneumonitis**
  - Lymphoproliferative disorders
  - Collagen vascular diseases
  - Radiation pneumonitis
- **≥25% lymphocytes** suggests granulomatous disease (sarcoidosis, HP, or chronic beryllium disease), cellular NSIP, drug reaction, lymphoid interstitial pneumonia, COP, or lymphoma.
- **>50% lymphocytes** → HP or cellular NSIP

Lymphocyte subsetting
(Lymphocyte subpopulations and immunohistochemistry)

- Lymphocyte subpopulations (CD3, CD4, CD8)
  - Immunofluorescent labeled monoclonal Abs
  - Flow cytometer, hand counting
  - CD4 to CD8 ratio (CD4+/CD8+ **= 0.9–2.5**)
- Sarcoidosis will have a **high CD4:CD8** ratio
- HP will have a **low CD4:CD8** ratio

Table 3 Effect of Bronchoalveolar Lavage CD4:CD8 Ratio on the Diagnosis of Various Interstitial Lung Diseases

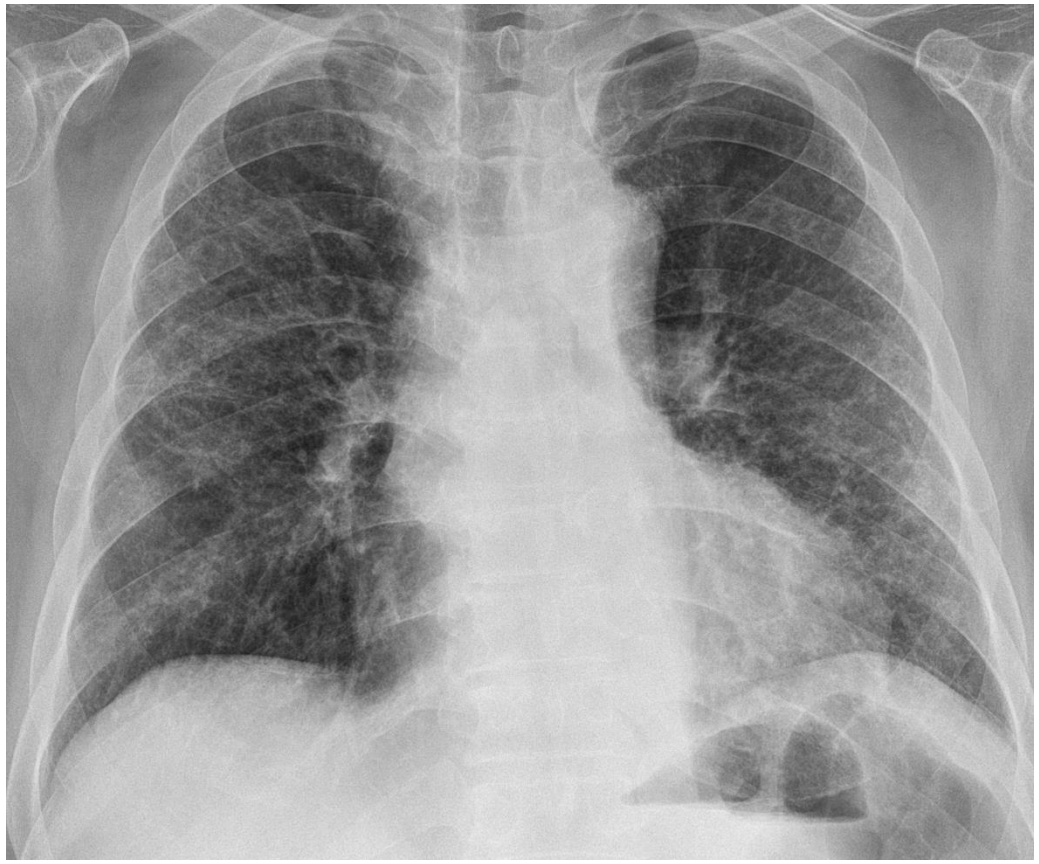
Diagnosis	Number of Patients	Odds Prior to BAL	< 0.5	0.5–3.5	> 3.5
Sarcoidosis	239	33.7	9.1	40.3	69.1*
Idiopathic pulmonary fibrosis	112	15.8	13.6	12.2	5.2†
Extrinsic allergic alveolitis	66	9.3	27.3†	17.2	12.5

*$p < .001$.
†$p < .05$.
Adapted from Welker et al.[77]

Semin Respir Crit Care Med 2007; 28(5): 475-485

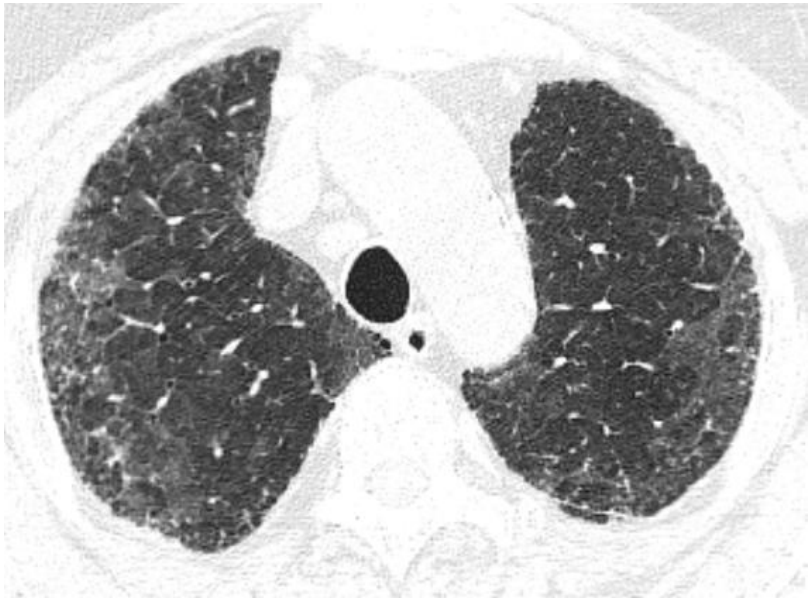
Case 1 – Dyspnea

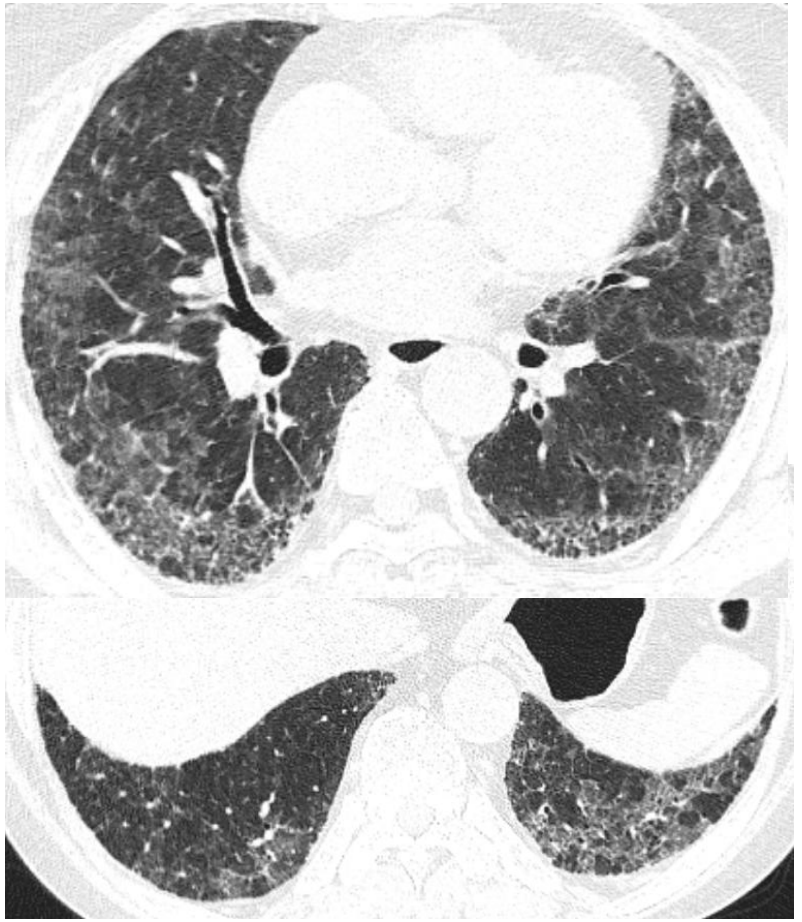
- M / 73
- C.C : Dyspnea
- 7일전부터 기침, 객담 및 호흡곤란→ILD의심
- Arthritis (-) Raynaud (-) sicca symptom (-)
- Current-smoker, 60 pyrs
- 가족력 · 직업 및 환경요인 (-)
- HTN(2010)



Diffuse reticular opacities in both lungs

Case 1 - CT





- Subpleural/peripheral reticulation and mild traction bronchiectasis with GGOs

→ Compatible with ILD such as **NSIP, possible IPF**

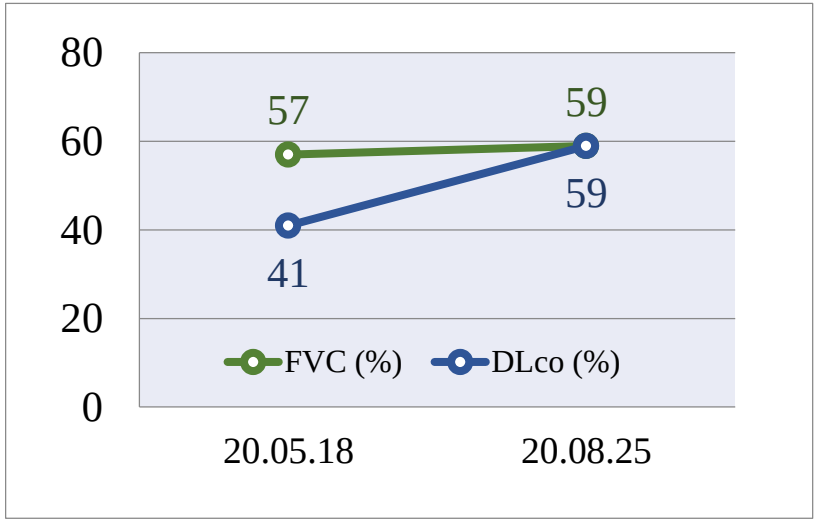
Case 1 – MDT → HP (NSIP)

- Radiology findings
  - NSIP, possible IPF
- Pulmonology findings
  - Alternative
- Pathology findings (Cryo-biopsy)
  - Centrilobular fibrosis
  - Multifocal anthracosis with mononuclear cell infiltrate and organizing pneumonia
  - Favor alternative diagnosis (inhalational injury) rather than UIP
- Auto AB
  - ANA Negative (1:40)
  - ANCA Negative
  - Anti CCP Ab 0.7 (참고치 < 5 U/mL)
  - RA < 10 (0 – 18 IU/ml)

- **BAL**

	환자	참고치
Macrophage	66 %	>85%
Neutrophil	3 %	10-15% (5-10%)
Lymphocyte	**27 %**	≤3%
Eosinophil	**3 %**	≤1%
Basophil	1 %	≤5%
CD4/CD8 ratio	**3.49**	0.9–2.5

- **PFT**



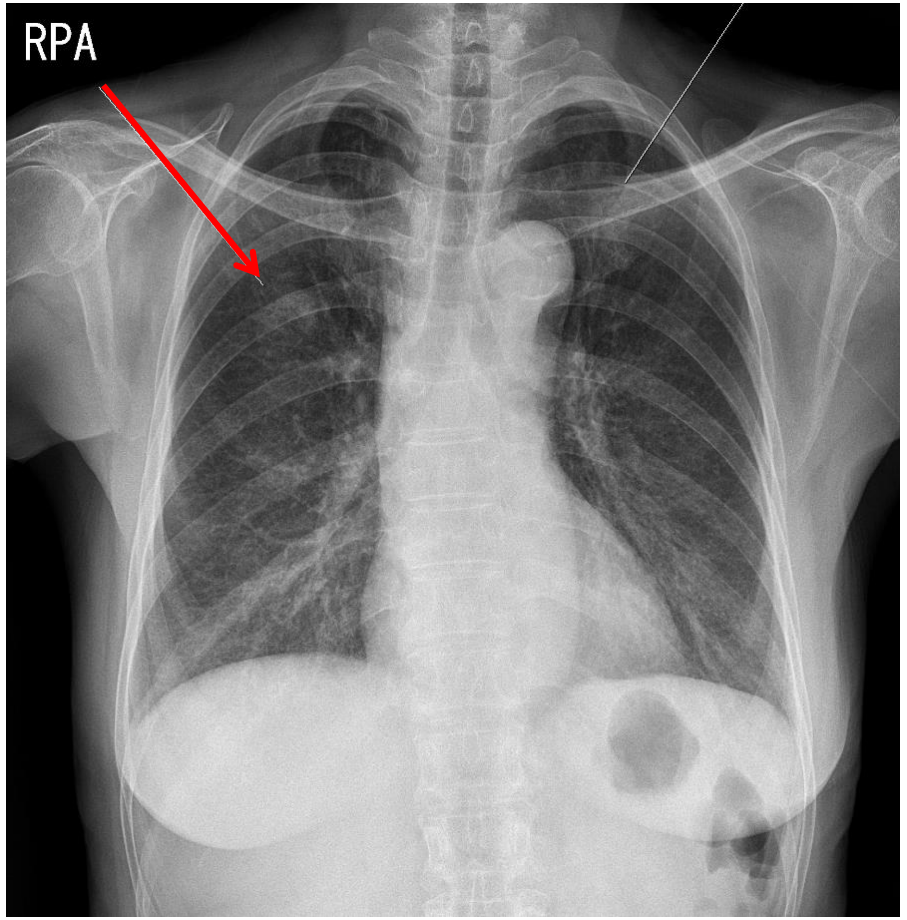
Eosinophilic cellular pattern

- **>1% eosinophils**
  - **Eosinophilic pneumonias**
  - **Drug-induced pneumonitis**
  - Bone marrow transplant
  - **Asthma**
  - Churg-Strauss syndrome
  - Allergic bronchopulmonary aspergillosis
  - **Bacterial, fungal, helminthic, pneumocystis infection**
  - Hodgkin’s disease

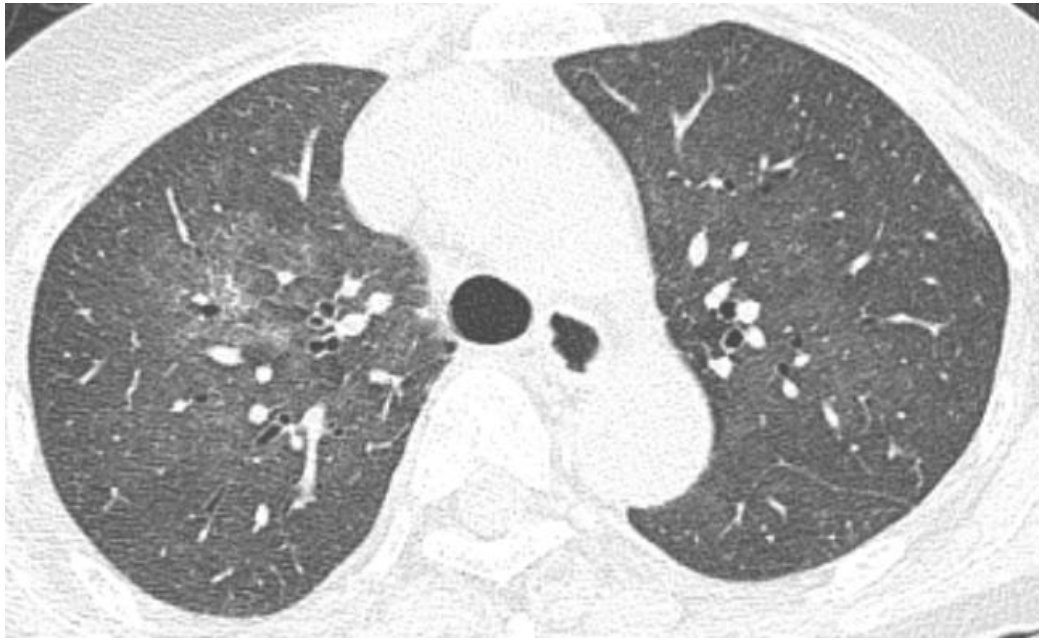
- **>25% eosinophils** → virtually diagnostic of acute or chronic eosinophilic pneumonia.

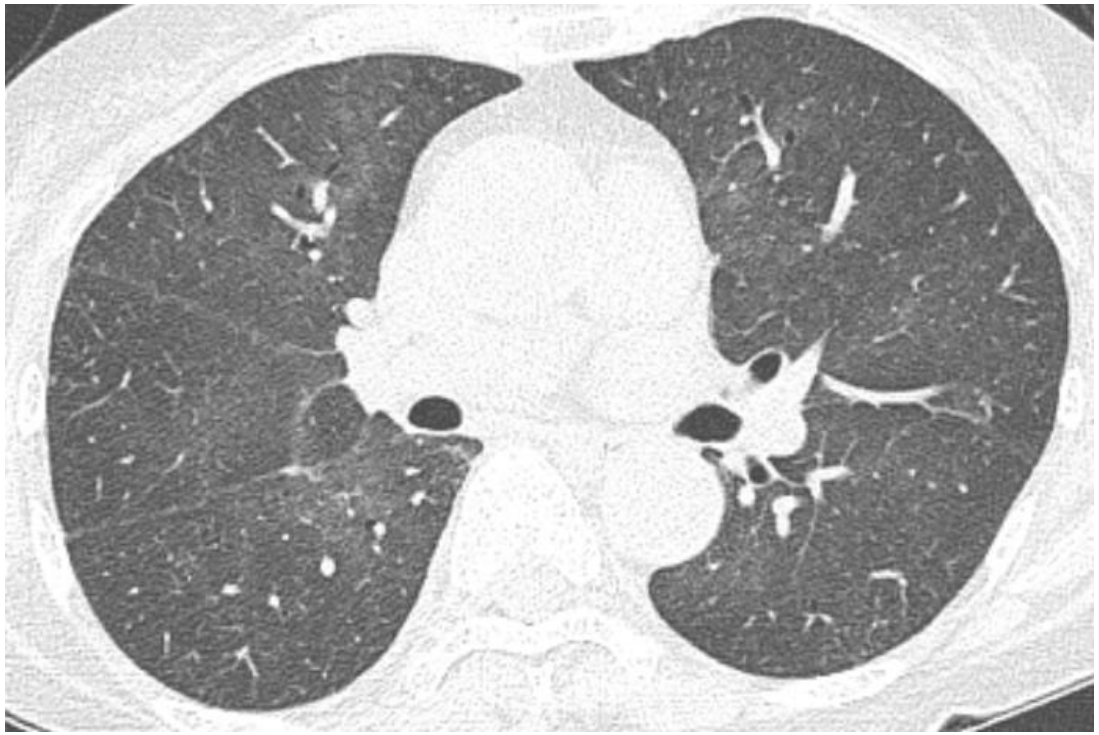
Case 2 - Abnormal chest x-ray

- F / 69
- C.C : Abnormal chest x-ray
- 5년 전 RA진단 후 타 병원에서 진료 받던 환자 → CXR 이상
- Arthritis (-) Raynaud (-) sicca symptom (-)
- None-smoker
- 가족력 : 부, 여동생 RA / 직업 및 환경요인 (-)
- Uterine cancer(1999, hysterectomy 후 완치판정), RA(2014), DM(2014)



Case 2 - CT

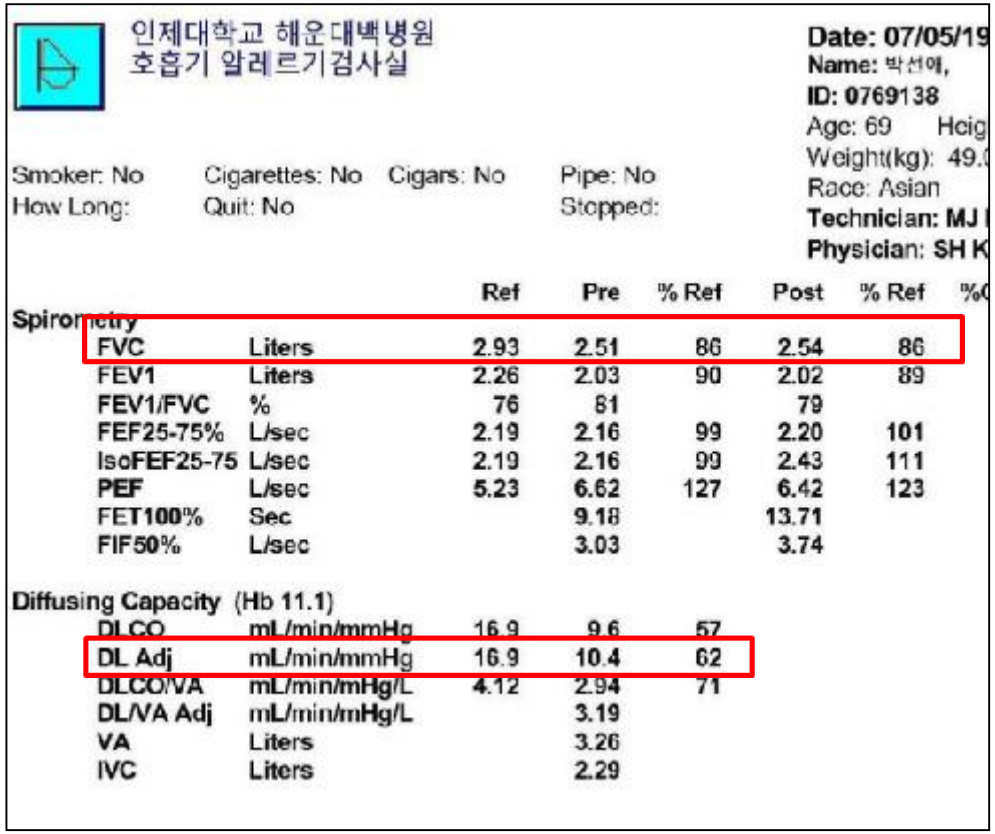




- Diffuse faint GGO in both lung
- Multiple tiny ill defined nodules with subpleural and centrilobular distribution in both upper and lower lobe
- DDx. 1. atypical pneumonia 2. HP 3.Drug induced ILD

Case 2 – MDT → MTX-induced ILD

- **PFT**



인제대학교 해운대백병원
호흡기 알레르기검사실

Date: 07/05/19
Name: 박선애,
ID: 0769138
Age: 69 Hcig
Weight(kg): 49.
Race: Asian
Technician: MJ
Physician: SH K

Smoker: No Cigarettes: No Cigars: No Pipe: No
How Long: Quit: No Stopped:

		Ref	Pre	% Ref	Post	% Ref	%(
Spirometry							
FVC	Liters	2.93	2.51	86	2.54	86	
FEV1	Liters	2.26	2.03	90	2.02	89	
FEV1/FVC	%	76	81		79		
FEF25-75%	L/sec	2.19	2.16	99	2.20	101	
IsoFEF25-75	L/sec	2.19	2.16	99	2.43	111	
PEF	L/sec	5.23	6.62	127	6.42	123	
FET100%	Sec		9.18		13.71		
FIF50%	L/sec		3.03		3.74		
Diffusing Capacity (Hb 11.1)							
DLCO	mL/min/mmHg	16.9	9.6	57			
DL Adj	mL/min/mmHg	16.9	10.4	62			
DLCO/VA	mL/min/mmHg/L	4.12	2.94	71			
DL/VA Adj	mL/min/mmHg/L		3.19				
VA	Liters		3.26				
IVC	Liters		2.29				

- **BAL**

	환자	참고치
Macrophage	11 %	>85%
Neutrophil	6 %	10-15% (5-10%)
Lymphocyte	**76 %**	≤3%
Eosinophil	**11 %**	≤1%
Basophil	2 %	≤5%
CD4/CD8 ratio	**4.36**	0.9–2.5

Neutrophilic cellular pattern

- **>3% neutrophils**
  - **Collagen vascular disease**
  - **Idiopathic pulmonary fibrosis**
  - **Aspiration pneumonia**
  - **Bacterial, fungal**
  - Bronchitis
  - Asbestosis
  - Acute respiratory distress syndrome(ARDS)
  - Diffuse alveolar damage(DAD)

- > 50% neutrophils → acute lung injury, aspiration pneumonia, or suppurative infection

Microbiologic analysis

Aspergillosis, CMV, PCP

Diagnostic value in several pathogens of BAL and BW

- BW
  - Specimens of the major airways not
  - Contamination by the upper airways
  - Useless in the diagnosis of not patho
- BAL
  - More distal specimen, became an op ory tract

BAL is superior in common pathogen ???
No evidence

BW+BAL

- Retrospective study was conducted at the University Medical Center of Groningen (UMCG) in the Netherlands
- Intra-class correlation coefficient (ICC) was used, culture and PCR

Micro-organism	Total No. BAL	Positive findings in BAL	Total No. BW	Positive findings in BW	ICC
Staphylococcus aureus	307	14	304	15	0.819
Pseudomonas aeruginosa	307	11	304	12	0.865
Stenotrophomonas maltophilia	307	2	304	5	0.568
Aspergillus fumigatus	306	22	304	24	0.624
Pneumocystis jirovecii	188	37	2	0	-

0 indicating no agreement
0–0.20 as poor agreement
0.20–0.41 as fair agreement
0.41–0.61 as moderate agreement
0.61–0.81 as substantial agreement
0.81–0.99 as near perfect agreement
1 as perfect agreement

BAL and miniBAL

Age/ sex	Underlying condition	Bacteriology		Mycology	
		BAL	Mini-BAL	BAL	Mini-BAL
60/F	Steroid treatment	MSSA	MSSA	–	–
43/F	H. malignancy	*A. baumannii*	*A. baumannii*	–	–
54/M	H. malignancy	*S. pneumoniae*	*S. pneumoniae*	*Candida* spp.	*Candida* spp.
74/M	H. malignancy	–	–	–	*Candida* spp.
21/M	Solid tumor	–	–	*Candida* spp.	*Candida* spp.
70/M	H. malignancy	*S. pneumoniae*	*S. pneumoniae*	*Candida* spp.	*Candida* spp.
81/F	H. malignancy	Yeast	Yeast	*Candida* spp.	*Candida* spp.
63/F	H. malignancy	*A. baumannii*	*A. baumannii*	*Candida* spp.	*Candida* spp.
63/M	Solid tumor	Yeast	Yeast	*Candida* spp.	*Candida* spp.
45/M	HIV(+)	Yeast	–	*Candida* spp.	*Candida* spp.
57/M	Solid tumor	MSSA	MSSA	*Candida* spp.	*Candida* spp.
50/F	H. malignancy	*E. faecium*	–	–	–
49/F	Steroid treatment	*A. baumannii*	*A. baumannii*	–	–
58/M	H. malignancy	–	–	–	*Aspergillus* spp.
53/M	Solid tumor	*P. aeruginosa*	*P. aeruginosa*	–	–

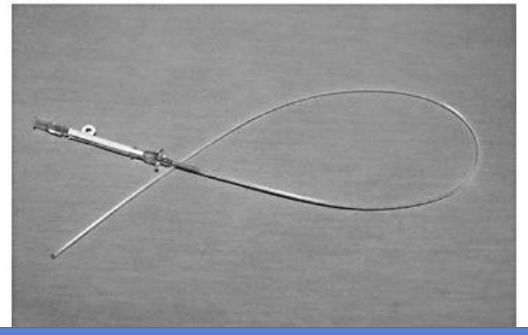
H. malignancy = Hematological malign… *baumannii*; *S. pneumoniae* = *Streptococcus*… *aeruginosa* = *Pseudomonas aeruginosa*

34.4% vs 31.3%

34.4% vs 40.6%

		Correlation coefficient (r)
BAL bacteriology	mini-BAL bacteriology	0.850
BAL bacteriology	ETA bacteriology	0.477
Mini-BAL bacteriology	ETA bacteriology	0.430
BAL mycology	mini-BAL mycology	0.821
BAL mycology	ETA mycology	0.095
Mini-BAL mycology	ETA mycology	−0.176

** endotracheal aspiration (ETA)



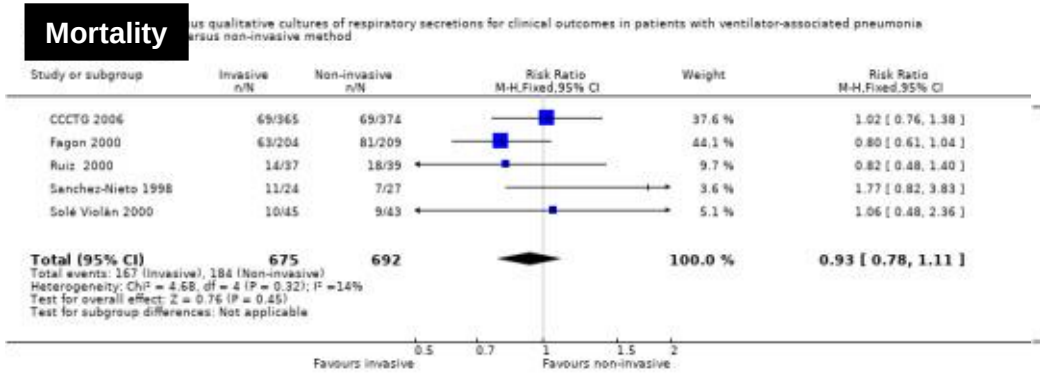
miniBAL can replace BAL for patients who are concerned about large amounts of saline

- 62 samples / 32 pts
- Immunocompromised ICU with MV
- miniBAL - lavage catheter, 20 ml 0.9% NaCl, blind
- BAL – BFS, 120-150ml 0.9% NaCL

M. Sezai Tasbakan Respiration. 2011;81(3):229-235

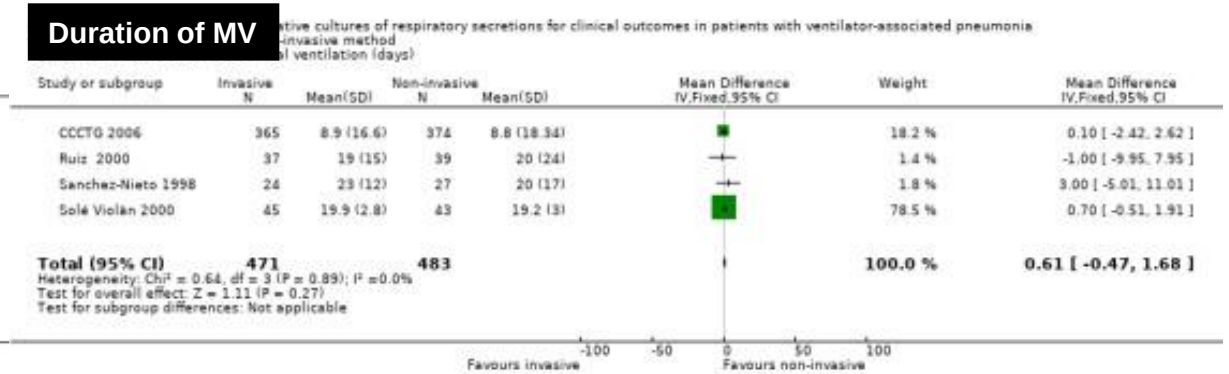
Clinical outcomes in patients with VAP

Mortality



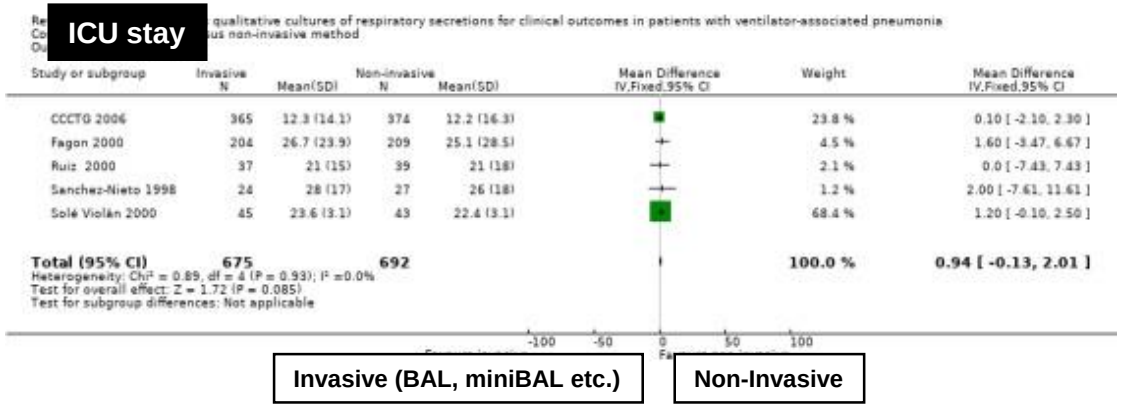
Invasive (BAL, miniBAL etc.) | Non-Invasive

Duration of MV



Invasive (BAL, miniBAL etc.) | Non-Invasive

ICU stay



Invasive (BAL, miniBAL etc.) | Non-Invasive

- **No evidence** that invasive strategies of respiratory secretions results in
  - Reduced mortality,
  - Reduced time in ICU and
  - Reduced time on MV
  - Higher rates of antibiotic change

Cochrane Database Syst Rev. 2014 Oct; 2014(10):CD006482.

Apergillosis

- Culture of Aspergillus spp from respiratory secretions (25~50% positive cultures)
- Galactomannan - polysaccharide that is a major constituent of Aspergillus cell walls, enzyme immunoassay (EIA), optical density (OD) ≥0.5 is considered to be a positive result
- European Organi-zation for Research and Treatment of Cancer/MycosesStudy Group (EORTC/MSG)

Table 1. EORTC/MSG criteria

Proven IA	Histopathologic or cytopathologic examination showing hyphae from needle aspiration or biopsy specimen with evidence of associated tissue damage; or positive culture result for a sample obtained by sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with infection
Probable IA	At least 1 host factor criterion; and 1 microbiological criterion; and 1 major (or 2 minor) clinical criteria from abnormal site consistent with infection
Possible IA	At least 1 host factor criterion; and 1 microbiological or 1 major (or 2 minor) clinical criteria from abnormal site consistent with infection. This category is not recommended for use in clinical trials of antifungal agents

Any patient

Immunocompromised

Clin Infect Dis. 2020 Sep 15; 71(6): 1367–1376.

Apergillosis

Clinical features of Pulmonary aspergillosis
The presence of 1 of the following 4 patterns on CT:
1. Dense, well-circumscribed lesions(s) with or without a halo sign
2. Air crescent sign 3.Cavity 4. Wedge-shaped and segmental or lobar consolidation
Mycological evidence Aspergillus species recovered by culture from sputum, BAL, bronchial brush, or aspirate

Galactomannan antigen	any 1 of the following:
Single serum or plasma: ≥1.0	
BAL fluid: ≥1.0	
Single serum or plasma: ≥0.7 and **BAL fluid ≥0.8**	
CSF: ≥1.0	
Aspergillus PCR	any 1 of the following:
Plasma, serum, or whole blood 2 or more consecutive PCR tests positive	
BAL fluid 2 or more duplicate PCR tests positive	
At least 1 PCR test positive in plasma, serum, or whole blood and 1 PCR test positive in BAL fluid	

OD ≥0.5 is considered to be a positive result

Table 2. Effect of definition of test positivity

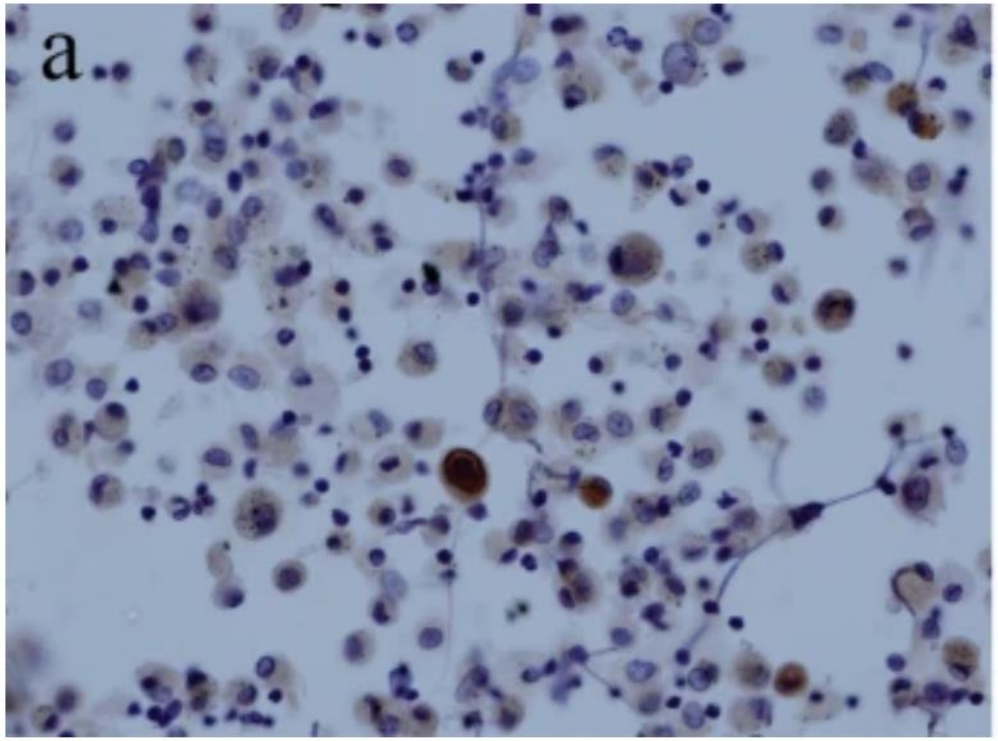
Cut-off	Analysis	Studies (n)	Sensitivity (95% CI)	Specificity (95% CI)
0.5		27	0.78 (0.70 to 0.85)	0.85 (0.78 to 0.91)
	Single sample	13	0.79 (0.69 to 0.88)	0.80 (0.71 to 0.90)
	Subsequent samples	14	0.77 (0.67 to 0.87)	0.88 (0.81 to 0.94)
1.0		8	0.71 (0.63 to 0.78)	0.90 (0.86 to 0.93)
	Single sample	4	0.72 (0.62 to 0.82)	0.87 (0.81 to 0.93)
	Subsequent samples	4	0.70 (0.59 to 0.80)	0.92 (0.88 to 0.96)

Cochrane Database of Systematic Reviews 2015, Issue 12

Cytomegalovirus(CMV) pulmonary infection

- CMV mainly affects **alveolar epithelial cells**
- Blood and body fluid (BAL) **CMV culture** → diagnosis
- Serology
  - Acute infection
    - CMV IgM - suggesting recent seroconversion
    - CMV IgG - fourfold or greater increase in titer (at least two to four weeks apart)
  - Past infection
    - CMV IgG
- CMV PCR (정량, 정성)
- Histologic examination of tissue biopsies

CMV immunocytochemistry show "owl's-eye" like structure.
CMV-IHCx40



BMC Pulmonary Medicine volume 22, Article number: 55(2022)

Pneumocystis carinii pneumonia

- Pneumocystis cannot be cultured
- Pneumocystis is primarily an alveolar pathogen

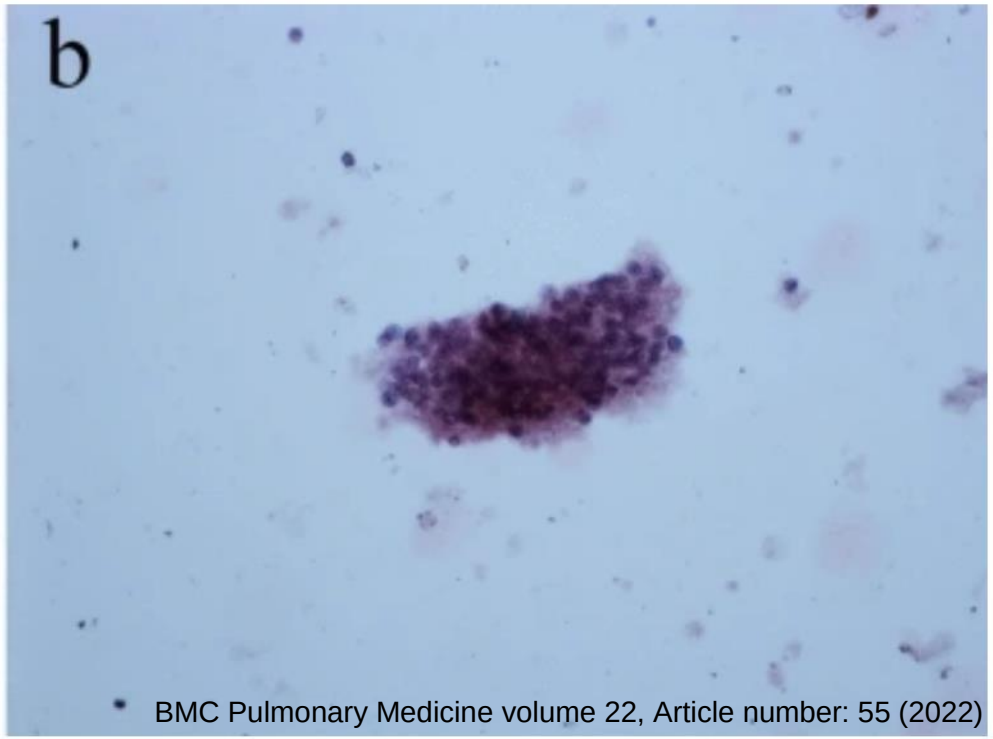
- Microbiologic identification of the organism
  - BAL fluid(optimal specimen for PCR analysis)

    >> Induced sputum(acceptable)
  - PCR >> staining(dye-based, fluorescent antibody)
  - PCR 94%–100% sensitivity / 79%–96% specificity

- Serum beta-D-glucan testing

  as the basis for presumptive diagnosis

The walls of the *Pneumocystis carinii* cysts stained
- black, regular or irregular, with obvious nuclei (GMSx40)



BMC Pulmonary Medicine volume 22, Article number: 55 (2022)

Sadatomo Tuberc Respir Dis 2020;83:132-140

BAL vs. BW for TB diagnosis

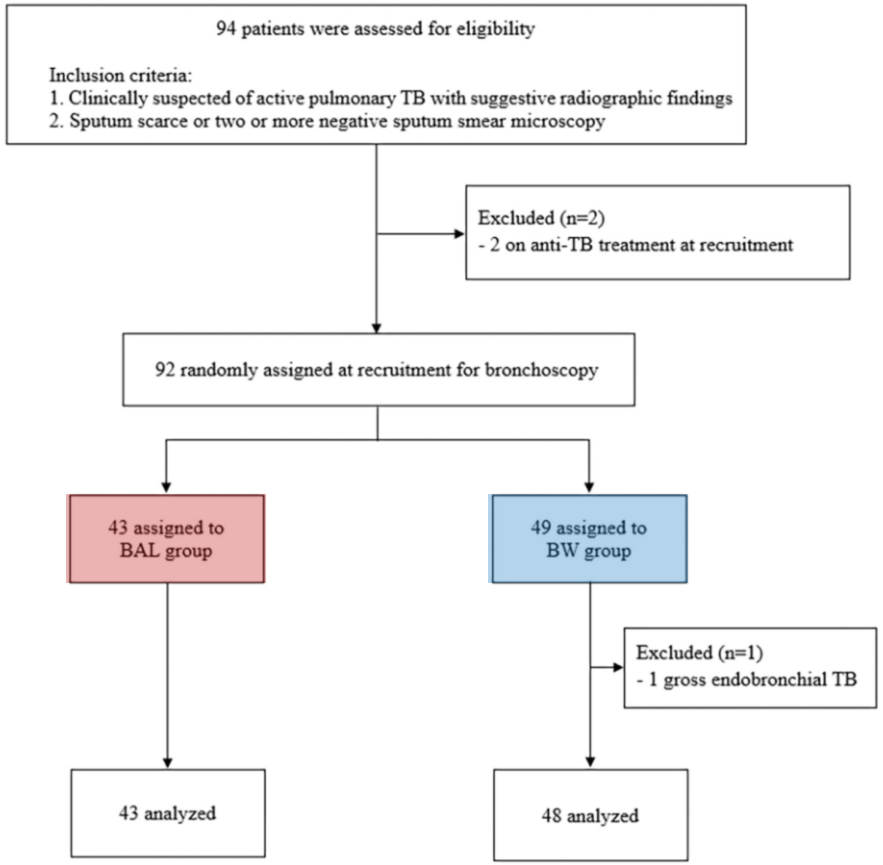


Fig. 1. Flow diagram of the study population.

Table 3
Diagnostic value of bronchoalveolar lavage and bronchial washing in pulmonary tuberculosis detection

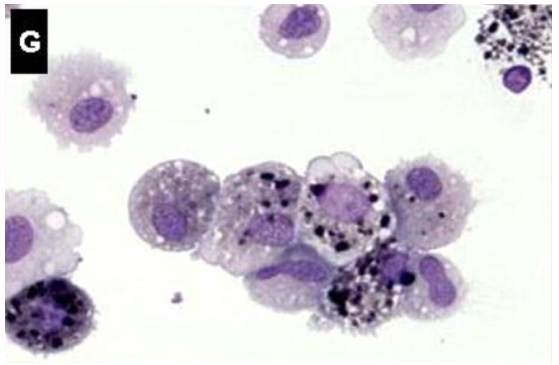
Diagnostic value	BAL group ($n = 43$)	BW group ($n = 48$)
Sensitivity, % (95% CI)	85.7 (18/21) (63.7–97.0)	50.0 (15/30) (31.3–68.7)
Specificity, % (95% CI)	100 (22/22) (84.6–100.0)	100 (18/18) (81.5–100.0)
Positive predictive value, % (95% CI)	100 (18/18) (81.5–100.0)	100 (15/15) (78.2–100.0)
Negative predictive value, % (95% CI)	88.0 (22/25) (68.8–97.5)	54.5 (18/33) (36.4–71.9)

BAL, bronchoalveolar lavage; BW, bronchial washing; CI, confidence interval.

Kim YW, et al. Clin Microbiol Infect. 2020;26:911-6.

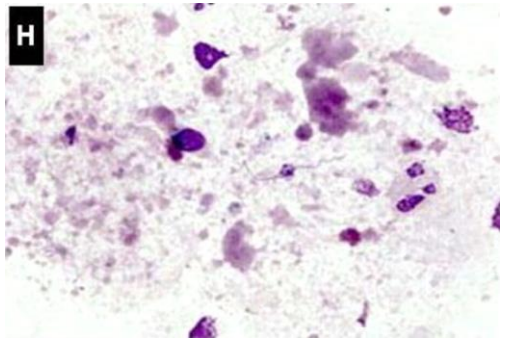
Cytologic analysis

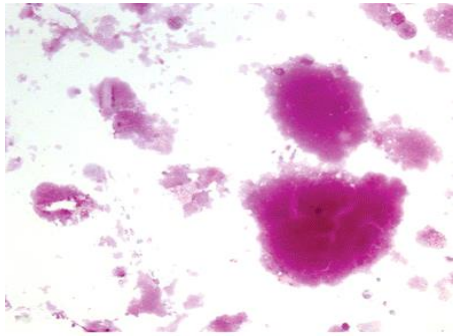
- Lung malignancies



- Diffuse alveolar hemorrhage
  - **Hemosiderin-laden macrophages**

    (Prussian blue staining)





- Pulmonary alveolar proteinosis
  - Amorphous, predominantly acellular debris
  - extracellular globular hyaline material homogeneously PAS positive

Diffuse alveolar hemorrhage

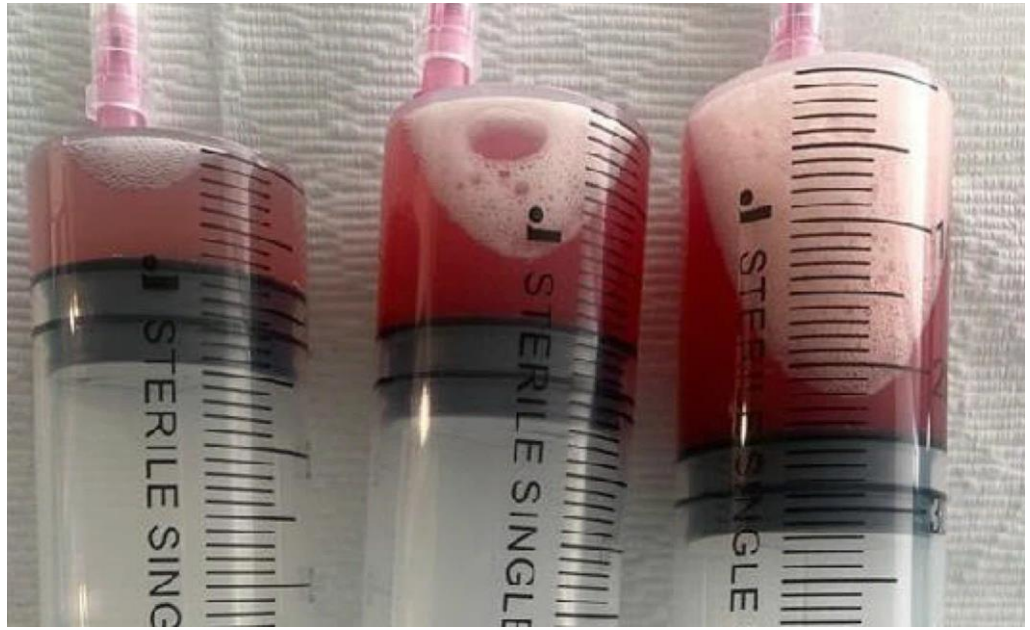
Table 16 Diffuse alveolar hemorrhage

Diffuse alveolar hemorrhage due to non-infectious causes
DAH with pulmonary capillaritis
Isolated pauci-immune necrotizing pulmonary capillaritis
Granulomatous polyangiitis
Microscopic polyangiitis
Mixed cryoglobulinemia
Behcet's syndrome
Henoch-Schönlein purpura
Goodpasture's syndrome*
Pauci-immune glomerulonephritis
Immune-complex-associated glomerulonephritis
Collagen-vascular disease (systemic lupus erythematosus*, polymyositis, rheumatoid arthritis, mixed-connective tissue disease, scleroderma)
Primary antiphospholipid antibody syndrome
Acute lung transplant rejection
Autologous bone marrow transplantation
Drugs (e.g., propylthiouracil with positive anti-neutrophilic cytoplasmic antibody)
DAH without capillaritis
Idiopathic pulmonary hemosiderosis
Systemic lupus erythematosus*
Goodpasture's syndrome*
Diffuse alveolar damage—e.g., after cytotoxic drug preconditioning therapy for bone marrow transplantation
Penicillamine—bland hemorrhage; uncommon; occurs after 1 year of therapy
Tuberous sclerosis
Trimellitic anhydride
Mitral stenosis
Coagulation disorders
Pulmonary veno-occlusive disease
Pulmonary capillary hemangiomatosis
Lymphangioleiomyomatosis—due to rupture of postcapillary venules, which are infiltrated by smooth muscles
Pulmonary embolism with infarction
Diffuse alveolar hemorrhage due to infectious causes (315)

With pulmonary capillitis

Without pulmonary capillitis

Infectious cause



J Thorac Dis. 2020 Sep; 12(9): 4991–5019

Pulmonary alveolar proteinosis

Summary(1)

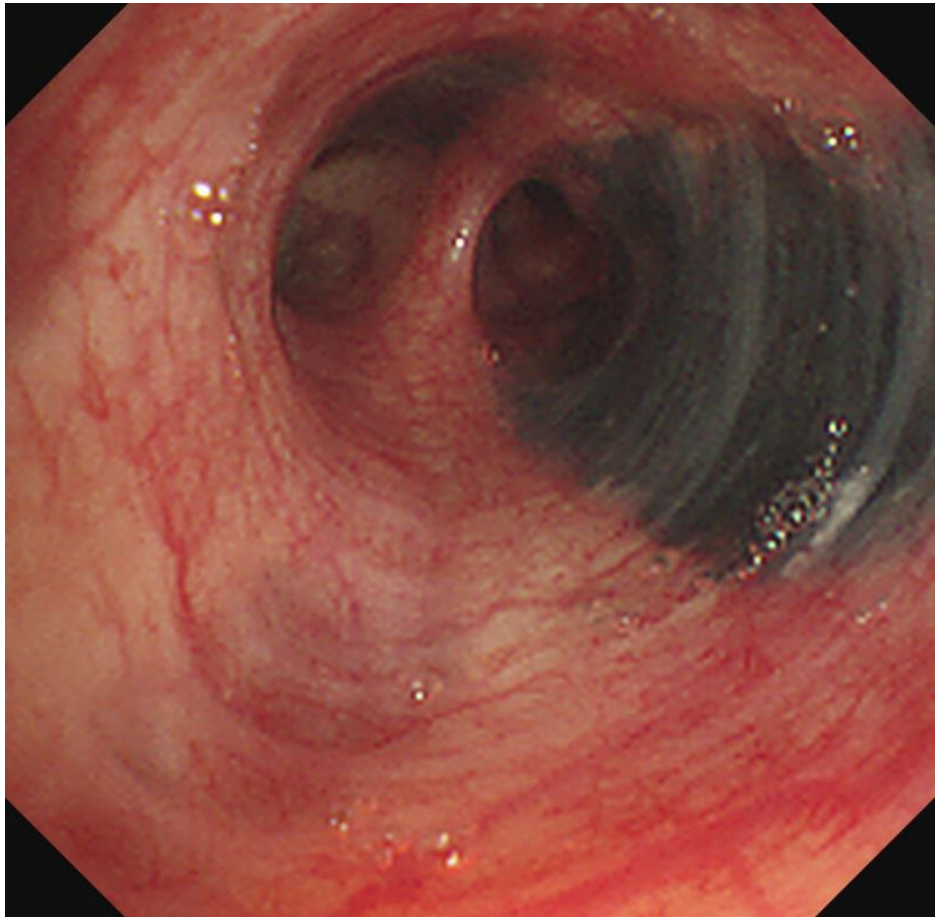
- BAL May provide strong support or clues for a diagnosis or help narrow the differential diagnosis, especially in ILD patients.

- BAL is effective for microbiological analysis and, in terms of sensitivity, is performed in parallel with bronchial washing.

- BAL is an effective and necessary test in diagnosis of aspergillosis, PCP, CMV and TB.

Diagnostic findings

Anthracofibrosis



Black pigmentation of the tracheobronchial tree

- Especially in Middle East and East Asia (korea and Iran)
- Both broncial mucosal and submucosal layers and lung parenchyma
- Biomass
  - Macrophages that are responsible for removing inhaled particles engulf the particles and remain in the submucosa
- Chronic infections
  - Tuberculosis (TB, 27%–60% have been found to have TB)
  - Slow grown subtype
  - Silica containing pigmentation

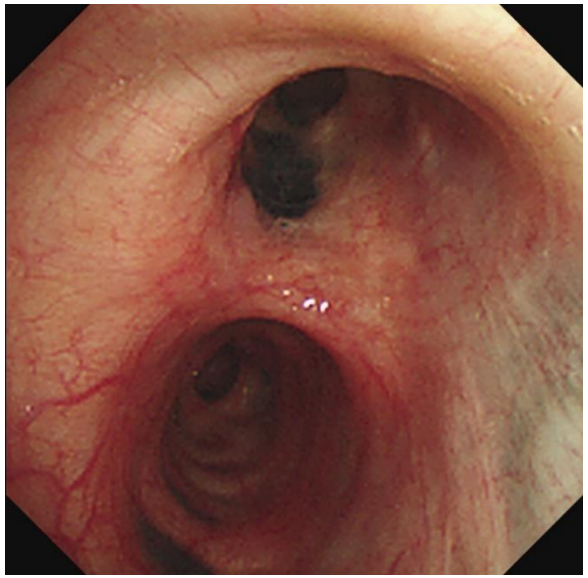
  → Alteration immune mechanisms

  → Prone to *M. tuberculosis* infection

Tanaffos 2017; 16(3): 175-189

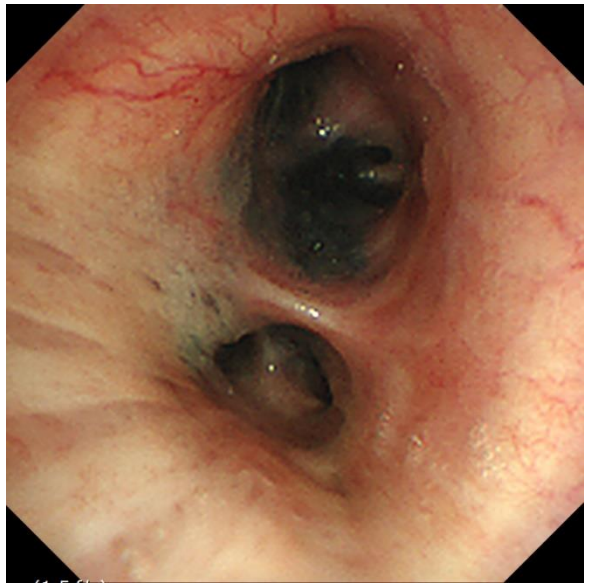
Anthracofibrosis

RUL, LUL, RML (m/c)

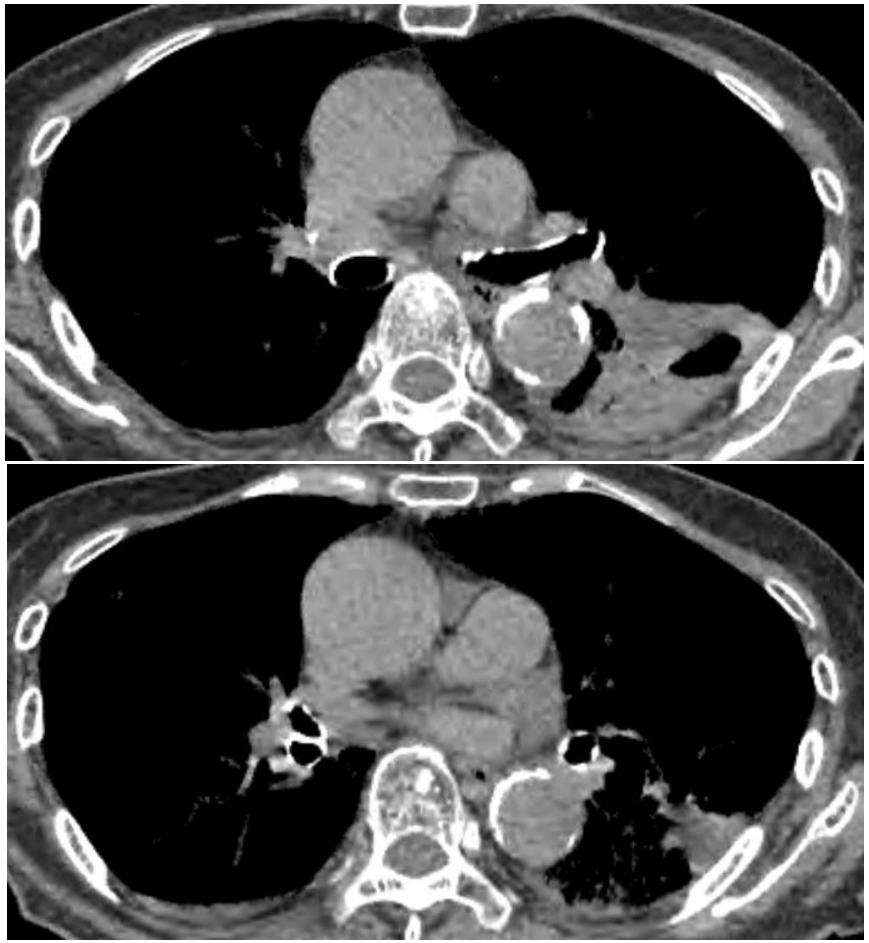


RUL anthracosis

LUL anthracofibrosis

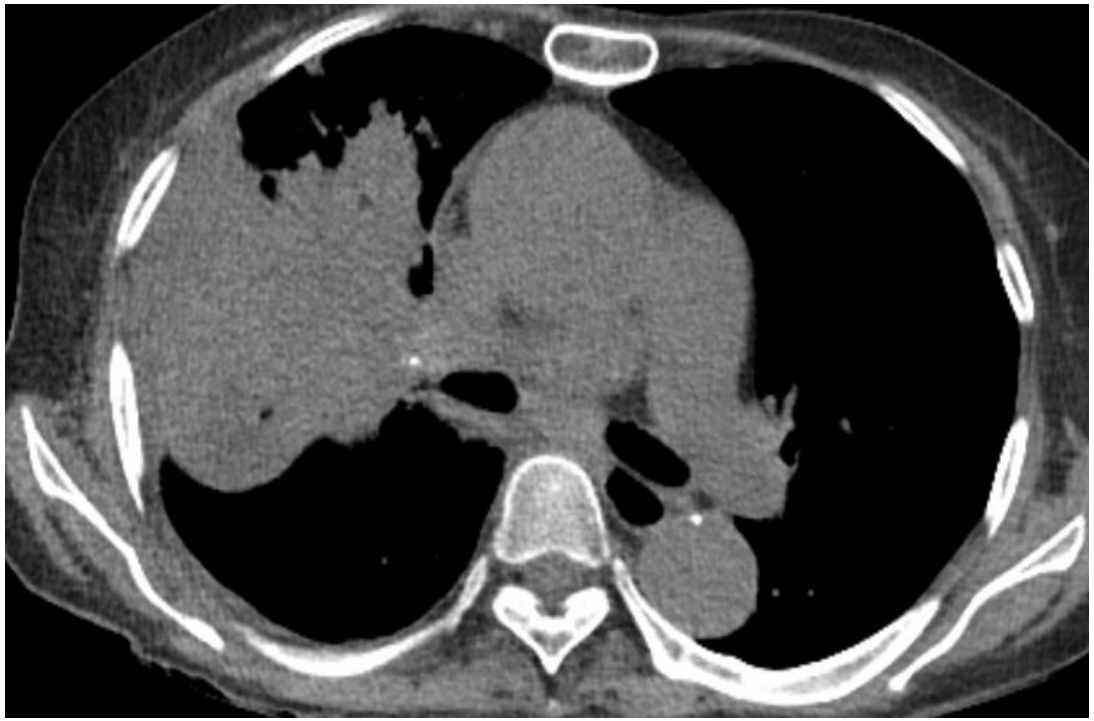


Peribronchial and LN calcification



F/75 RUL atelectasis

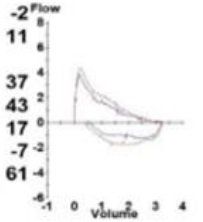
RUL atelectasis

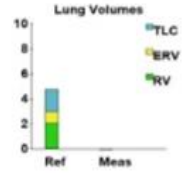


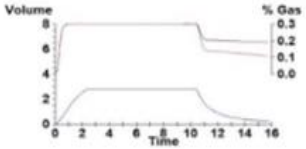
Obstructive spirometry

(can be restrictive and combined in anthracofibrosis)

		Ref	Pre	% Ref	Post	% Ref	%Chg
Spirometry							
FVC	Liters	2.96	3.25	110	3.18	108	-2
FEV1	Liters	2.20	1.66	75	1.84	84	11
FEV1/FVC	%	74	51		58		
FEF25-75%	L/sec	2.08	0.69	33	0.94	45	37
IsoFEF25-75	L/sec	2.08	0.69	33	0.99	48	43
PEF	L/sec	5.23	3.83	73	4.48	86	17
FET100%	Sec		14.55		13.54		-7
FIF50%	L/sec		1.05		1.69		61
Diffusing Capacity							
DLCO	mL/min/mmHg	16.7	12.9	77			
DL Adj	mL/min/mmHg	16.7	12.9	77			
DLCO/VA	mL/min/mHg/L	4.03	3.17	79			
DL/VA Adj	mL/min/mHg/L		3.17				
VA	Liters		4.07				
IVC	Liters		2.96				

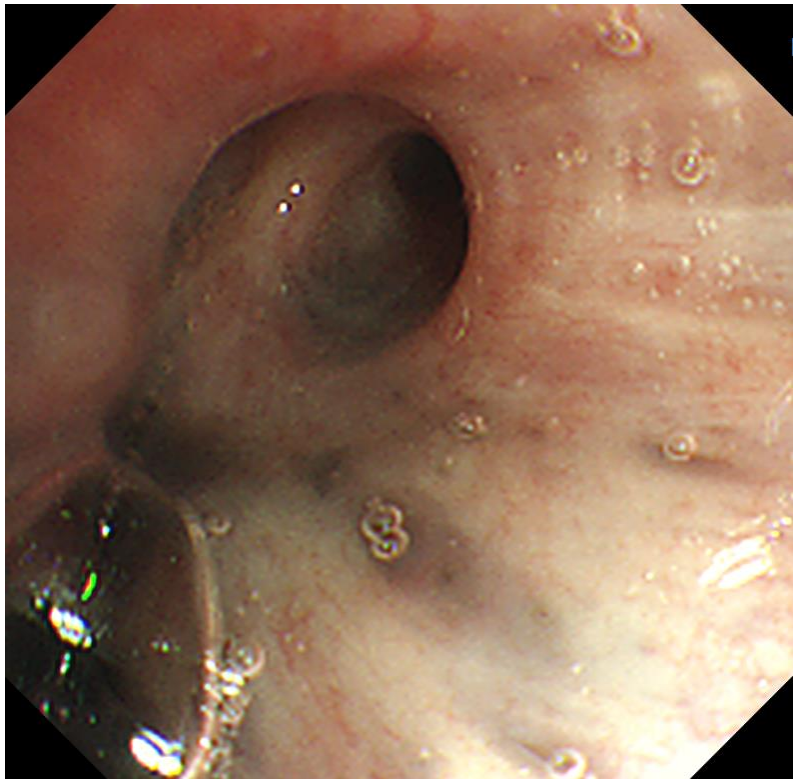




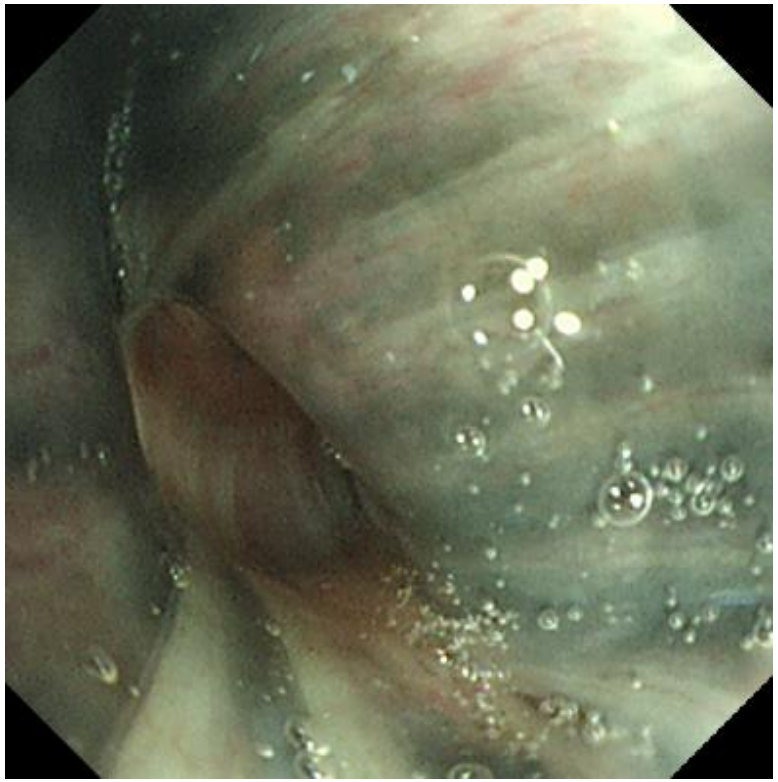


F/75 RUL atelectasis

RUL



RUL anterior segment

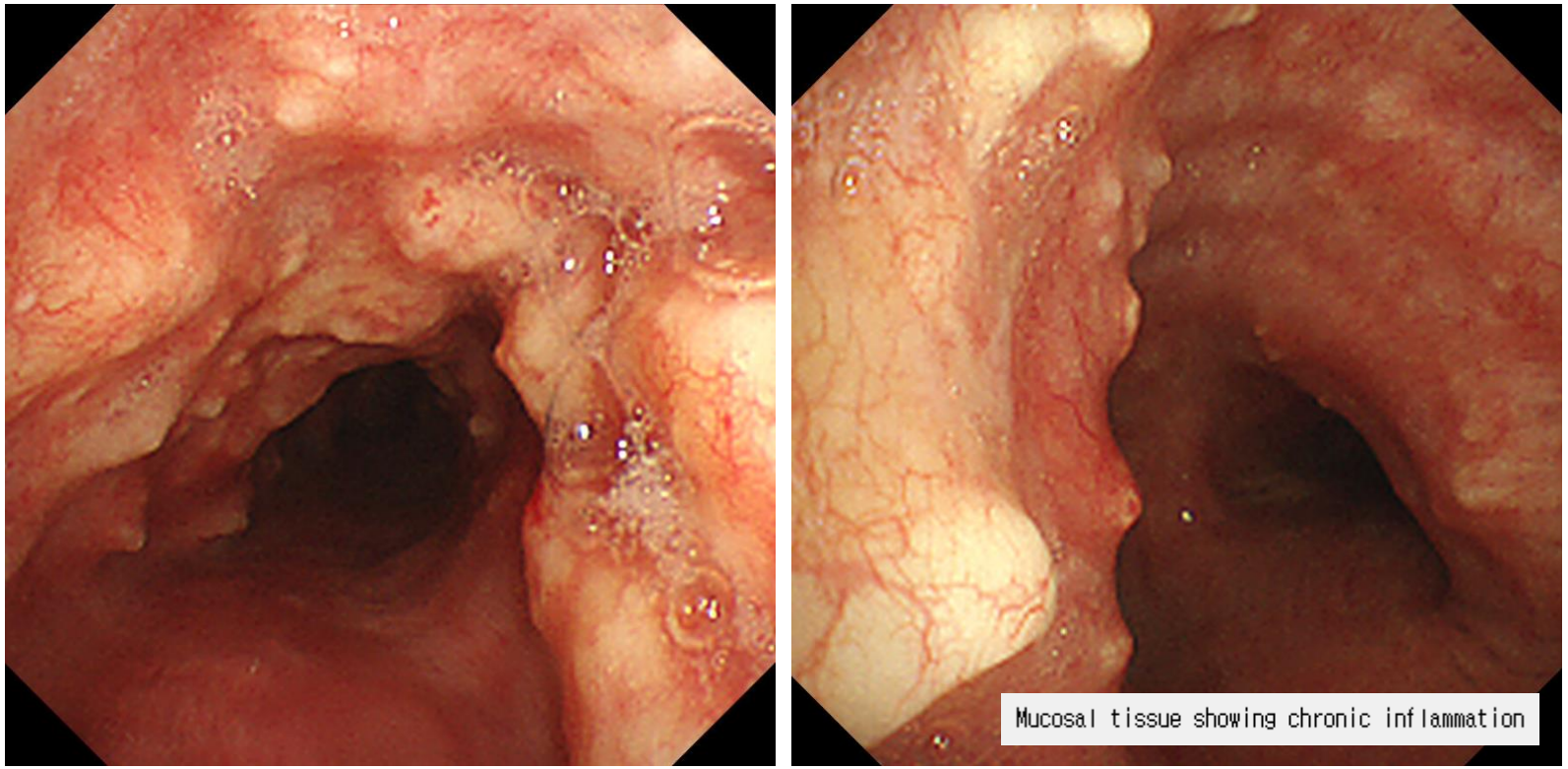


Anthracosis → mucosal proliferation → luminal stenosis and/or obstruction

→ Anthracofibrosis

Tracheobronchopathia osteochondroplastica

M/68 RUL mass w/u, incidental finding



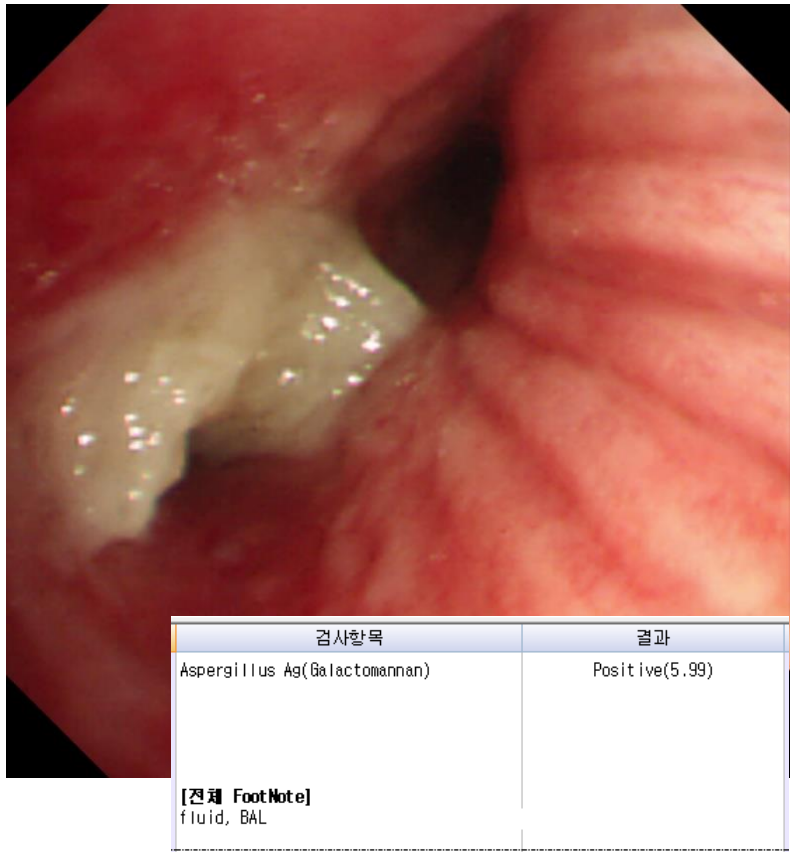
Numerous sessile, cartilaginous, or bony submucosal nodules (anterolateral)

- Rare benign disease, unknown cause
- DDx.
  - Papillomatoses
  - Sarcoidosis
  - Chondrosarcoma
  - Hamartomas
  - Amyloidosis
  - Tuberculoid calcifications
  - Dermatomyositis
  - Scleroderma
  - Wegener's granulomatosis
  - Paratracheal calcified lymph nodes

Aspergillosis, fungal infection

F/63 pneumonia (ovarian cancer, MDS)

Lt. 2nd carina

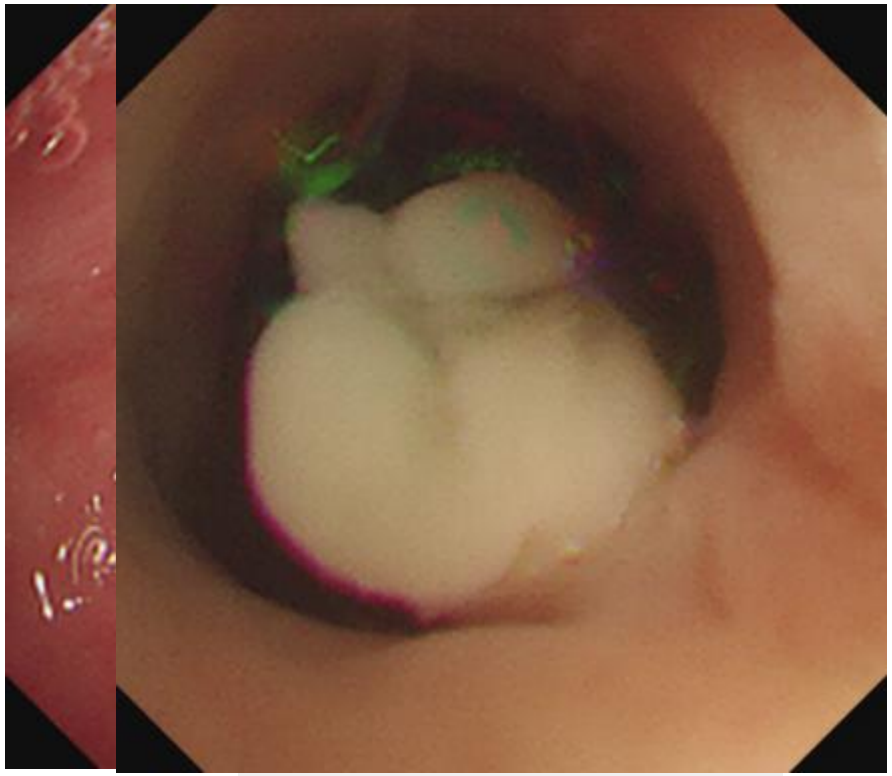


검사항목	결과
Aspergillus Ag(Galactomannan)	Positive(5.99)

[전체 FootNote]
fluid, BAL

M/58 hemoptysis

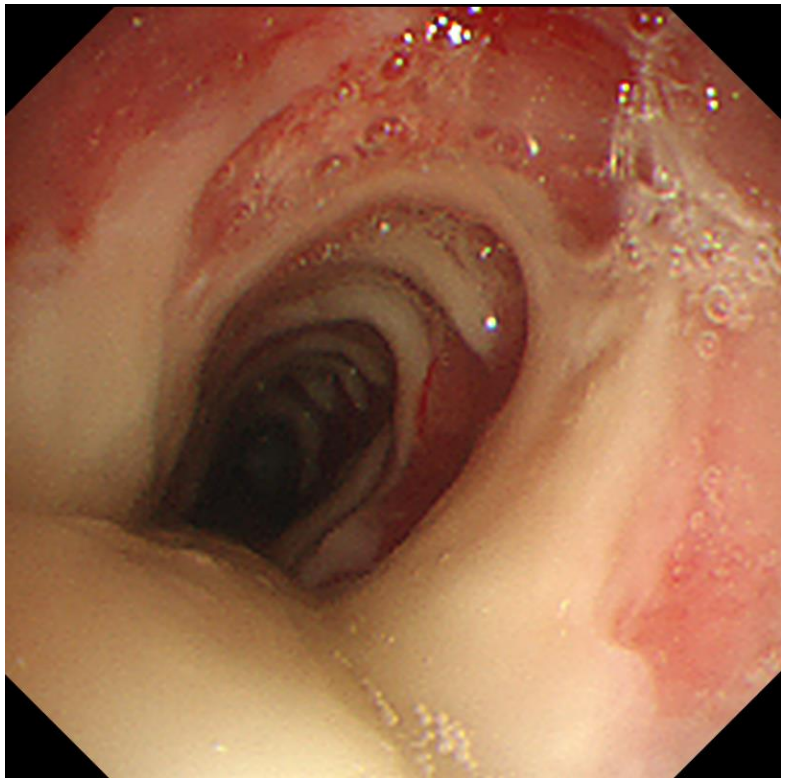
RUL bronchus stenosis with whitish material



Fungal ball, consistent with aspergilloma

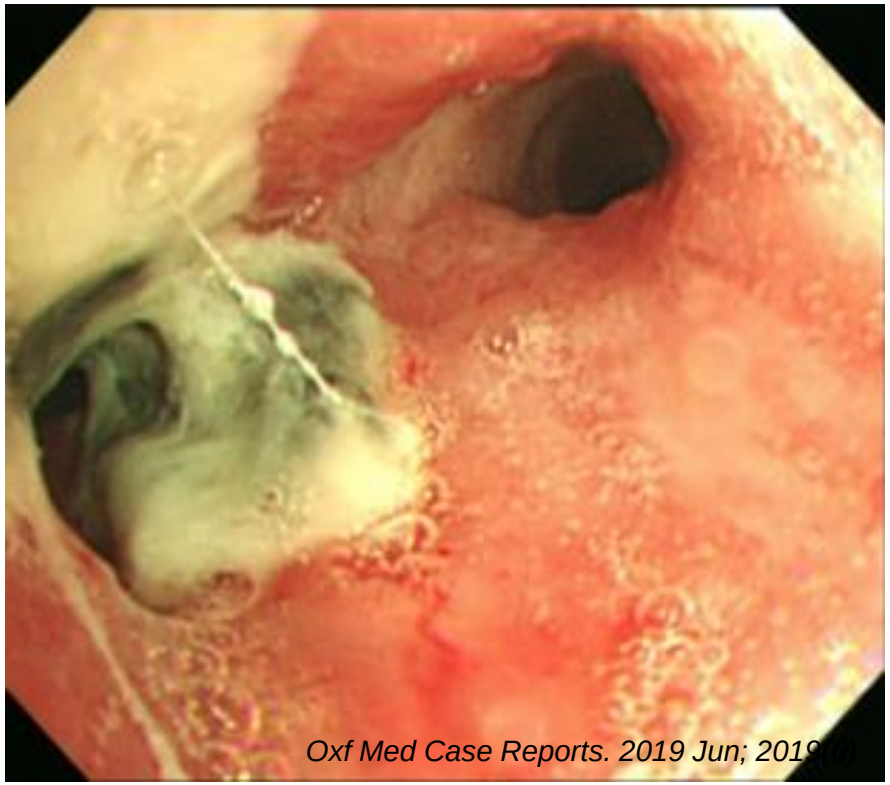
Aspergillosis, fungal infection

M/73 NSCLC, Candida albicans



Pseudomembranous form

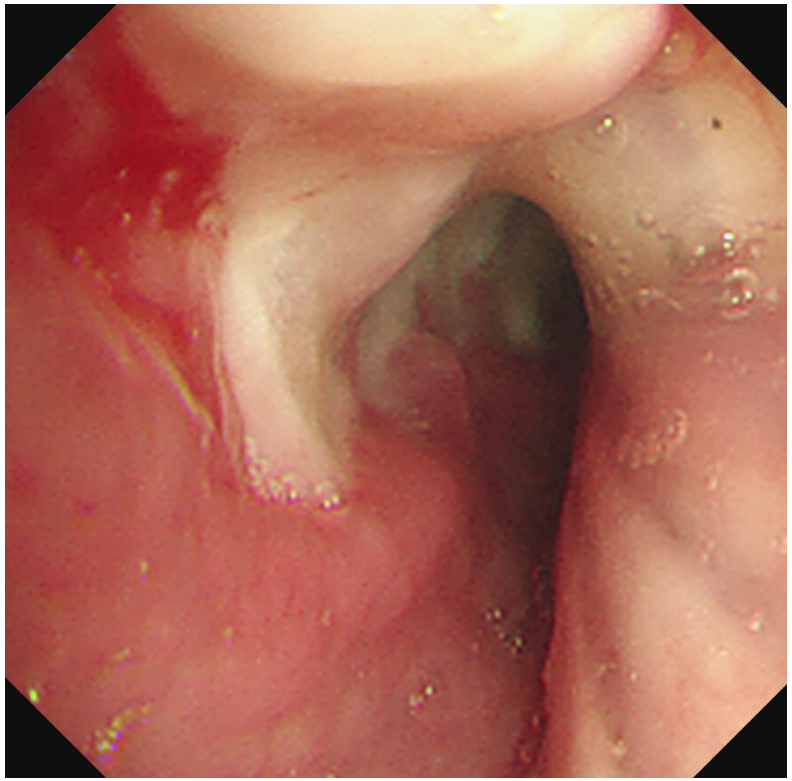
Candida albicans vs. aspergillosis



Necrotic, ulcerative form

Endobronchial TB

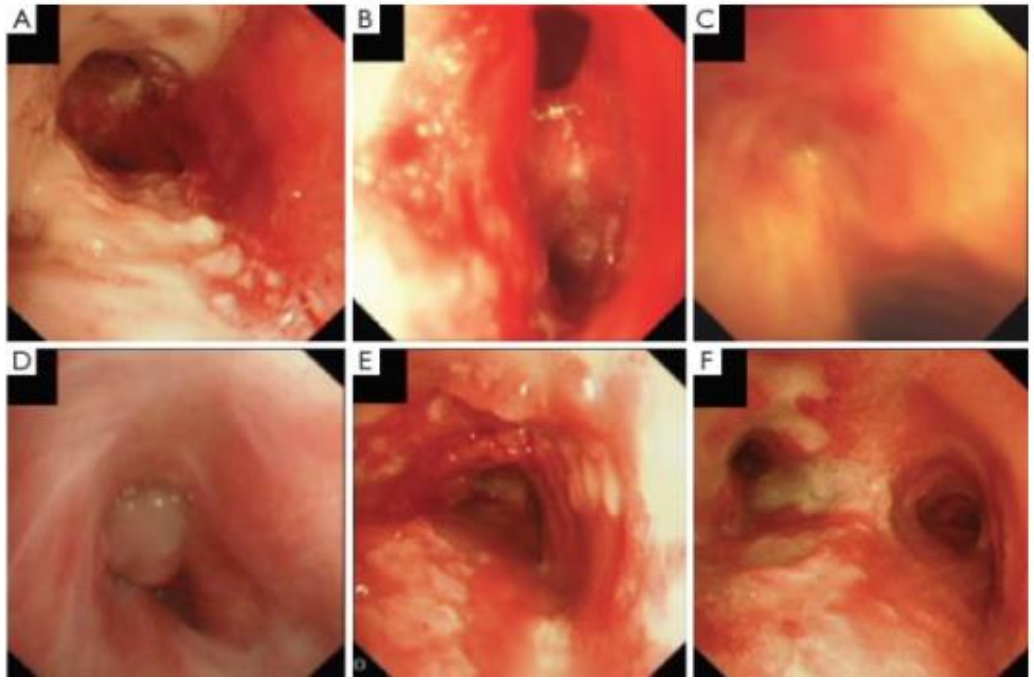
F/83



A. Caseosa active (m/c) **B. hyperemia-edema**

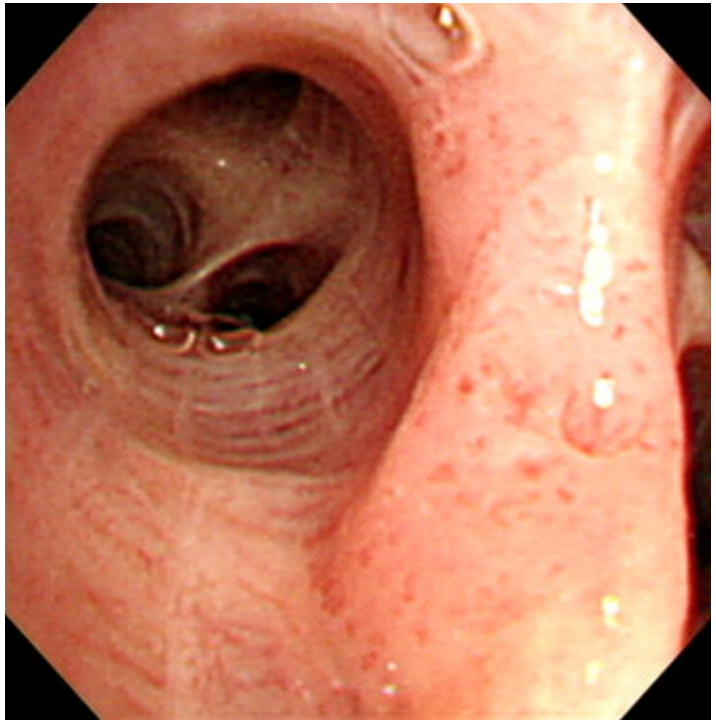
C. Fibro-stenotic **D. tumorous**

E. Granular **F. ulcerative**



Squamous cell carcinoma

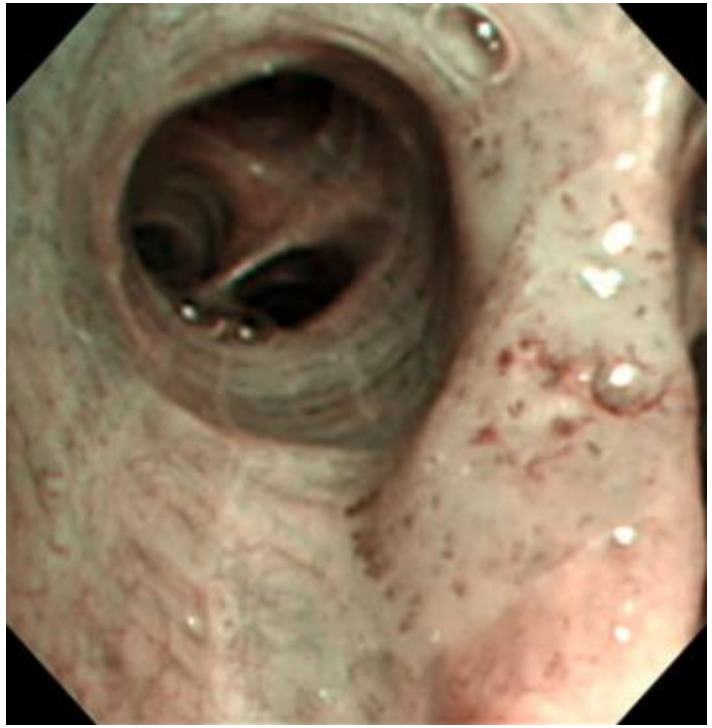
M/63 incidental finding



Bronchus, right upper lobe, bronchoscopic biopsy;

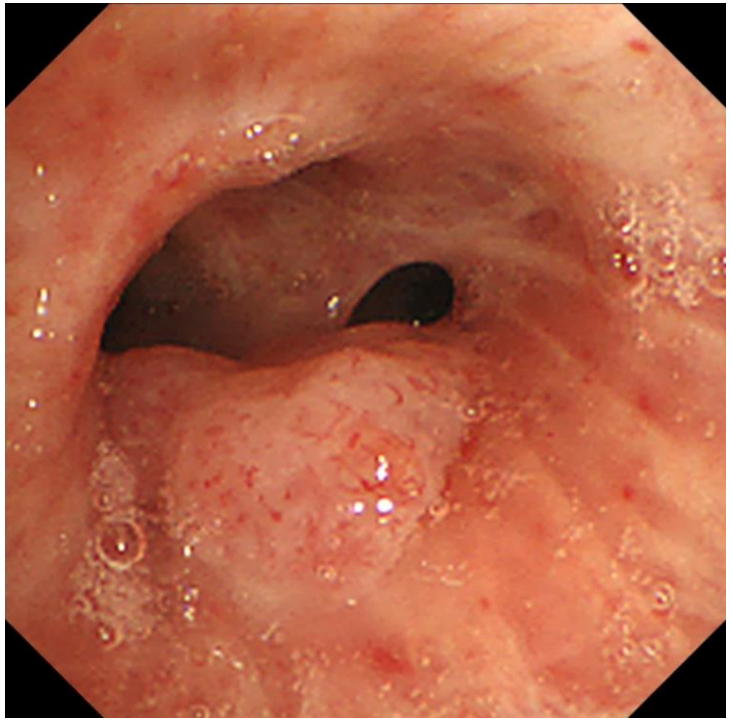
Squamous epithelial hyperplasia with dysplasia, consistent with squamous cell carcinoma in situ

Narrow band image



M/67 CT RUL

r/o secretion on CT scan



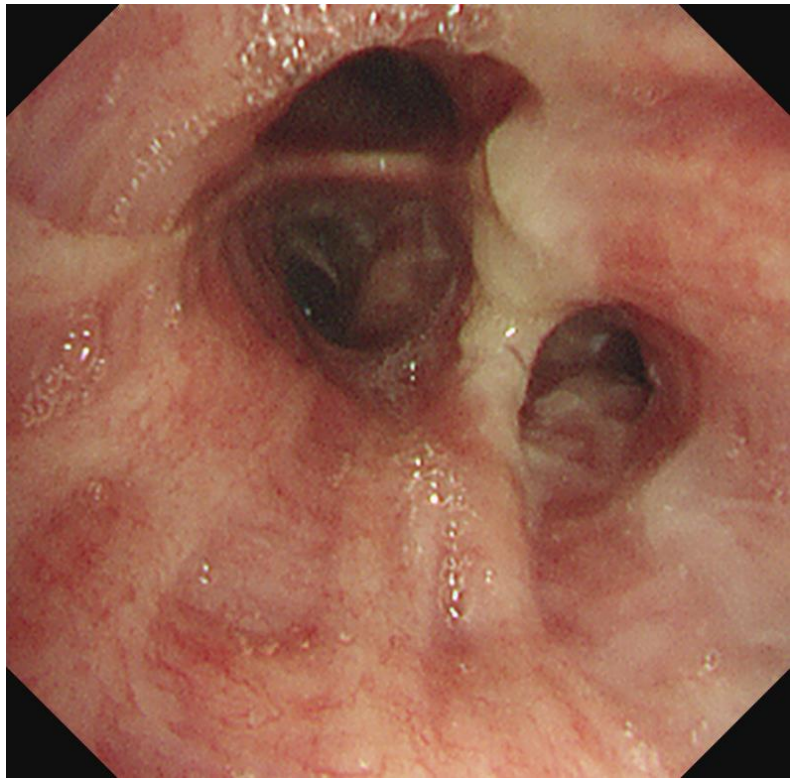
Bronchus, right upper lobe, biopsy;

Squamous cell carcinoma

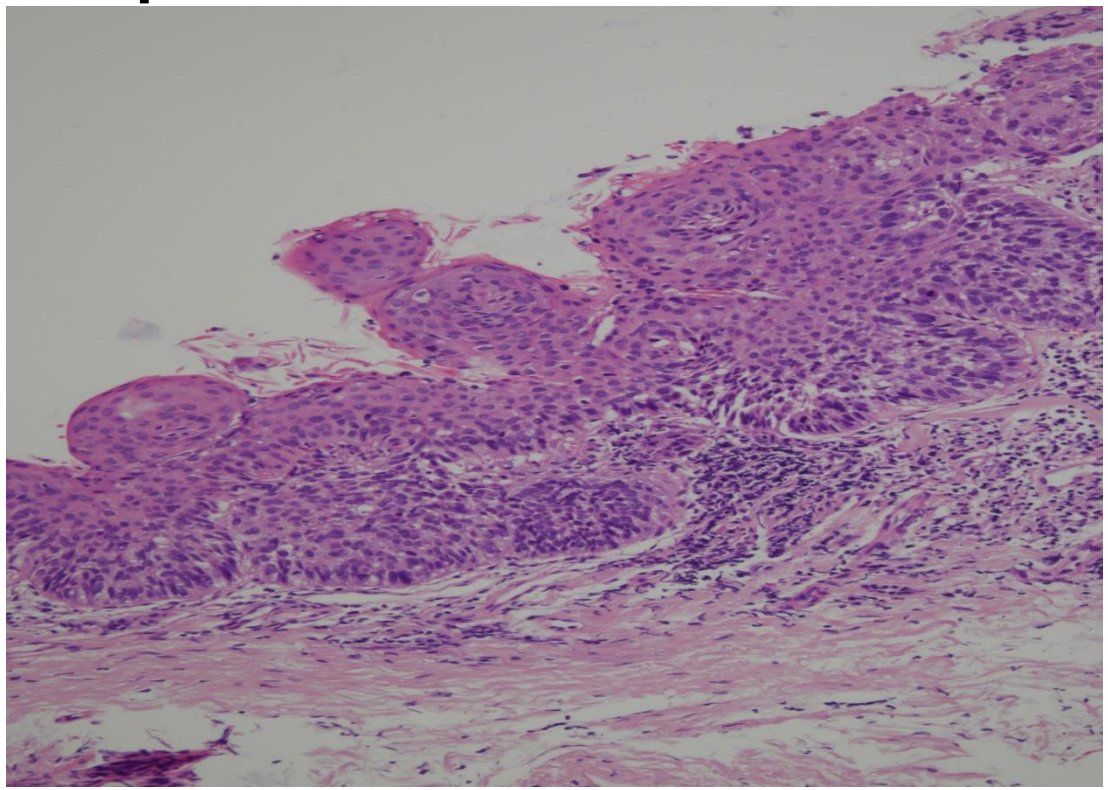
Squamous cell carcinoma

M/70 s/p SqCC, RLLobectomy 2021.4

RUL consolidation, LLL incidental finding



Squamous cell carcinoma with suspicious stromal invasion



Summary(2)

- BAL May provide strong support or clues for a diagnosis or help narrow the differential diagnosis, especially in ILD patients.
- BAL is effective for microbiological analysis and, in terms of sensitivity, is performed in parallel with bronchial washing.
- BAL is an effective and necessary test in diagnosis of aspergillosis, PCP, CMV and TB.
- Be aware of the characteristic findings of bronchoscopy.

Thank you for your time and attention