Lung Manifestations of systemic disease – Regional Royal College Meeting 2019

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North West Anglia Foundation Trusts
Addenbrooke’s Hospital and Peterborough City Hospital
Multi-systemic conditions tend to be treated by organ specific specialists.

Purpose of today is to raise awareness of lung involvement and differential diagnoses.

Case based approach.

Focus on multi-system diseases involve the lung and their management.
Lung Manifestations of systemic disease

- Connective Tissue disease
- Vasculitis
- Gastroenterological - Pharyngeal pouch, pancreatitis, IBD
- Liver disease - Pulmonary AVM, effusion, hypertension
- Endocrine - Obesity, Thyroid, Acromegaly
- Renal - Dialysis, chronic anaemia, renal artery stenosis
- Haematological - Lymphoma, leukaemia, drugs
- Neurological – muscle weakness
- Cardiac – Valvular lung disease, drugs
Lung Manifestations of systemic disease

- Is it disease process?
- Is it the treatment side effect?
- Is it opportunistic infection?
Lung development and structure
Lung development and structure

- Embryonic: E 0-12, wk 8-27
- Pseudoglandular: E 12-15, wk 5-17
- Canalicual: E 15-17, wk 16-26
- Alveolar: E Birth-30, wk 36-3 years

Langman's fig 13-06
Langman's fig 13-07
The circulation of the lung

Leval MR (2005)
Case 1

- 29 year old
- Background renal calculi
- Cough > 8 weeks and fever treated for LRTI x2
- Red lesions on shins
- Redness of eyes and swelling of cheeks
- Foreign travel – Gap year taught English as foreign Language in Uganda age 19 for 6 months
- Attended ED
Case 2

- Looked well
- Parotid swelling
- Erythema nodosum
- BP 121/88
- HR 84
- T 36.3
- SpO2 98% (air)
- Chest clear

- ECG
  - Normal

- Bloods tests
  - CRP 50
  - Full blood count mild lymphopenia 0.9
  - Liver function tests normal
  - Bone profile normal

- D-Dimer
  - 698
Case 1
What would be best fit diagnosis

① Sarcoid
② Tuberculosis
③ Lymphoma
④ IgG4 related disease
⑤ Granulomatosis with polyangiitis (formerly known as Wegener’s)
What would be your next test?

① Serum ACE
② Echocardiogram and 24 hour tape
③ 24 hour urine for hypercalciuria
④ Endobronchial ultrasound and lymph node biopsy
⑤ All the above
⑥ None of the above it is sarcoid
Chest radiographic appearance of sarcoid

<table>
<thead>
<tr>
<th>Stage</th>
<th>Features</th>
<th>Spontaneous resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>normal</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>BHL</td>
<td>Up to 90%</td>
</tr>
<tr>
<td>II</td>
<td>BHL + infiltrates</td>
<td>Up to 70%</td>
</tr>
<tr>
<td>III</td>
<td>Pulmonary infiltrates</td>
<td>Up to 20%</td>
</tr>
<tr>
<td>IV</td>
<td>Pulmonary fibrosis</td>
<td>&lt; 5%</td>
</tr>
</tbody>
</table>
Sarcoid – Clinical features

- Lymph nodes: 95%+ mediastinal, 30% peripheral
- Lungs: > 90%
- Liver: 50-80%
- Kidneys: 10-20% hypercalcaemia, 7-30% renal granuloma
- Musculoskeletal: 25-40%
- Central Nervous System: 10%
- Eyes: 20-50%
- Parotid: < 5%
- Cardiac: 5-10%
- Spleen: 5-10%
- Blood: 4-40%
- Skin: 25%

N Eng J Med 2007 357:2143
### Table 3. Initial Therapy According to Organ and Clinical Status. *

<table>
<thead>
<tr>
<th>Organ</th>
<th>Clinical Findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lungs</td>
<td>Dyspnea plus FEV₁, FVC &lt;70%</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
<tr>
<td></td>
<td>Cough, wheezing</td>
<td>Inhaled corticosteroid</td>
</tr>
<tr>
<td>Eyes</td>
<td>Anterior uveitis</td>
<td>Topical corticosteroid</td>
</tr>
<tr>
<td></td>
<td>Posterior uveitis</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
<tr>
<td></td>
<td>Optic neuritis</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
<tr>
<td>Skin</td>
<td>Lupus pernio</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
<tr>
<td></td>
<td>Plaques, nodules</td>
<td>Hydroxychloroquine, 400 mg/day</td>
</tr>
<tr>
<td></td>
<td>Erythema nodosum</td>
<td>Thalidomide, 100–150 mg/day</td>
</tr>
<tr>
<td></td>
<td>Central nervous system</td>
<td>Methotrexate, 10–15 mg/wk</td>
</tr>
<tr>
<td></td>
<td>Cranial-nerve palsies</td>
<td>Prednisone, 20–40 mg/day</td>
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<tr>
<td></td>
<td>Intracerebral involvement</td>
<td>Hydroxychloroquine, 400 mg/day</td>
</tr>
<tr>
<td>Heart</td>
<td>Complete heart block</td>
<td>NSAID</td>
</tr>
<tr>
<td></td>
<td>Ventricular fibrillation, tachycardia</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
<tr>
<td></td>
<td>Decreased LVEF (&lt;35%)</td>
<td>Azathioprine, 150 mg/day</td>
</tr>
<tr>
<td>Liver</td>
<td>Cholestatic hepatitis with constitutional symptoms</td>
<td>Hydroxychloroquine, 400 mg/day</td>
</tr>
<tr>
<td>Joints and muscles</td>
<td>Arthralgias</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
<tr>
<td></td>
<td>Granulomatous arthritis</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
<tr>
<td></td>
<td>Myositis, myopathy</td>
<td>Prednisone, 20–40 mg/day</td>
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<tr>
<td>Hypercalcuiara and hypercalcemia</td>
<td>Kidney stones, fatigue</td>
<td>Prednisone, 20–40 mg/day</td>
</tr>
</tbody>
</table>

* FEV₁ denotes forced expiratory volume in 1 second, FVC forced vital capacity, LVEF left ventricular ejection fraction, AICD automatic implantable cardiac defibrillator, and NSAID nonsteroidal antiinflammatory drug.

† Most authorities recommend a dual-chamber pacemaker–defibrillator.
Case 2

- 56 yr man
- 1 week history
  Haemoptysis, weight loss over 2 months, variable sweating 3, fatigue, arthralgia
- GP chest X-ray abnormal
- 2 WW referral for lung cancer
Case 2- What investigation should be ordered when reviewed?

① Screening bloods FBC, LFTs, and vasculitis screen
② CT scan
③ PET CT
④ All the above
⑤ Another test
Investigations

- **Bloods**
  - FBC: neutrophilia
  - CRP: 60
  - LFT: normal
  - Electrolytes: Creatinine 120 (risen from baseline 76)
- **CT scan**
- **PET-CT scan**
- **Biopsy**
- **ANCA positive**
- **Urine dip positive for blood and protein**
Anti-neutrophil cytoplasm Ab
**ANCA**
- Proteinase 3 (PR-3)
- Myeloperoxidase (MPO)
- Vasculitis

Neutrophil specific Ab
**NSA**
- Cytoplasmic and nuclear antigens
- Inflammatory bowel disease, Liver disease, Rheumatoid arthritis, Cystic fibrosis etc.

**Caution**
- The utility of ANCA depends on its application in high risk populations to maximise its positive predictive value.
- A negative ANCA does not exclude a vasculitis

Wiik Autoimmunity 2002
Granulomatosis with polyangiitis – Clinical features

ENT - 90% all
- 70% epistaxis
- deafness/OM 32%

Lungs - 68% All
- haemoptysis 37%
- Cavities/nodules 26%
- Infiltrates/effusion 56%
- PE 8%

Kidneys – 70%
- 28% hypertension

Musculoskeletal -39%

Neurological – 28%
- Central Nervous System 5%
- Peripheral 25%

Eyes 30%
- scleritis, lacrimal duct, uveitis

Cardiac 6-24%

Abdominal 2-7%

Skin 20-32%

Arthritis and Rheumatism 2011; 67:257-26
Case 3
Case 4

- 37 year man
- Progressive dyspnoea over 7 days
- Fever, cough
- Seen by GP started amoxycillin 500 mg tds
- Intermittent haemoptysis
- PaO$_2$ 8.5 PaCO$_2$ 3.8 on Fi O$_2$ 0.4
What further tests would you do?

① urine dip, FBC, CRP, Electrolytes, ANCA
② CT scan
③ Bronchoscopy
④ ECHO
⑤ All of the above
⑥ Other
Investigations for vasculitis

All patients
- Urine Dipstick and microscopy
- CXR
- Blood - FBC, CRP, UE

Selected tests depending on presentation
- Blood
  - ANCA (AASV), Anti GBM, complement, cryoglobulin
  - Blood culture, Hepatitis B and C, HIV
  - IgE (EGPA-CSS)
- Pulmonary physiology
  - Dynamic test, Flow volume loop
- Bronchoscopy
  - To exclude infection and confirm alveolar haemorrhage. Rarely are mucosal or transbronchial biopsies useful.
- Biopsy of relevant tissue - Nasal, Lung, kidney
- Radiology
  - HRCT
- Neurological
  - Nerve conduction
- Cardiology
  - Echocardiogram
An Approach for Investigation of infiltrates

Acute history with Pulmonary infiltrates

Unstable
- Begin empirical treatment for infection
  - Start comprehensive evaluation
  - procalcitonin

Stable
- Comprehensive evaluation
  - CT Scan
  - Vasculitis screen
  - Blood cultures
  - Viral screen
  - bronchoscopy

Adjust therapy on basis of investigations and response to therapy

Consider surgical biopsy

Modified from Chest 2004
BJ Haem 2016
56 female
Haemosiderin laden macrophages

- Usually found after day 3, peak day 7, present for up to 2 months
- Also found in other condition
- Needs to be used with other tests
Transbronchial biopsy

- Diffuse alveolar haemorrhage with alveolar walls infiltrated
What is the likely diagnosis

1. Granulomatosis with polyangiitis
2. Microscopic polyangiitis
3. Anti-GBM disease
4. SLE
5. unsure
Key point: If ANCA positive check anti-GBM

Papris et al 2008, Critical Care
Comparison of the main causes of pulmonary-renal haemorrhage

<table>
<thead>
<tr>
<th></th>
<th>GPA</th>
<th>MPA</th>
<th>EGPA</th>
<th>AntiGBM</th>
<th>SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence Per 10^6 population</strong></td>
<td>8.5-10.3</td>
<td>6.8-8.9</td>
<td>0.5-3.7</td>
<td>3-4</td>
<td>60-350</td>
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<tr>
<td><strong>Organ involvement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs - haemorrhage</td>
<td>17-50%</td>
<td>25-50%</td>
<td>rare</td>
<td>80-94%</td>
<td>4-30%</td>
</tr>
<tr>
<td>Lung - infiltrates</td>
<td>&gt;15%</td>
<td>&gt;50%</td>
<td>40%</td>
<td>90-94%</td>
<td>50-70%</td>
</tr>
<tr>
<td>kidneys</td>
<td>70-80%</td>
<td>80-90%</td>
<td>25%</td>
<td>41-71%</td>
<td>often</td>
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<tr>
<td>Other organs</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
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<tr>
<td>Asthma</td>
<td>no</td>
<td>no</td>
<td>yes</td>
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<td><strong>Laboratory findings</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Anti-GBM</td>
<td>no</td>
<td>possible</td>
<td>no</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>P-ANCA (MPO)</td>
<td>possible</td>
<td>yes</td>
<td>possible</td>
<td>no</td>
<td>no</td>
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<tr>
<td>C-ANCA (PR3)</td>
<td>yes</td>
<td>possible</td>
<td>possible</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>ANA</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>5 year survival</td>
<td>50%</td>
<td>40%</td>
<td>20-30%</td>
<td>80%</td>
<td>80%</td>
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</table>
# Treatment of ANCA associated systemic vasculitis (AASV)

<table>
<thead>
<tr>
<th>Clinical Class</th>
<th>Localised</th>
<th>Early systemic</th>
<th>Generalised systemic</th>
<th>Severe</th>
<th>Refractory</th>
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<tbody>
<tr>
<td>Constitutional</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Renal function</td>
<td>Creatinine &lt; 120 umol/l</td>
<td>Creatinine &lt; 500 umol/l</td>
<td>Creatinine &gt; 500 umol/l</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Threatened vital organ function</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Induction</td>
<td>Single agent (CS, AZA, MTX)</td>
<td>CYC or MTX + CS</td>
<td>CYC+CS</td>
<td>CYC+CS+PE</td>
<td>Investigational drugs iv IgG, RTX, DSG, anti-TNFα</td>
</tr>
<tr>
<td>Dosage</td>
<td>CS (1mg/kg/day) tapered down to 0.25 mg/kg od by 12 weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended</td>
<td>AZA (1mg/kg/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MTX (20–25 mg/week)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Oral CYC (1.5–2mg/kg/day)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>PE Seven exchanges with first 2 weeks with 60ml/kg plasma exchanged for 5% HAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
<td>Once remission for is achieved for 3 to 6 months transition to maintenance treatment with AZA (1-2 mg/kg/day) or MTX (20–25mg/week) should be considered</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Del Piero et al 2009
Case 4
18yr female
Case 6 PFTs

<table>
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<tr>
<th></th>
<th>July</th>
<th>Dec</th>
<th>%</th>
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<tbody>
<tr>
<td>FEV₁</td>
<td>3.02</td>
<td>1.21</td>
<td>37</td>
</tr>
<tr>
<td>FVC</td>
<td>3.92</td>
<td>2.34</td>
<td>68</td>
</tr>
<tr>
<td>PEFR</td>
<td>240</td>
<td>76</td>
<td>24</td>
</tr>
</tbody>
</table>
What is wrong with her lung function?

- a) Obstructive – large airways
- b) Obstructive – small airways
- c) Restrictive
- d) Mixed
- e) Don’t know

<table>
<thead>
<tr>
<th></th>
<th>July</th>
<th>Dec</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>FEV(_1)</td>
<td>3.02</td>
<td>1.21</td>
<td>37</td>
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<tr>
<td>FVC</td>
<td>3.92</td>
<td>2.34</td>
<td>68</td>
</tr>
<tr>
<td>PEFR</td>
<td>240</td>
<td>76</td>
<td>24</td>
</tr>
</tbody>
</table>
NORMAL TRACHEAL ANATOMY

TOP FIVE DIFFERENTIAL DIAGNOSES

1. Inflammatory Bowel Disease: UC, Crohn’s
2. Amyloidosis
3. Granulomatosis with Polyangitis
4. Relapsing Polychondritis
5. Tracheobronchopathica Osteobronchoplastica

Differentials of Diffuse Tracheal Thickening (1)

NORMAL TRACHEA ON CT

ULCERATIVE COLITIS/CROHNS

Differentials of Diffuse Tracheal Thickening

AMYLOIDOSIS

GRANULOMATOSIS WITH POLYANGITIS

Differentials of Diffuse Tracheal Thickening (3)

RELAPSING POLYCHONDRITE | TRACHEOBRONCHOPATHICA OSTEOCHRONDROPLASTICA:

Sub-glottic balloon dilatation
Flow volume loop after 2 weeks

<table>
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<tr>
<th></th>
<th>July</th>
<th>pre</th>
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<tr>
<td>FEV₁</td>
<td>3.02</td>
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<td>2.61</td>
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<tr>
<td>FVC</td>
<td>3.92</td>
<td>2.34</td>
<td>4.12</td>
</tr>
<tr>
<td>PEFR</td>
<td>240</td>
<td>76</td>
<td>160</td>
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</tbody>
</table>
Subglottic stenosis in GPA

- Upto 20% of patients will develop disease
- Female preponderance 2:1
- Age of diagnosis <30
- Invariably have otolaryngeal disease
- Stenosis frequently occurs in the absence of disease activity at other sites
- Presenting clinical symptoms dyspnoea, hoarseness, stridor, wheeze, haemoptysis
- Plain CXR was normal in 18% of patients with tracheobronchial disease.
- Disease responds to immunosuppression therapy in 1/4 of cases.
Review of Connective tissue disease lung
Lung involvement in connective tissue disease

**Small airways disease**
- Bronchiolitis (RhA)
- Bronchiectasis (RhA)

**Lung parenchyma**
- Alveolitis
- Fibrosis
- Organising pneumonia
- Haemorrhage
- Drug reactions

**Other**
- Infection
- Respiratory muscle dysfunction
- Atelectasis

**Large airways disease – RhA <1%**

**Nodular lung disease**
- Rheumatoid nodules

**Pulmonary hypertension**
- Systemic sclerosis

**Pleural disease**
- SLE, RhA
### PFT Patterns in Lung Disease

<table>
<thead>
<tr>
<th></th>
<th>Fibrosis</th>
<th>Acute Alveolitis</th>
<th>Obstruction</th>
<th>Pulmonary Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>N</td>
</tr>
<tr>
<td>FVC</td>
<td>↓</td>
<td>↓</td>
<td>↔</td>
<td>N</td>
</tr>
<tr>
<td>PEFR</td>
<td>↔ ↔</td>
<td>↔ ↔</td>
<td>↓</td>
<td>N</td>
</tr>
<tr>
<td>TLC</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>N</td>
</tr>
<tr>
<td>RV</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>N</td>
</tr>
<tr>
<td>TLCO</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
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<tr>
<td>KCO</td>
<td>↓</td>
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</table>
Life expectancy with extra-articular manifestations of RA
HRCT Rheumatoid
Comparison of connective tissue lung disease

Table 1
Frequency of Pulmonary Disease Involvement in Various Collagen Vascular Diseases

<table>
<thead>
<tr>
<th>Pulmonary Disease</th>
<th>Systemic Lupus Erythematosus</th>
<th>Rheumatoid Arthritis</th>
<th>Progressive Systemic Sclerosis</th>
<th>Polymyositis or Dermatomyositis</th>
<th>Sjögren Syndrome</th>
<th>Mixed Connective Tissue Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual interstitial pneumonia</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>++</td>
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<tr>
<td>Nonspecific interstitial pneumonia</td>
<td>+</td>
<td>+</td>
<td>++++</td>
<td>++++</td>
<td>+</td>
<td>++++</td>
</tr>
<tr>
<td>Diffuse alveolar damage</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>. .</td>
<td>. .</td>
</tr>
<tr>
<td>BOOP</td>
<td>+</td>
<td>. .</td>
<td>+</td>
<td>+</td>
<td>. .</td>
<td>. .</td>
</tr>
<tr>
<td>Lymphocytic interstitial pneumonia</td>
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<td>. .</td>
<td>. .</td>
<td>. .</td>
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<tr>
<td>Hemorrhage</td>
<td>+++</td>
<td>. .</td>
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<tr>
<td>Airway disease</td>
<td>. .</td>
<td>++</td>
<td>. .</td>
<td>. .</td>
<td>. .</td>
<td>. .</td>
</tr>
</tbody>
</table>

Note.—Plus signs (+) indicate relative frequency of pulmonary disease involvement (+ = lowest frequency, ++++ = highest frequency). Empty cells ( . . ) indicate no pulmonary disease involvement.
UIP
apicobasal, honeycombing, traction bronchiectasis, reticulation and ground glass
- UIP
  - Heterogenous
  - Honeycombing
  - Traction bronchiectasis
- Patchy fibrosis
- Fibroblastic focus of loose organising connective tissue hallmark
- NSIP
  - Homogenous
  - Sub pleural Reticulation
  - Micronodules
  - Ground glass

NSIP
Cellular NSIP uniform appearance of interstitial inflammation
Key point – Connective tissue disease associated has better prognosis than similar UIP or NSIP
- Methotrexate pneumonitis rare (0.53%)
- Risks for development include
  - Age >60
  - Previous use DMARDs
  - Hypoalbuminaemia
  - DM
  - Pleural disease
  - Prior ILD related to RA
- Treatment withdrawal
  MTX + steroids
- Outcome good with full recovery in >82%
Bronchiliosis

- Mosaicism
- Expiratory air trapping
- Small airways disease
  - Reduced FEV
  - Reduced FVC
  - Reduced MEF
  - Reduced TLCO
  - Increased RV/TLC
Rheumatoid Pleural effusion

- Glucose
  - <2mmol/l in 40% thought to arise from
    - 1) relative block of glucose transport from blood to pleural space
    - 2) increased utilization
- LDH >2 ULN
  - the efflux of glucose metabolism products are relatively blocked
- Total protein of >30g/l
- pH of <7.0 - CO2 transport from the pleural space is blocked
- Positive rheumatoid factor, low complement, cholesterol crystals, predominant lymphocytes, and characteristically few mesothelial cells
Case 5
Case 5 - Is this vasculitis?

- 54 yr old female
- Background
  - Seronegative arthritis
  - Insulin Dependent DM (20’s)
  - CKD3 with nephrotic range proteinuria
  - Pancreatic insufficiency
  - Pleuropericarditis
  - Asthma
- Fatigue and cough
Based on history and radiology what is the best diagnosis?

1. Sarcoid
2. Connective tissue disease with serositis (inflammation – pleura and pericardium)
3. Granulomatosis with polyangiitis
4. IgG4 disease
5. Infection
IgG4 related disease - Overview

**Pituitary gland**
Headache, visual field deficit, lactation, diabetes insipidus (IgG4-related hypophysitis)

**Lacrimal gland**
Swollen upper eyelids, dry eyes (IgG4-related dacryoadenitis)

**Salivary gland**
Swollen submandibular portions, dry mouth (IgG4-related sialadenitis)

**Thyroid**
Neck tightness, malaise, oedema (IgG4-related thyroid disease)

**Respiratory tract**
Cough; similar to bronchial asthma

**Kidney**
Often asymptomatic; hydrenephrosis in renal hilum involvement (IgG4-related kidney disease)

**Lung**
Cough, often asymptomatic (IgG4-related lung disease)

**Retroperitoneal cavity**
Fever, malaise, aneurysm in cases with periaortitis (IgG4-related retroperitoneal fibrosis)

**Biliary tract**
Obstructive jaundice (IgG4-related sclerosing cholangitis)

**Pancreas**
Upper abdominal discomfort, obstructive jaundice, impaired glucose tolerance (type I autoimmune pancreatitis)

**Prostate gland**
Frequent urination, feelings of residual urine (IgG4-related prostatitis)

**Lymph nodes**
Swollen lymph nodes (IgG4-related lymphadenopathy)
Case 6
Lung involvement in IgG4 related disease

**Small airways disease**
- Asthma
- Combined asthma emphysema

**Large airways disease** — stenosis

**Lung parenchyma**
- Alveolitis
- Fibrosis
- Organising pneumonia

**Pseudotumours**
- Nodules / mass

**Mediastinal lymphadenopathy**
**Medistinal fibrosis**

**Pleural disease**
- Effusions
- Pleural thickening
- Pleural masses
IgG4 sclerosing disease

- Male predominance (70-80%) with Median age 60-65
- Elevated IgG4 (70-90%)
  - compared to 5% normal population
  - Can be normal in serum with disease

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Definitive</th>
<th>Probable</th>
<th>Possible</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dense lymphoplasmacytic infiltrate</td>
<td>2 or more</td>
<td>1 feature Radiology</td>
<td></td>
</tr>
<tr>
<td>2. Storiform fibrosis</td>
<td></td>
<td>1 or more feature radiology</td>
<td></td>
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<tr>
<td>3. Obliterative phlebitis</td>
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<tr>
<td>1. Immunostaining</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>IgG4+/IgG+plasma cell ratio &gt;40</td>
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<td>2. IgG4+ cell &gt; 10 HPF</td>
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<tr>
<td>IgG4 &gt; 1.35 g/l</td>
<td>no</td>
<td>yes</td>
<td>Yes</td>
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</tbody>
</table>

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Treatment of IgG4 ISD

- Prednisolone 1mg/kg 2 weeks
- Weaned to <10mg /day over 3 months
- Low dose maintenance dose 5-10mg/day associated with less relapse
- Treatment failure
  - Cyclophosphamide, cyclosporin
  - rituximab
The lung can be directly involved by disease processes. I have overviewed the main processes which are auto-immune. Diseases considered mainly of the lung such as can present atypically and involve other organs. The problem remains how to differentiate between infection, direct involvement of the lung by disease, drug reaction, or other causes. A detailed history and examination are important. The appropriate investigation in the clinical context is important to maximise utility of these tests. Treatment is guided by the severity of disease and organ involvement.
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www.vasculitis.org