IIP CLASSIFICATION REVISION: SUMMARY OF NEW ASPECTS

- ATS/ERS IIP Classification Revision: Updates existing entities
  - NSIP accepted and defined
    - Smoking-related IPs – better understood
    - Acute exacerbation – better defined
- Validates CRP/multidisciplinary approach
- Recognition of new entities and histologic patterns
- Mixed patterns and cases that are difficult to classify – addressed in more detail than in 2002
Disease overlap in Interstitial Lung Disease

Sameness... Coexistence... Transformation....
Disease overlap in Interstitial Lung Disease

Sameness... Coexistence... Transformation....
Disease overlap in Interstitial Lung Disease

Sameness..., Coexistence..., Transformation....
Disease overlap in Interstitial Lung Disease

LIP AIP RB-ILD OP
UIP DIP sarcoid NSIP
LAM HP Idiopathic pulmonary haemorrhage

Langerhans cell histiocytosis

Sameness... Coexistence... Transformation.....
ATS/ERS subdivision of NSIP

Cellular

Fibrotic

ATS/ERS workshop ï AJRCCM 2008;177:1338-47

Sixty-seven cases (out of 305)

Mean age was 52 years, 67% were women, 69% were never smokers,

Dyspnea (96%) and cough (87%); 69% had restriction.

HRCT - lower lung predominant, reticular pattern (87%) with traction bronchiectasis (82%) and volume loss (77%).

Five-year survival was 82.3%.

Distinct clinical entity that occurs mostly in middle-aged women who are never-smokers. The prognosis of NSIP is very good.
NSIP versus DIP
Smoking-related interstitial lung disease
Histopathology: F-NSIP

MDT review:
- HRCT favours chr HP
- History of bird exposure

Levels cut on blocké

FINAL DIAGNOSIS:
CHRONIC HYPERSENSITIVITY PNEUMONITIS
ATS/ERS workshop – relatively few at the centre of the circle
2 year old female

Increasing shortness of breath, ?ILD

c.218T>C in the SFTP gene

Fibrotic NSIP
Surfactant protein deficiency
Diffuse lung disease in infancy and childhood: expanding the chILD classification (0-2 years/2-18 years/mimics of ILD).

Deutsch G et al. AJRCCM 2007:176:1120-8


Diffuse Lung Disease in Biopsied Children 2 to 18 Years of Age. Application of the chILD Classification Scheme.

AIMS OF PRESENTATION

• Review classifications in thoracic pathology and how they have changed in the past 15 years.
• Understand how and why classifications are formed and evolve
• Consider the requirements for future classifications
• Update on thoracic pathology
FUTURE CLASSIFICATION ISSUES

Increasing importance of immunohistochemistry and genetics in the diagnosis of lung tumours.

TREATMENT OPTIONS will also drive changes in classification

Conventional chemotherapy
- Pemetrexed (non-squamous NSCLC),
- Bevacizumab (non-squamous NSCLC)

Targeted agents
- EGFR mutations: Gefitinib, Erlotinib, Afatinib (T790M mutation)
- ALK translocations: Crizotinib, Alectinib
- ROS translocations: Crizotinib

Immunomodulatory drugs
- Therapeutic vaccines priming the immune response
  - e.g., MAGE-A3 (vaccine targeting MAGE-A3), TG4010 (vaccine encoding MUC-1 and IL-2), IMA901 (peptide vaccine), racotumomab (anti-idiotypic vaccine), sipuleucel-T (Provenge, cellular therapeutic vaccine), nelipepimut-S (E75/NeuVax, peptide vaccine)
- Agents targeting T-cell checkpoint dysregulation
  - e.g., nivolumab (anti-PD-1), pembrolizumab (anti-PD-1), MPDL3280A (anti-PD-L1), MEDI4736 (anti-PD-L1), ipilimumab (anti-CTLA-4), tremelimumab (anti-CTLA-4)
What is the most efficient way of testing for the ALK translocation?

NEED FOR AGREEMENT ON STANDARDISED METHODOLOGIES IF IHC/FISH/NGS ARE TO BE USED AS PART OF TUMOUR CLASSIFICATION SYSTEMS
FUTURE CLASSIFICATION ISSUES

Increasing importance of immunohistochemistry and genetics in the diagnosis of lung tumours.

TREATMENT OPTIONS

- Conventional chemotherapy
- Targeted agents
  - EGFR mutations: Gefitinib, Erlotinib, Afatinib (T790M mutation)
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TISSUE SAMPLES AND TESTING OPTIONS
# Sampling and analysis

<table>
<thead>
<tr>
<th>2004</th>
<th>2014</th>
<th>2015-25</th>
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<tbody>
<tr>
<td>Sputum</td>
<td>Washings</td>
<td>Washings</td>
</tr>
<tr>
<td>Brushings, Washings</td>
<td>Biopsies</td>
<td>Biopsies</td>
</tr>
<tr>
<td>Biopsies</td>
<td>Core needle</td>
<td>Core needle</td>
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<tr>
<td>Core needle</td>
<td>TBNA (cytology)</td>
<td>TBNA (biopsy)</td>
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<tr>
<td>Mediastinoscopy</td>
<td>VATS/open resection</td>
<td>VATS/open resection</td>
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<tr>
<td>Open resections</td>
<td>Systematic nodal resection</td>
<td>Systematic nodal resection</td>
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<tr>
<td></td>
<td>Circulating tumour cells</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Blood/plasma (ctDNA)</td>
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<tr>
<td></td>
<td>Breath</td>
<td></td>
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<tr>
<td></td>
<td>No tissue (Cyber knife/RFA)</td>
<td>No tissue (Cyber knife/RFA)</td>
</tr>
</tbody>
</table>
Is there a future for the (lung) pathologist...?
The cycle of change

CLINICAL
Pre-examination → Examination → Post-examination

HISTOPATHOLOGY
Diagnosis, Tissue Handling, Timeliness, Interpretation, Sample types,

Basic Science

Translational

Service Development

RESEARCH

UNDERPINNED BY ROBUST AND CLINICALLY RELEVANT CLASSIFICATION SYSTEMS
Get involved...!

Å Researché Service Developmenté Service Evaluationé Audité.

Å Critical review of classifications (interobserver studies), atypical presentations, new antibodies and is a very good way to learn, present and publish


CONCLUSIONS

AIMS
- Review important classifications in thoracic pathology and how they have changed in the past 15 years.
- Understand how and why classifications are formed and evolve
- Consider the requirements for future classifications
- Update on thoracic pathology

A CLASSIFICATION NEEDS TO BE
- REPRODUCIBLE (strict and recognisable set of criteria)
- GLOBALLY APPLICABLE (everyone can apply)
- THOROUGH (which can deal with atypical variants)
- DYNAMIC
  - MORPHOLOGY...BIOLOGY...MOLECULAR PATHOLOGY...MULTIDISCIPLINARY
  - CAN BECOME SIMPLER NOT MORE COMPLICATED
  - DOES NOT HAVE TO CHANGE IF IT IS WORKING
  - SPEED OF CHANGE EVER INCREASING
  - CHANGES IN ONE CLASSIFICATION SYSTEM MAY AFFECT ANOTHER
- NOT EMBARRASSING (evidence-based and validated)
  - GREATER Sized COHORTS THROUGH INTERNATIONAL COLLABORATIONS
CLASSIFICATION LARGELY DEVELOPED WITHIN THE IASLC PATHOLOGY COMMITTEE

Forty Years of the International Association for Study of Lung Cancer Pathology Committee

Ming-Sound Tsao, MD, FRCPC,* William D. Travis, MD,† Elisabeth Brambilla, MD, PhD,‡ Andrew G. Nicholson, MD, FRCPath,§ Masayuki Noguchi, MD, PhD,|| and Fred R. Hirsch, MD, PhD,¶ on behalf of the IASLC Pathology Committee

The “international” multidisciplinary approach that represents the IASLC culture in research, education, and practice in clinical management of lung cancer patients have paved the way for integrating pathology practice into the new era of personalized cancer care. JTO 9:1740-1749, 2015
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