



PNEUMOLOGIA 2016

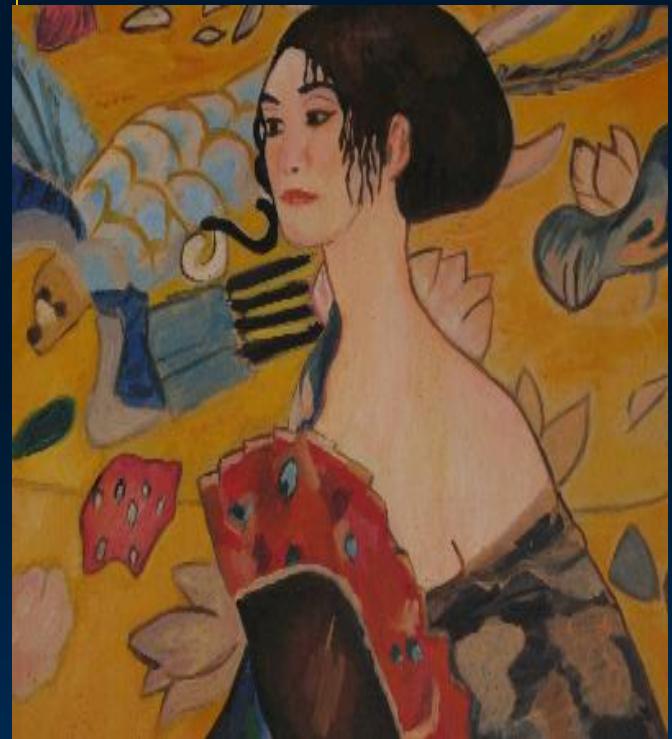
Milano, 16 – 18 giugno 2016 · Centro Congressi Palazzo delle Stelline

AAE: diagnosi e terapia

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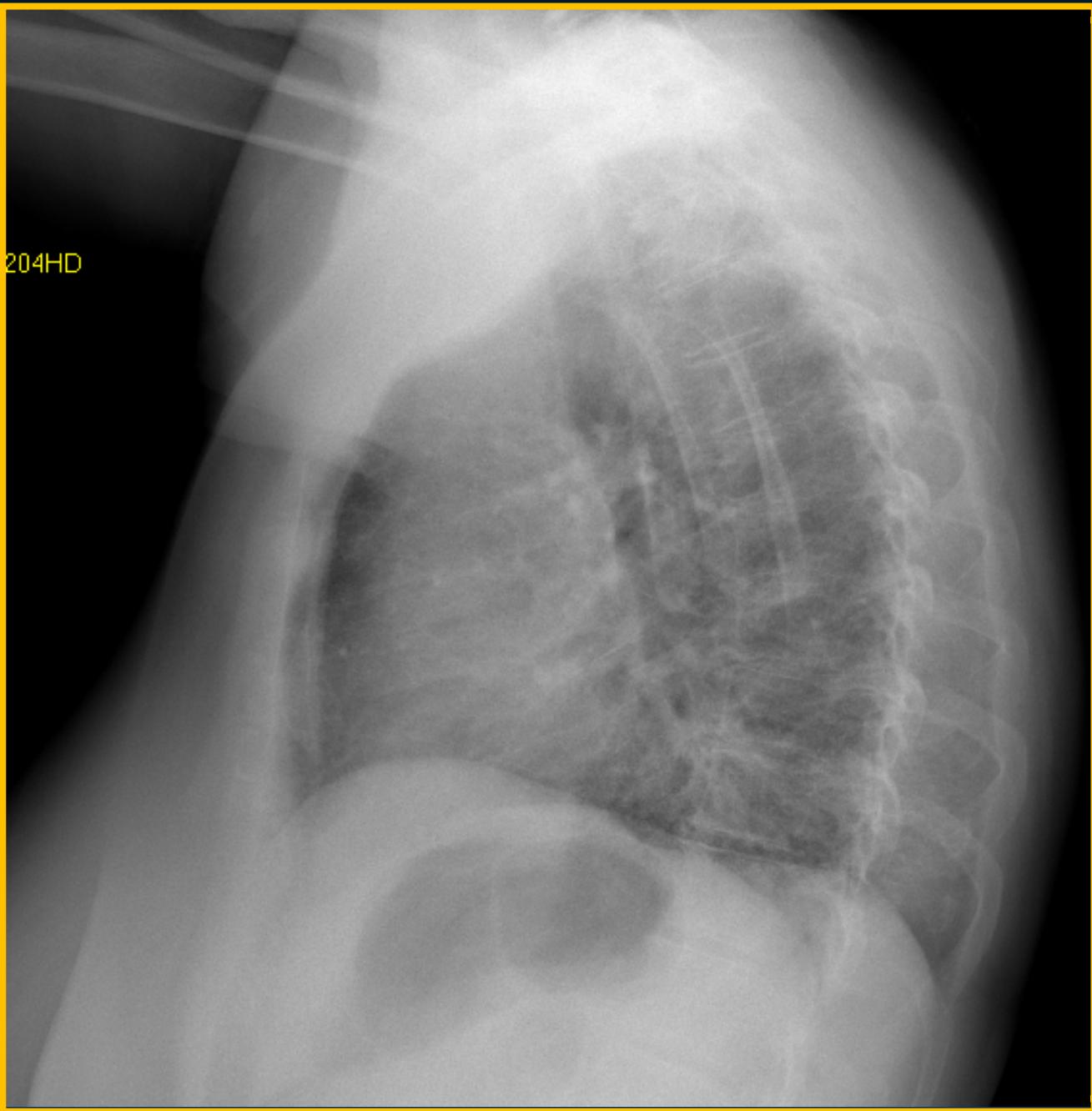
- Donna di 58 anni, non fumatrice
- Non intolleranze farmacologiche note
- Casalinga
- Frattura traumatica del piede destro sottoposta ad osteosintesi
- Ipertensione arteriosa sistemica in terapia con ACE-inibitore



- Ad ottobre 2011: episodio simil-influenzale cui residua tosse produttiva di secrezioni mucose
- Successiva comparsa di dispnea da sforzo ingravescente



204HD



- ◆ Relativo benessere fino a maggio 2012 quando per la comparsa dei medesimi sintomi esegue nuovo Rx torace: invariato
- ◆ PFR: FEV1 81%, VC 79%, FVC 80%, TLC 70%

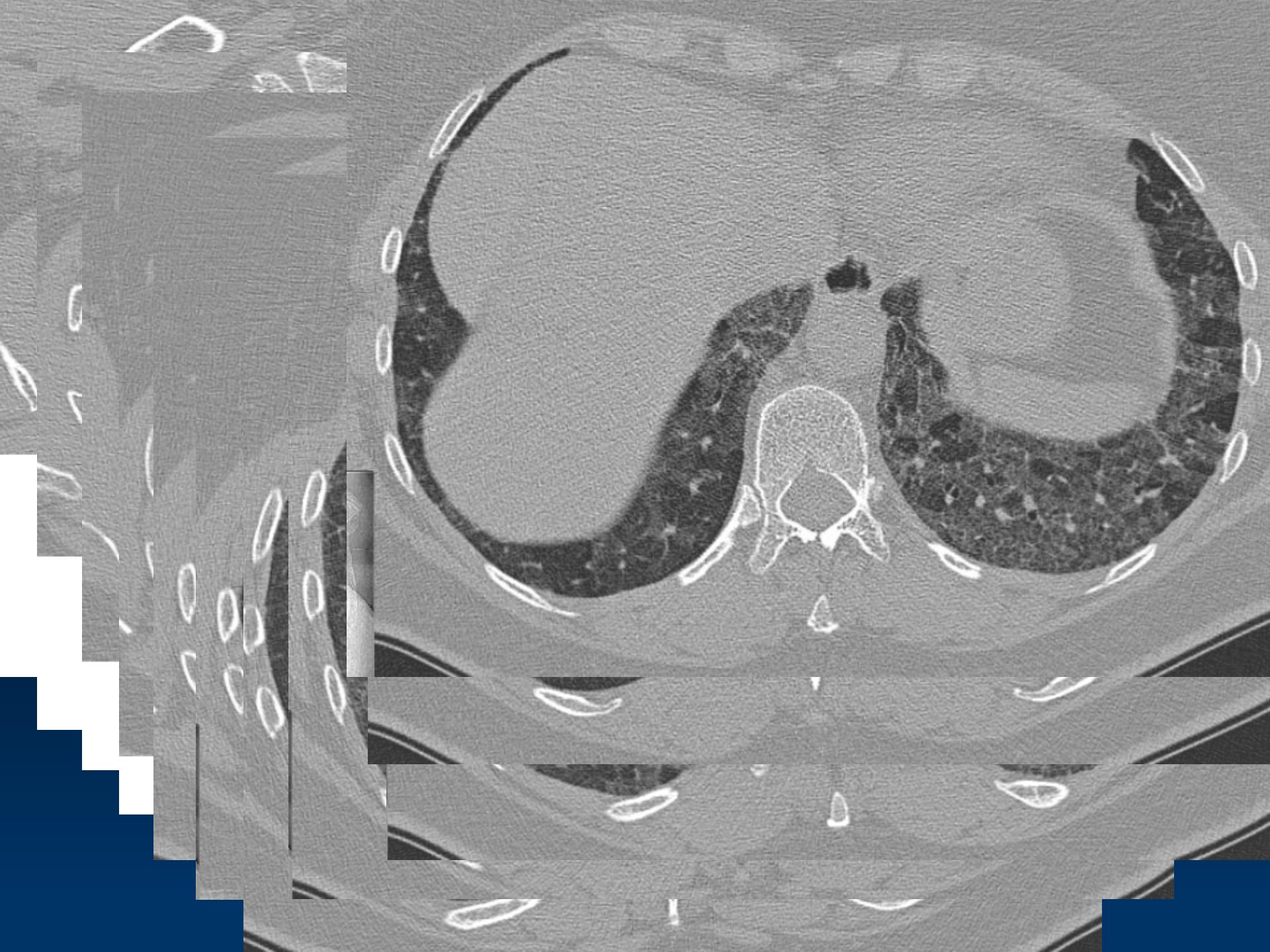


- Prescritta c/o altra Struttura terapia inalatoria con salmeterolo/fluticasone senza beneficio
- Sospeso ACE-inibitore



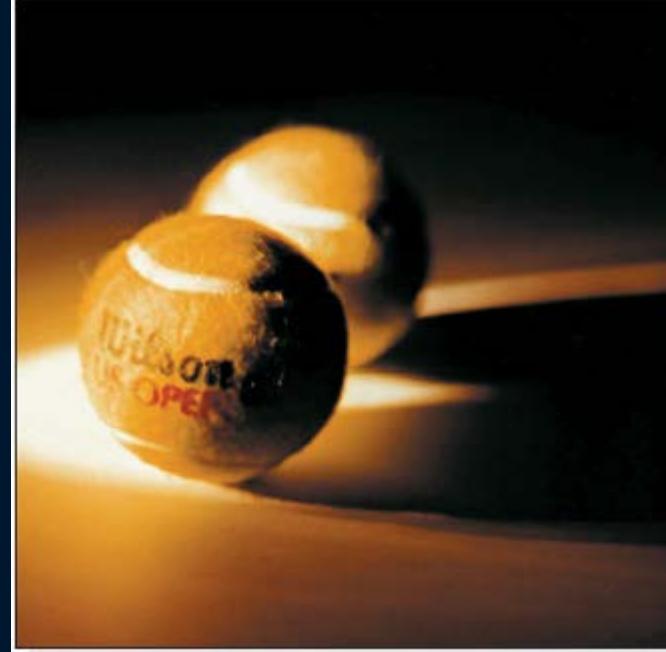
- ◆ Riferisce benessere durante soggiorno in ambiente marino
- ◆ A novembre 2012 nuovo Rx torace: invariato (interstiziopatia bi-basale !)
- ◆ A gennaio 2013 esegue HRCT del torace







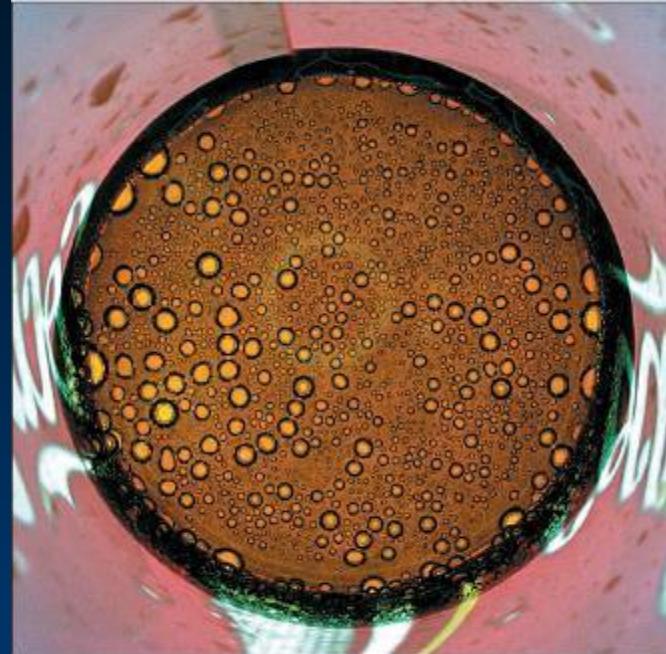
Reticular pattern □



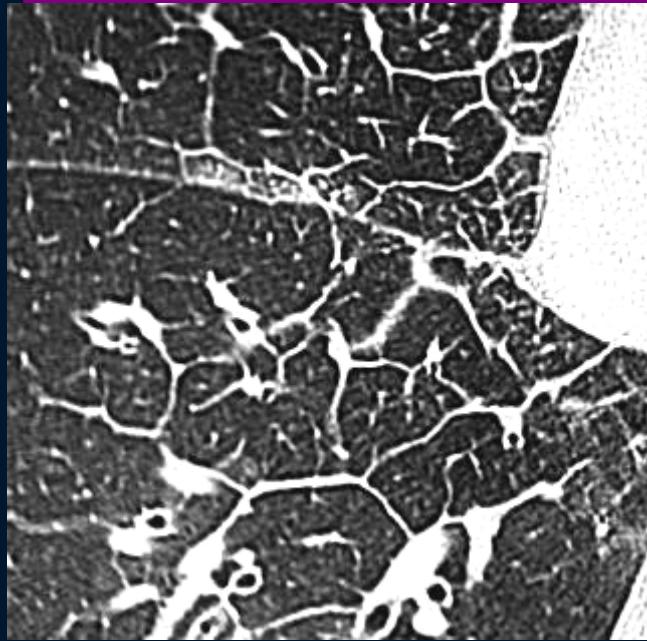
Nodular pattern ●



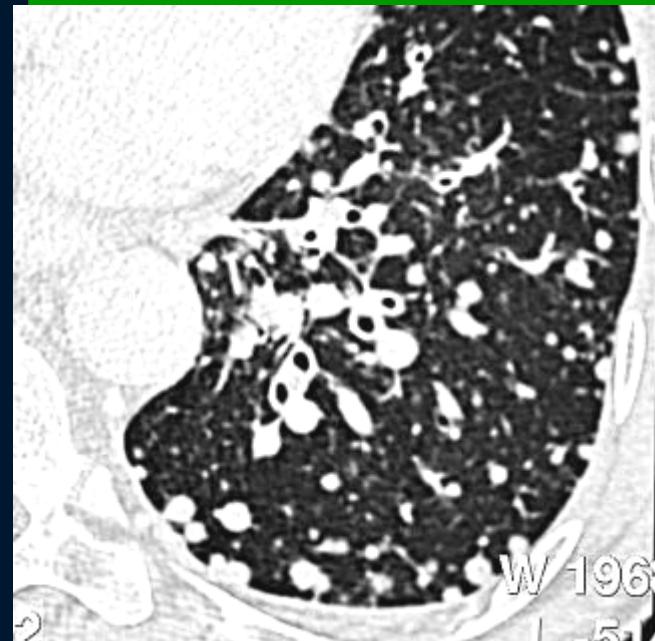
Alveolar pattern ☺



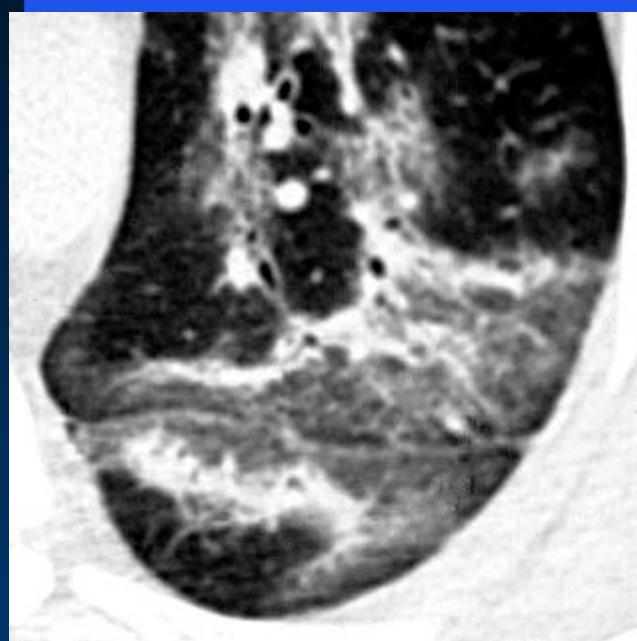
Cystic pattern ○



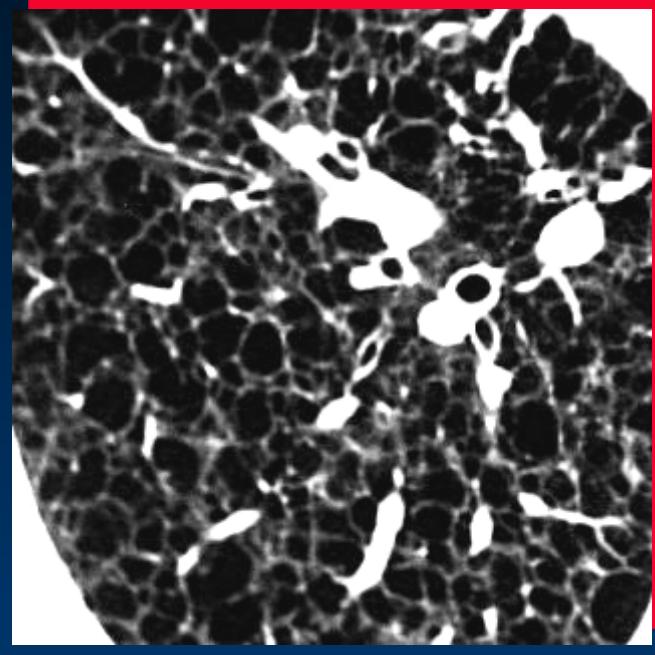
Reticular pattern □



Nodular pattern ●



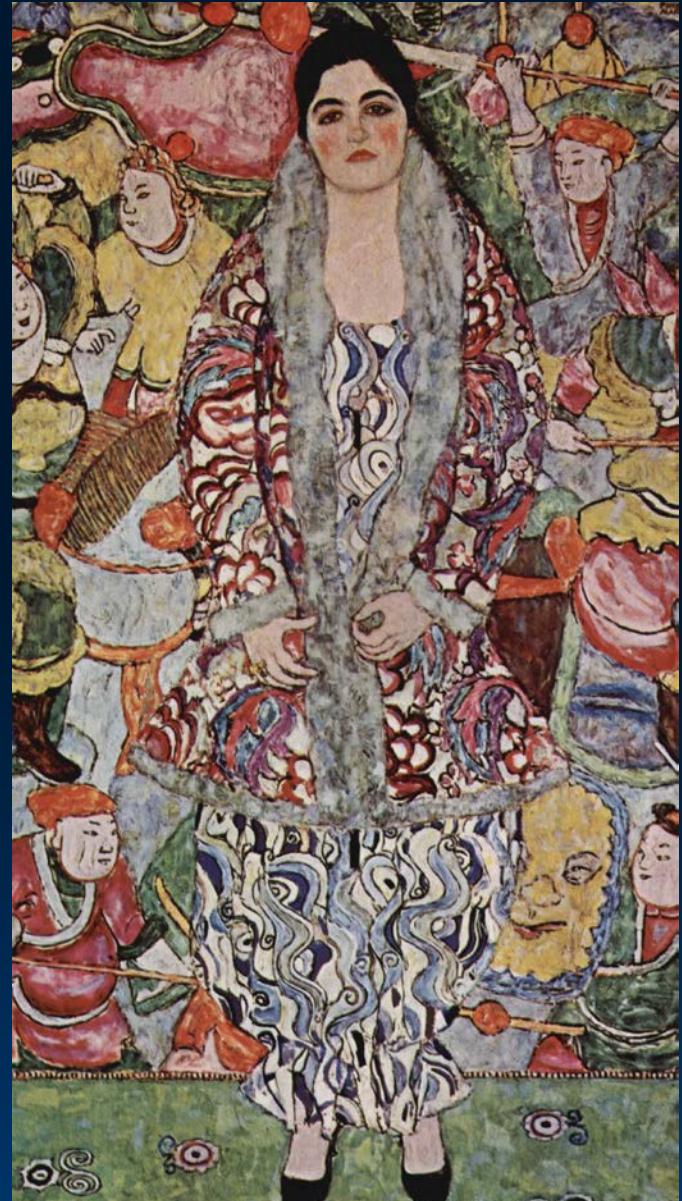
Alveolar pattern ☓



Cystic pattern ○

From: Maffessanti & Dalpiaz, Diffuse Lung Diseases, Springer 2006

- Buone condizioni generali, eupnoica a riposo
- Decubito indifferente attivo
- Emitoraci simmetrici, ipoespandibili
- Fini crepitii bi-basali
- Toni cardiaci validi, ritmici, nornoespandibili
- Non edemi declivi
- Parametri vitali: PA 115/80, FC 76 bpm, Sat. O₂ in AA 95%, FR 22 atti/min, apiretica. Peso 74 kg



- EGA in aria ambiente: PaO₂ 70.5 mmHg, PaCO₂ 41.5 mmHg, pH 7.42, Sat.O₂ 94.6%.
- 6MWT in AA: Sat.O₂ iniziale 95%, Sat.O₂ finale 83%; test interrotto dopo 200 metri e al III° minuto per desaturazione
- 6MWT in O₂-terapia 4L/min: Sat.O₂ iniziale 99%, finale 89%, percorsi 450 metri
- PFR: lieve deficit restrittivo associato a **severa** riduzione di DLCO (FVC 1.28L 76%, FEV1/FVC 84%, TLC 2.93L 69%, RV 79%, DLCO 32%)

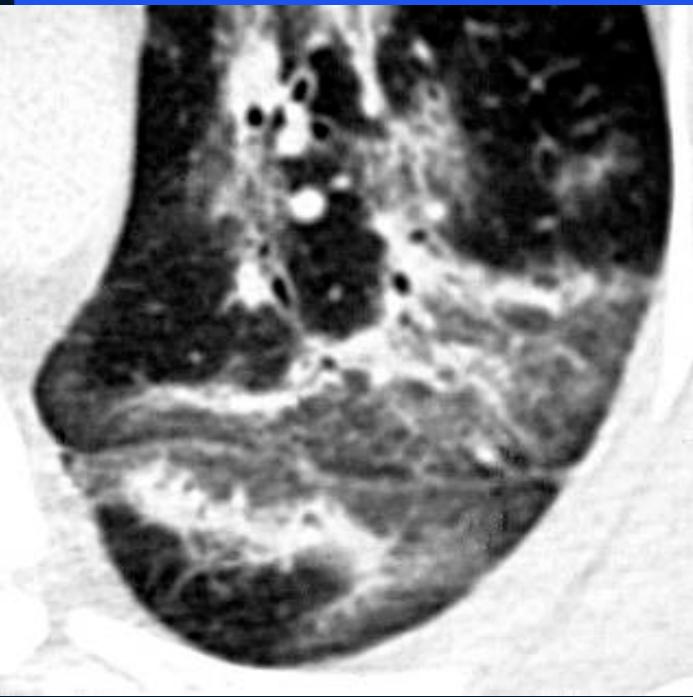


- Nulla di rilevante, indici di flogosi nella norma.
- ANA positivi 1/160, pattern omogeneo
- Restante autoimmunità negativa

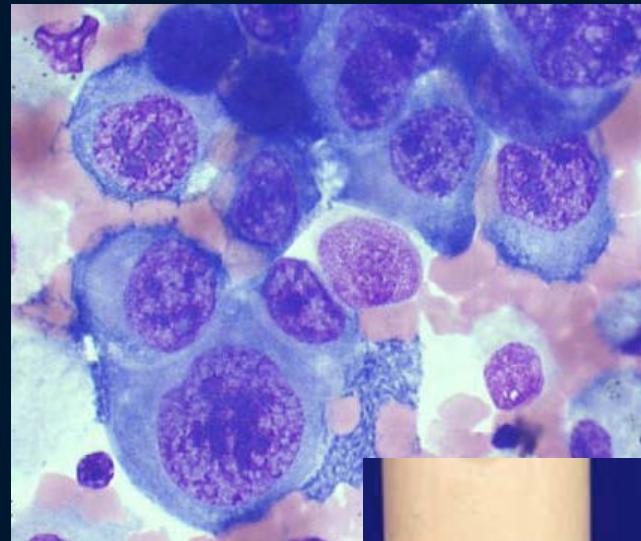
FBS per BAL

- Cellularità totale: 145500/mL
- Conta cellulare: Linfoцитi 70%, Macrofagi 24%, PMN 6%
- Sottoclassi linfoцитarie: CD8 60%, CD4 30.5%





Alveolar pattern ✎



AAE acuta, AIP, ARDS,
BAC, CEP, DIP, EPA
alveolare, farmaci
(pneumopatia da
amiodarone), MALToma,
OP, proteinosi alveolare,
PCP, vasculite emorragica

Lymphocytic cellular pattern

- >15% lymphocytes
- Sarcoidosis
- Nonspecific interstitial pneumonia (NSIP)
- Hypersensitivity pneumonitis
- Drug induced pneumonitis
- Collagen vascular diseases
- Radiation pneumonitis
- Cryptogenic organizing pneumonia (COP)
- Lymphoproliferative disorders

Am J Respir Crit Care Med 2012; 185; 1004-14

From: Maffessanti & Dalpiaz, Diffuse Lung Diseases, Springer 2006

Positività delle precipitine
(IgG) rivolte vs Ag di
derivazione aviaria



POLMONITE DA IPERSENSIBILITA'

Definizione

The report of the NHLBI/ORD* workshop stated that

"~~Hypersensitivity pneumonitis is a type of pulmonary disease known as extrinsic allergic alveolitis, is a complex health syndrome involving symptoms of dyspnea and cough resulting from the inhalation response of antigen to which the patient has been previously sensitized~~ parenchyma in response to inhalation exposure to a large variety of antigens."

*National Heart, Lung and Blood Institute in collaboration with the Office of Rare Diseases
Lacasse Y et al. Chest 2012; 142: 208

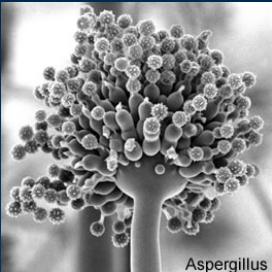
POLMONITE DA IPERSENSIBILITA' definizione

- 1) HP is a pulmonary disease with or without systemic manifestations (such as fever and weight loss);
- 2) It is caused by the inhalation of an antigen to which the subject is sensitized and hyperresponsive;
- 3) Sensitization and exposure alone in the absence of symptoms do not define the disease

POLMONITE DA IPERSENSIBILITA' principali antigeni responsabili

BATTERI e Micobatteri, MUFFE, LIEVITI E PROTEINE
DI DERIVAZIONE AVIARIA, sostanze chimiche

- *Saccharopolyspora rectivirgula*
- *Saccharomyces cerevisiae*
- *Penicillium casei*, sp et al.
- *Alternaria* sp
- *Candida albicans*
- *Aspergillus niger* e *fumigatus*
- *Curvularia lunata*
-



POLMONITE DA IPERSENSIBILITA' principali antigeni responsabili

Table 1. Common Types of Hypersensitivity Pneumonitis According to Major Classes of Antigens

Class of Antigens	Specific Antigens	Sources	Type of Disease
Bacteria	<i>Saccharopolyspora rectivirgula</i> , <i>Thermoactinomyces vulgaris</i>	Moldy hay, grain	Farmer's lung
Fungi, yeasts	<i>Aspergillus</i> species	Moldy hay, grain	Farmer's lung
	<i>Aspergillus</i> species	Moldy compost and mushrooms	Mushrooms worker's lung
	<i>Trichosporon cutaneum</i>	Contaminated houses	Japanese summer-type HP
	<i>Penicillium</i> species	Moldy cork	Suberosis
	<i>Penicillium casei</i>	Moldy cheese or cheese casings	Cheese washer's lung
	<i>Alternaria</i> species	Contaminated wood pulp or dust	Woodworker's lung
Mycobacteria	<i>Mycobacterium avium-intracellularare</i>	Mold on ceiling, tub water	Hot tub lung
	<i>Mycobacterium avium-intracellularare</i>	Mist from pool water, sprays and fountains	Swimming pool lung
Animal proteins	Proteins in avian droppings and serum and on feathers	Parakeets, budgerigars, pigeons, parrots, cockatiels, ducks	Pigeon breeder's lung, bird fancier's lung
	Avian proteins	Feather beds, pillow, duvets	Feather duvet lung
	Silkworm proteins	Dust from silkworm larvae and cocoons	Silk production HP
Chemicals	Diisocyanates, trimellitic anhydride	Polyurethane foams, spray paints, dyes, glues	Chemical worker's lung

POLMONITE DA IPERSENSIBILITA'

caratteristiche epidemiologiche e cliniche

Characteristics	HP study (n= 199)	Mayo Clinic (n= 85)
Sex, % women	56	62
Age, mean ± SD, y	55 ± 14	53 ± 14
Current smokers	6	2
Symptoms		
Dyspnea	98	93
Cough	91	65
Flulike symptoms	34	33
Chest discomfort	35	24
Signs		
Crackles	87	56
Wheezes	16	13
Digital clubbing	21	5

POLMONITE DA IPERSENSIBILITA'

cause e alterazioni funzionali

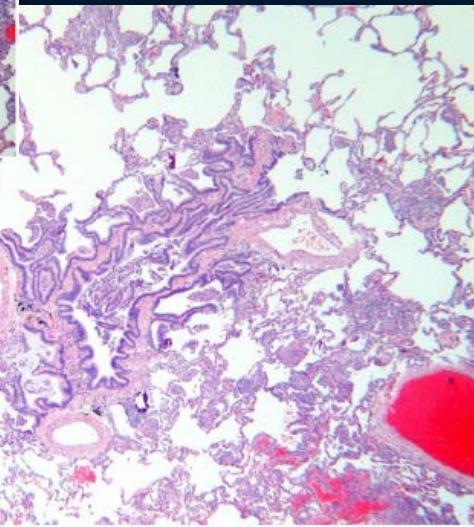
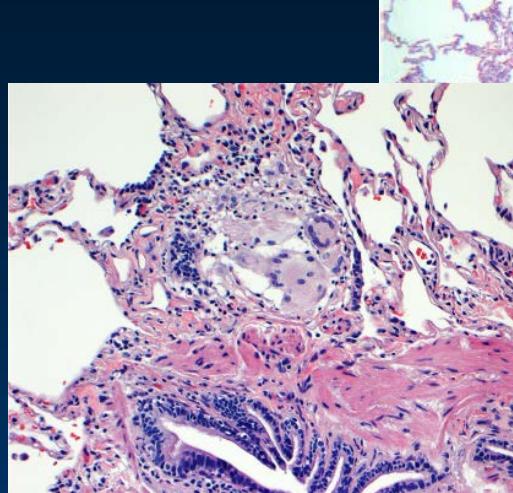
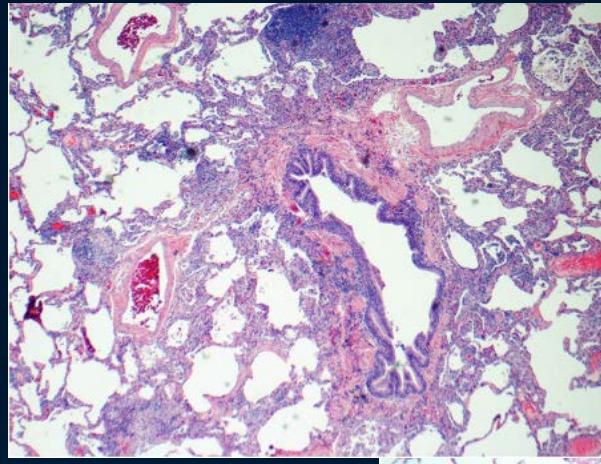
Characteristics	HP study (n= 199)	Mayo Clinic (n= 85)
Causes		
Not identified	1.5	25
Avian antigens	66	34
Farmers' lung	19	11
Hot tub lung	0	21
Molds	13	9
Pulmonary function		
Obstructive pattern	1	16
Restrictive pattern	64	53
Mixed pattern	1	Not reported
Nonspecific abnormalities	1	12
Normal	34	10

POLMONITE DA IPERSENSIBILITA' aspetti anatomo-patologici

1. Cellular bronchiolitis (possible variable degrees of peribronchiolar fibrosis)
2. Diffuse chronic interstitial infiltrates
3. Poorly circumscribed interstitial non necrotizing granulomas
4. Giant cells in the alveoli or interstitium (Schaumann bodies)

NB: emphysema!

NB: NSIP, UIP, BOOP might be the sole histological expressions of the disease



POLMONITE DA IPERSENSIBILITA' aspetti tomografici

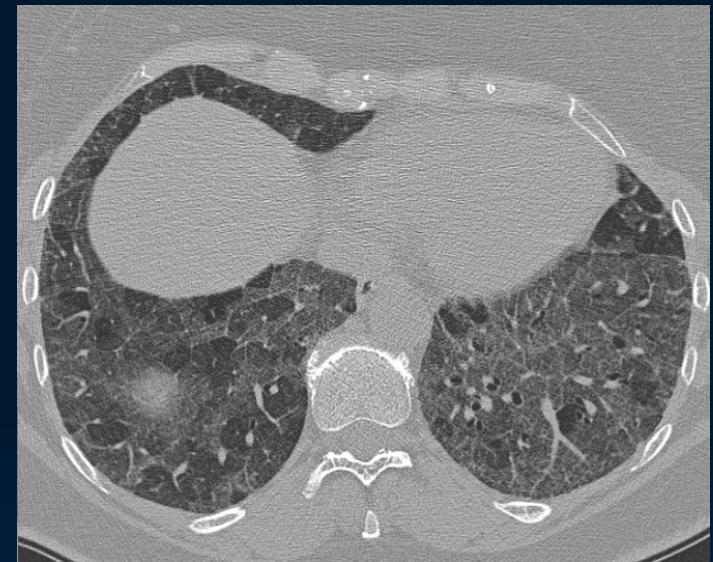
Numerous small round centrolobular opacities, usually < 5 mm, sometimes with well-defined borders and referred to as nodules (cellular bronchiolitis)



Ground-glass opacities usually bilateral and symmetric, sometimes patchy (that represent chronic interstitial inflammation)

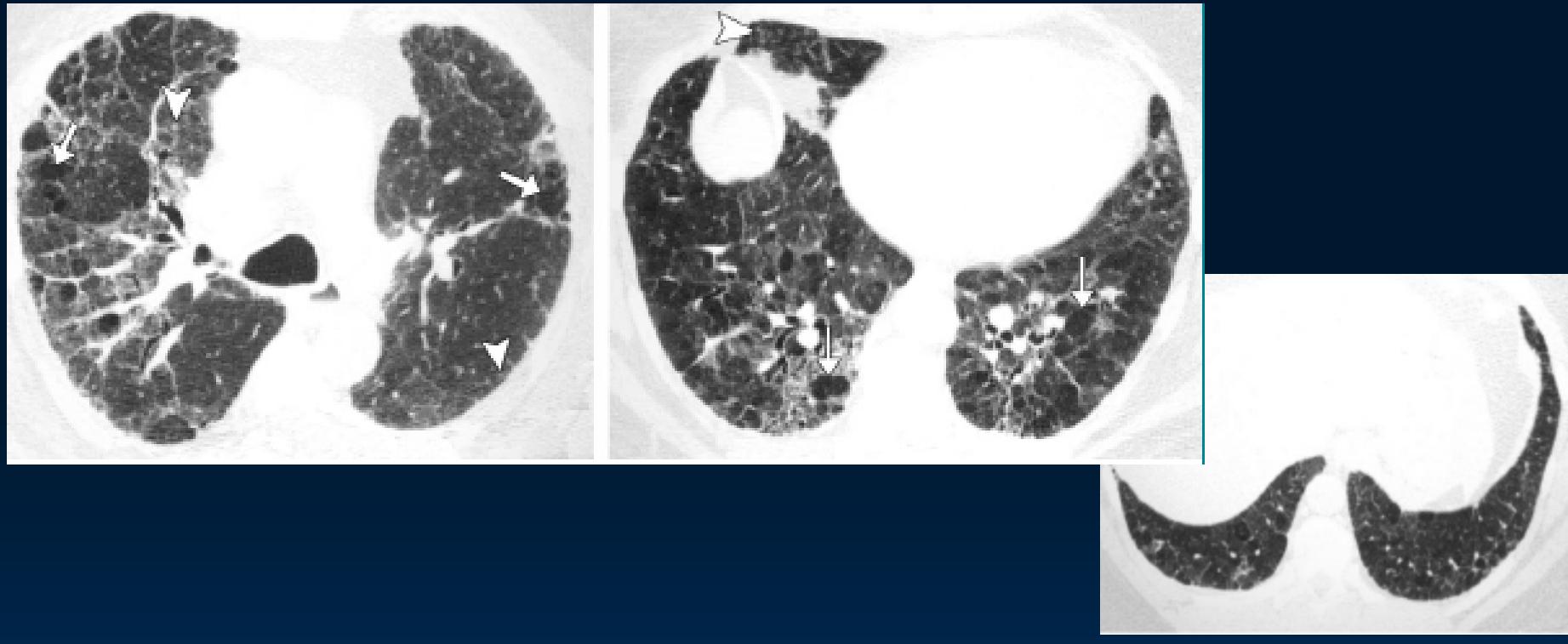
POLMONITE DA IPERSENSIBILITA' aspetti tomografici

Hypoattenuation and
hypovascularity of scattered
secondary lobules:
MOSAIC ASPECT
HEADCHEESE SIGN



When fibrosis is present,
we can see reticulation,
mainly in the middle
portion of the lungs

Chronic hypersensitivity pneumonitis: differentiation from UIP and NSIP using thin-section CT



The HRCT findings most helpful in differentiating chronic HP from IPF and NSIP are lobular areas with decreased attenuation and vascularity, centrilobular nodules and lack of lower zone predominance of abnormalities

Chronic hypersensitivity pneumonitis: differentiation from UIP

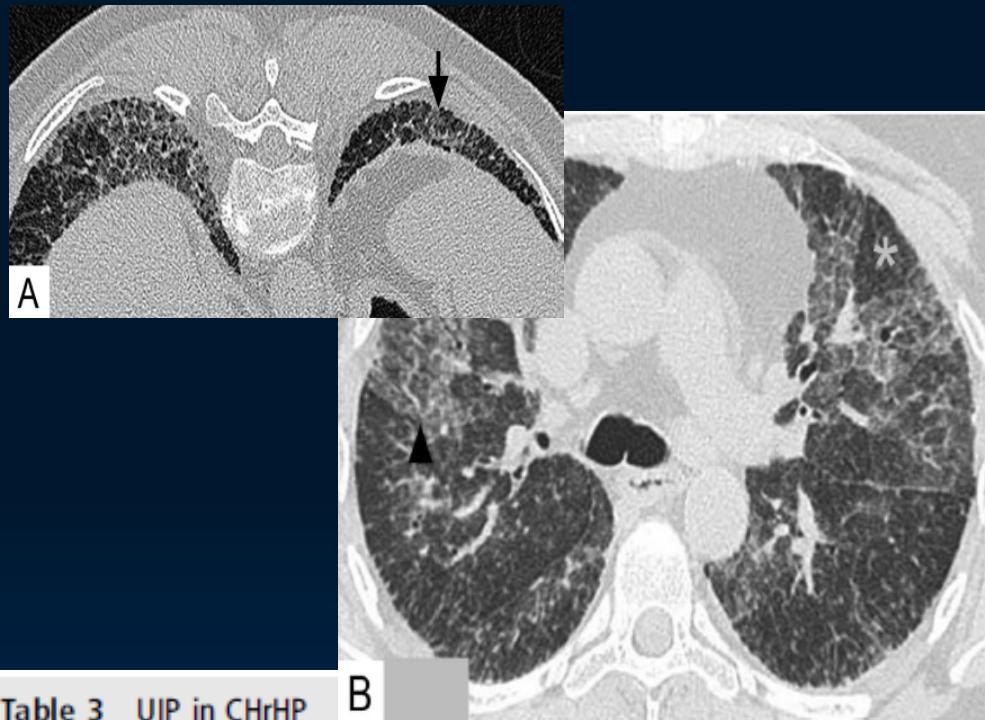
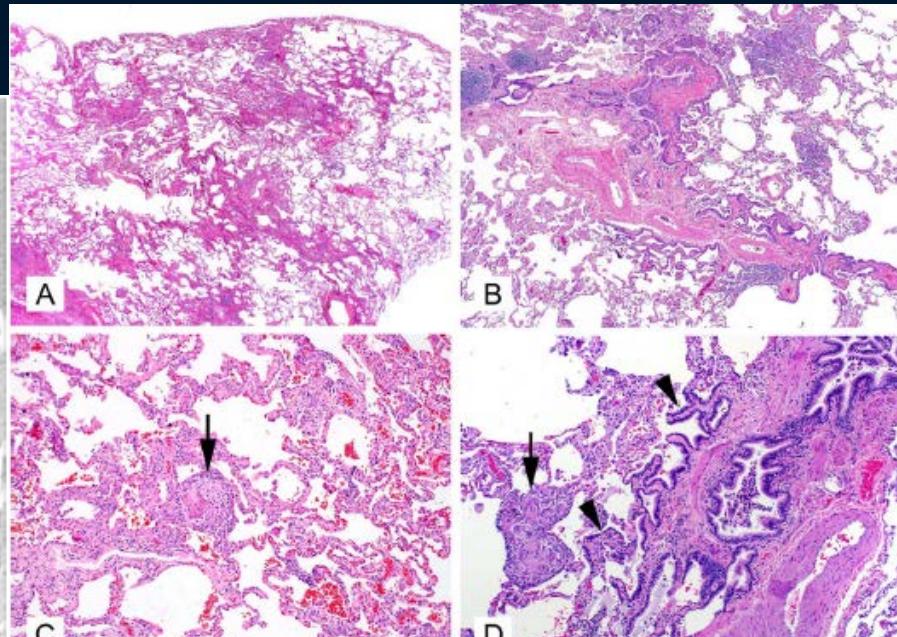


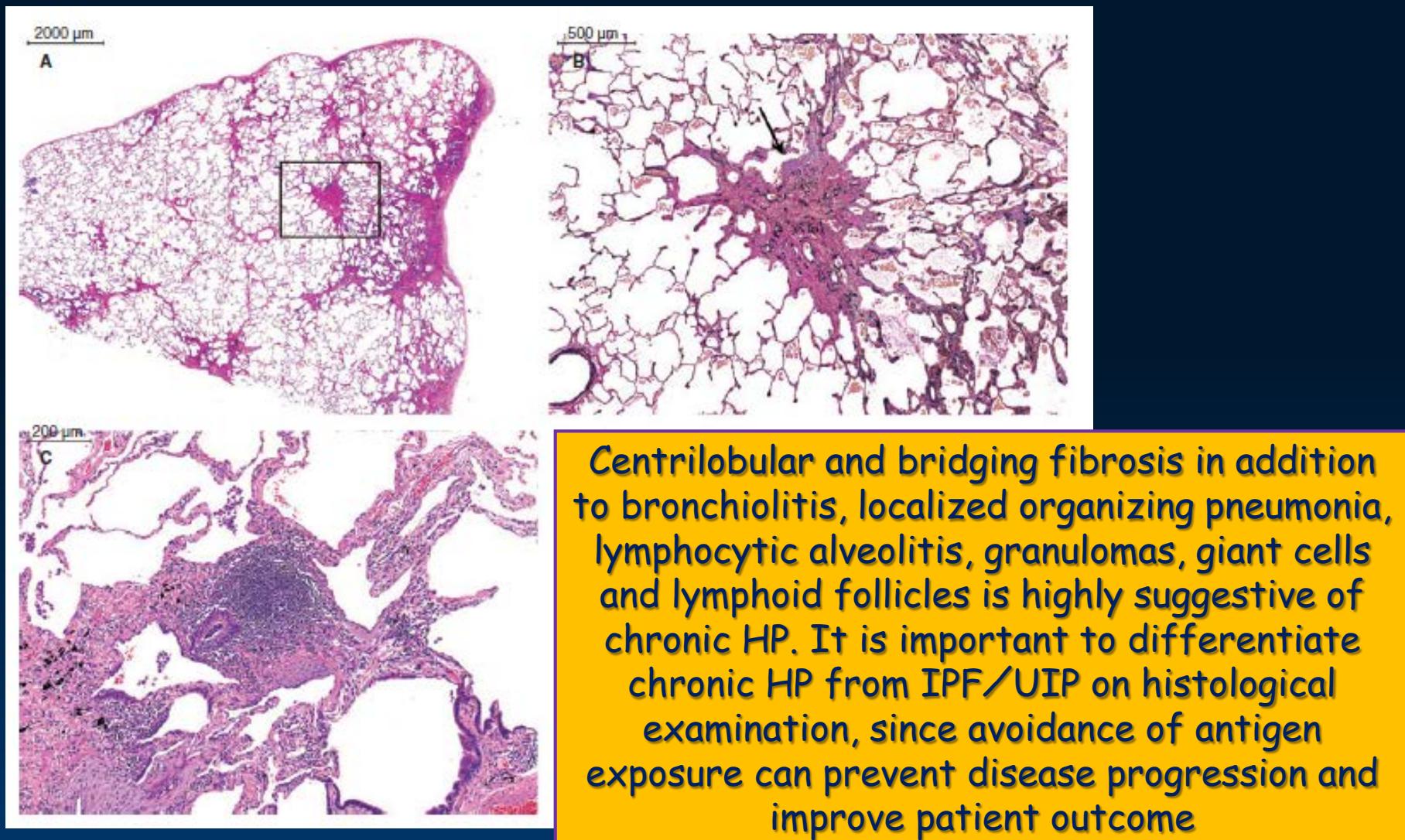
Table 3 UIP in ChHP

There is often fibrosis and honeycombing in the lung bases similar to idiopathic pulmonary fibrosis, however in the same patient there is also fibrosis in the upper lobes and air-trapping



Characteristics of advanced fibrosis in chronic hypersensitivity pneumonitis include centrilobular fibrosis with relative sparing of the septum and pleura, centrilobular interstitial inflammation with extensive peribronchiolar metaplasia and poorly formed granulomas

Chronic hypersensitivity pneumonitis: differentiation from UIP



POLMONITE DA IPERSENSIBILITA' criteri diagnostici

A number of diagnostic criteria recommendations
for HP have been published.

None of these sets of criteria has been validated.

Clinical history is of outmost importance in the
diagnosis of HP.

Currently, no "gold standard" exists for diagnosing HP

POLMONITE DA IPERSENSIBILITA' criteri diagnostici

Table 29.4 Suggested working diagnostic criteria of hypersensitivity pneumonitis

1. Exposure to offending antigens: revealed by history^a and/or microbiological investigations of the environment and/or presence of serum precipitins against antigen(s) from a standardized panel of antigen(s), or against antigen(s) present in the own environment of the individual
2. Symptoms compatible with HP and basal crepitant rales^b
3. BAL fluid lymphocytosis^c
4. Findings compatible with HP on HRCT
5. Decreased DLCO and/or arterial hypoxemia (or decreased blood saturation) at rest or during exercise

Adapted from Thaon et al. [37] with permission

Criteria 3 and 4 represent the “gold standard” for the diagnosis and are obligatory

Diagnosis of HP is definite when the five criteria are present. In absence, diagnosis requires a positive natural challenge and if negative, pulmonary samples for histological confirmation

^aRequires the use of a comprehensive list of etiologies like that from the GERM’O’P questionnaire summarized Table 29.5 or like that published in Ref [37]

^bBasal crepitant rales cannot be considered as an obligatory criteria as it is an operator-dependant indicator and must be considered as an additional criteria

^cExcept if BAL is performed very shortly after acute phase or exposure. In this case, BAL may to be done again some days later

POLMONITE DA IPERSENSIBILITA' "nuova" classificazione

	Type 1 HP (e.g., farmer's lung)	Type 2 HP (e.g., bird fancier-s lung)
Exposure	Usually massive and intermittent Usually microorganisms (fungi and actinomycetes)	Usually chronic insidious Usually lowdose of avian antigens
Clinical behaviour	Primarily acute/subacute : higher frequency of fever and recurrent episodes. Usual phlegm More recurrent systemic symptoms (chills, body aches)	Recurrent BFL: cough and mild exertional dyspnea, low-grade fever Insidious BFL: progressive dyspnea; clubbing
Lung function tests	Mild restrictive abnormalities that resolve Airflow obstruction (usually mild) seen in chronic disease	Restrictive pattern Hypoxemia at rest or exercise common
Lung imaging studies	Chest X-ray: frequently normal HRCT: ground glass opacities, predominating in the lower lobes, fine centrilobular nodules, hyperlucent areas Most frequent long-term sequelae: mild emphysema often sparing the upper parts of the lung	Chest X-ray: frequently abnormal HRCT: irregular reticular opacities, traction bronchiectasis and honeycombing superimposed to subacute changes (e.g. ground-glass opacities, nodules, hyperlucent areas)
BAL and precipitins	Non-specific for differentiating both types	Non-specific for differentiating both types
Lung biopsy	Small, poorly-formed noncaseating granulomas located near bronchioles Peripheral airways: proliferative bronchiolitis obliterans, characterized by fibroblast proliferation and an organizing intraluminal exudate that occludes bronchioles from within	Ill-formed granulomas (may be difficult to identify) Fibrotic pattern: NSIP-pattern or UIP-like pattern
Outcome	Usually resolves Chronic exposure may lead to chronic bronchitis or emphysema	Peripheral airways: constrictive bronchiolitis Poor, often progress to fibrosis Possible acute exacerbation of chronic form without further exposure

POLMONITE DA IPERSENSIBILITA'

Terapia



➤ Allontanamento
dell'agente causale !!

➤ Tp steroidea

POLMONITE DA IPERSENSIBILITA'

Terapia

- Corticosteroids may be indicated for acute symptomatic relief and in patients with subacute progressive and chronic disease, but they do not appear to impact on the long-term outcome
- A reasonable empiric treatment scheme may consist of prednisone 0.5-1 mg/Kg/d for 1-2 weeks in acute HP or for 4-8 weeks in subacute/chronic HP, followed by a gradual taper

POLMONITE DA IPERSENSIBILITA' aspetti anatomo-patologici

- Long-term treatment should be guided by clinical response, pulmonary function and radiographic improvement
- Progressive pulmonary fibrosis that characterizes chronic advanced HP does not respond to treatment, and lung transplantation should be considered in such cases

POLMONITE DA IPERSENSIBILITA' Terapie future ?



Nuovi farmaci
antifibrotici ??

A large, colorful word cloud centered around the words "thank you" in various languages. The word "thank" is in red, "you" is in yellow, and "thank you" together is in red. The surrounding words are in different colors and fonts, representing numerous languages from around the world. Some examples include "danke" in German, "спасибо" in Russian, "merci" in French, "gracias" in Spanish, "mochchakkeram" in Korean, and "merci" in French. The word cloud is set against a white background.