Chronic Pulmonary Aspregillosis (CPA)

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Chronic Pulmonary Aspergillosis (CPA)

History

I. **1842 Edinburgh, UK**
   - 1st report of CPA as a fatal condition

II. **1938 France**
   - radiological description of aspergilloma described as a "mega-mycetome intra-bronchiectasique

III. **1957 London, UK**
   - 1st CPA complicating tuberculosis (TB) treated with amphotericin

IV. **1960s London, UK**
   - *Aspergillus* antibody has been discovered

V. **Early 1980s**
   - term semi-invasive pulmonary aspergillosis/CPA

VI. **2003**
   - Criteria for the diagnosis and categorisation of patients

VII. **2016**
   - **ESCMID/ERS guidelines**

Chronic Pulmonary Aspergillosis (CPA)

Risk factors for CPA development

The predominant risk factors

a. Tuberculosis
b. Non Tuberculous Mycobacterium infection
c. Allergic Bronchopulmonary Aspergillosis (ABPA)
d. COPD
e. Prior pneumothorax
f. Treated lung cancer

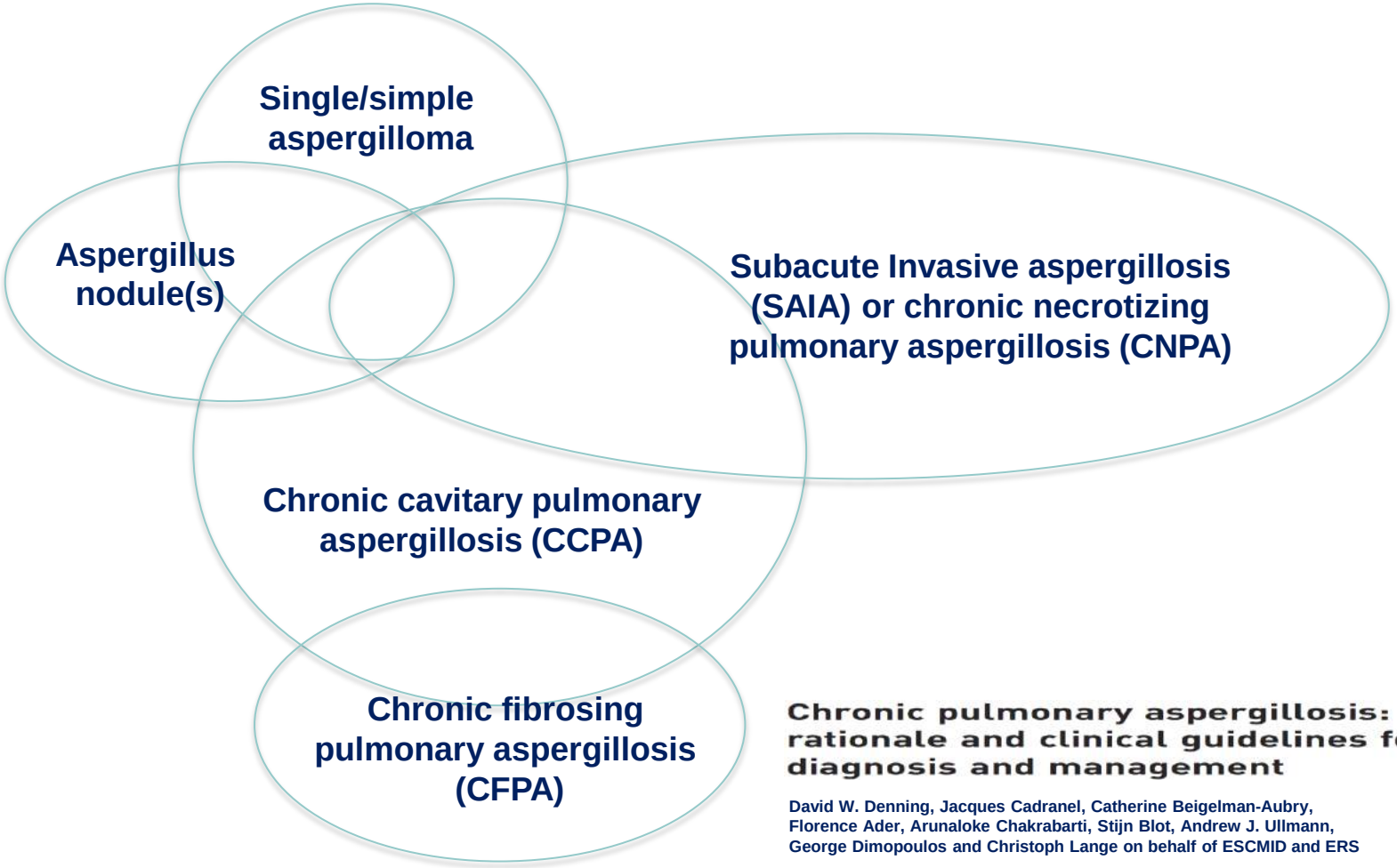
Less common risk factors

a. Fibrocystic sarcoidosis
b. Ankylosing spondylitis
c. Pneumoconiosis
d. Progressive massive fibrosis in silicosis

Smith NL et al Eur Respir J 2011; 37: 865–872, Kato T, et al. Chest 2002; 121: 118–127, Parakh UK et al Indian J Chest Dis Allied Sci 2005; 47: 199–203, Lachkar S et al. Rev Mal Respir 2007; 24: 943–953, Bal A et al Mycoses 2008; 51: 357–35

Chronic Pulmonary Aspergillosis (CPA)

Clinical phenotypes of CPA



Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management

David W. Denning, Jacques Cadranel, Catherine Beigelman-Aubry, Florence Ader, Arunaloke Chakrabarti, Stijn Blot, Andrew J. Ullmann, George Dimopoulos and Christoph Lange on behalf of ESCMID and ERS

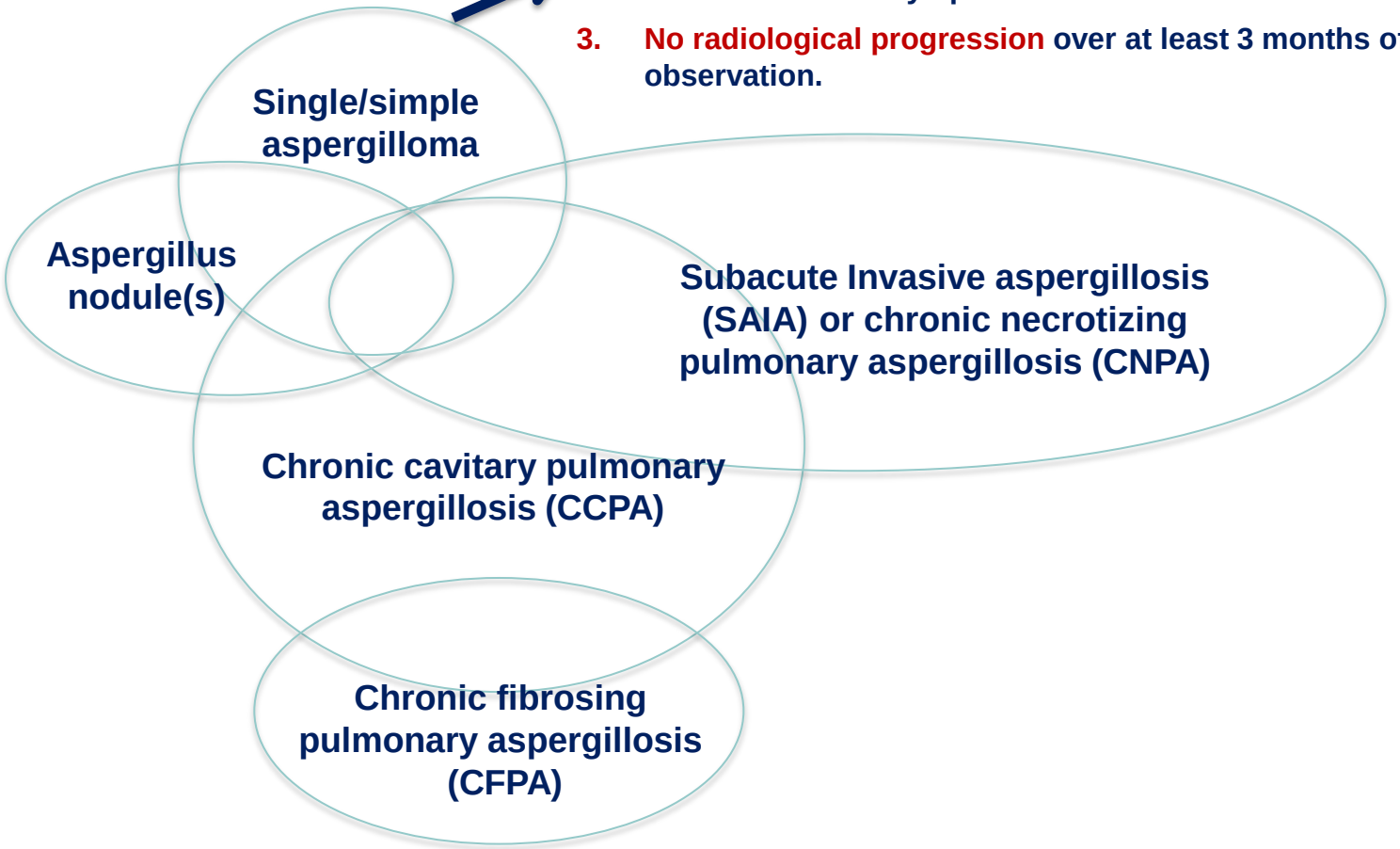
Eur Respir J 2016; 47: 45–68

TASK FORCE REPORT
ESCMID/ERS GUIDELINES

Chronic Pulmonary Aspergillosis (CPA)

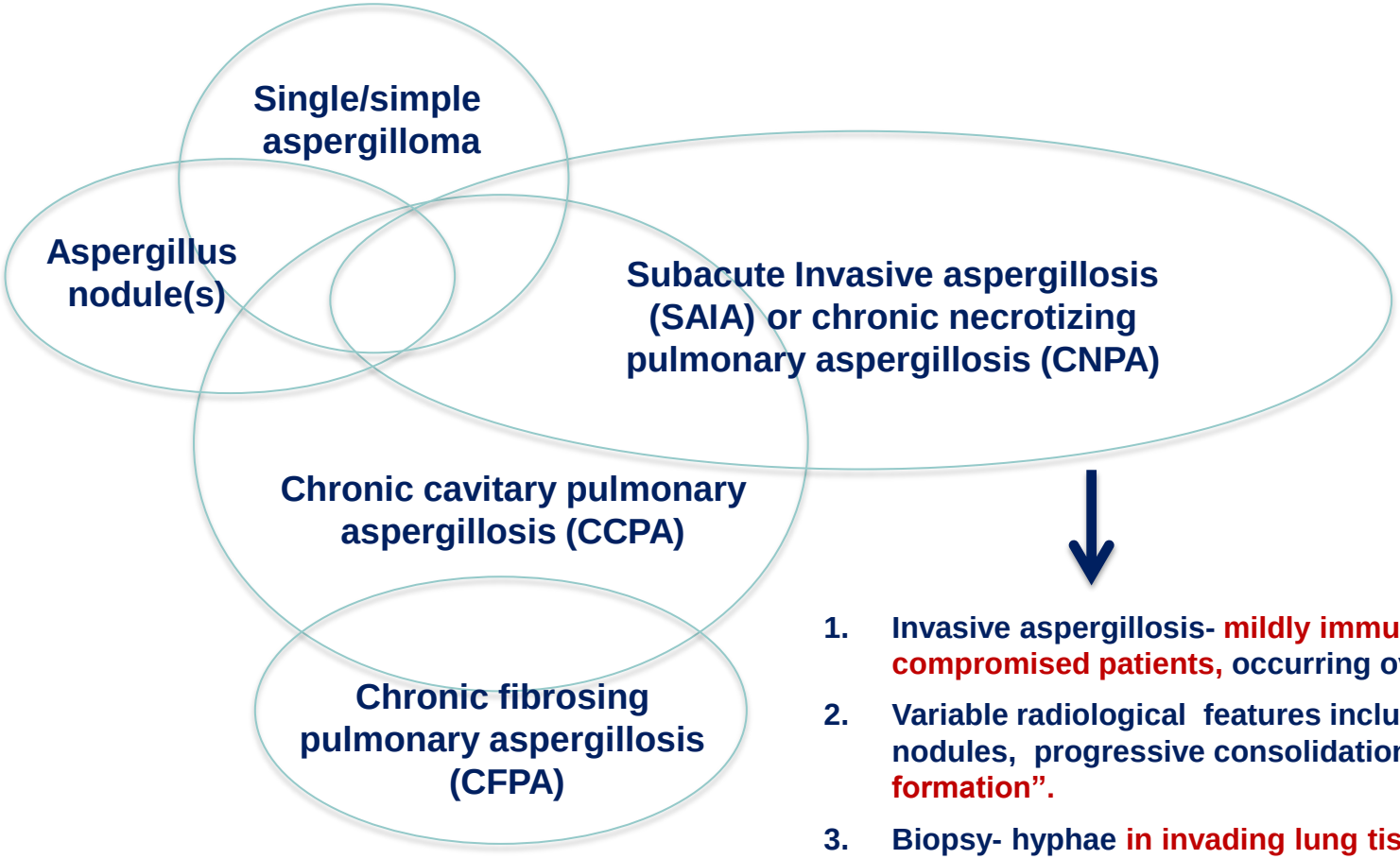
Definitions – Aspergilloma

1. Single pulmonary cavity **containing a fungal ball**
2. Serological/microbiological evidence implicating *Aspergillus* spp. in **a non-immunocompromised patient** with minor or no symptoms
3. **No radiological progression** over at least 3 months of observation.



Chronic Pulmonary Aspergillosis (CPA)

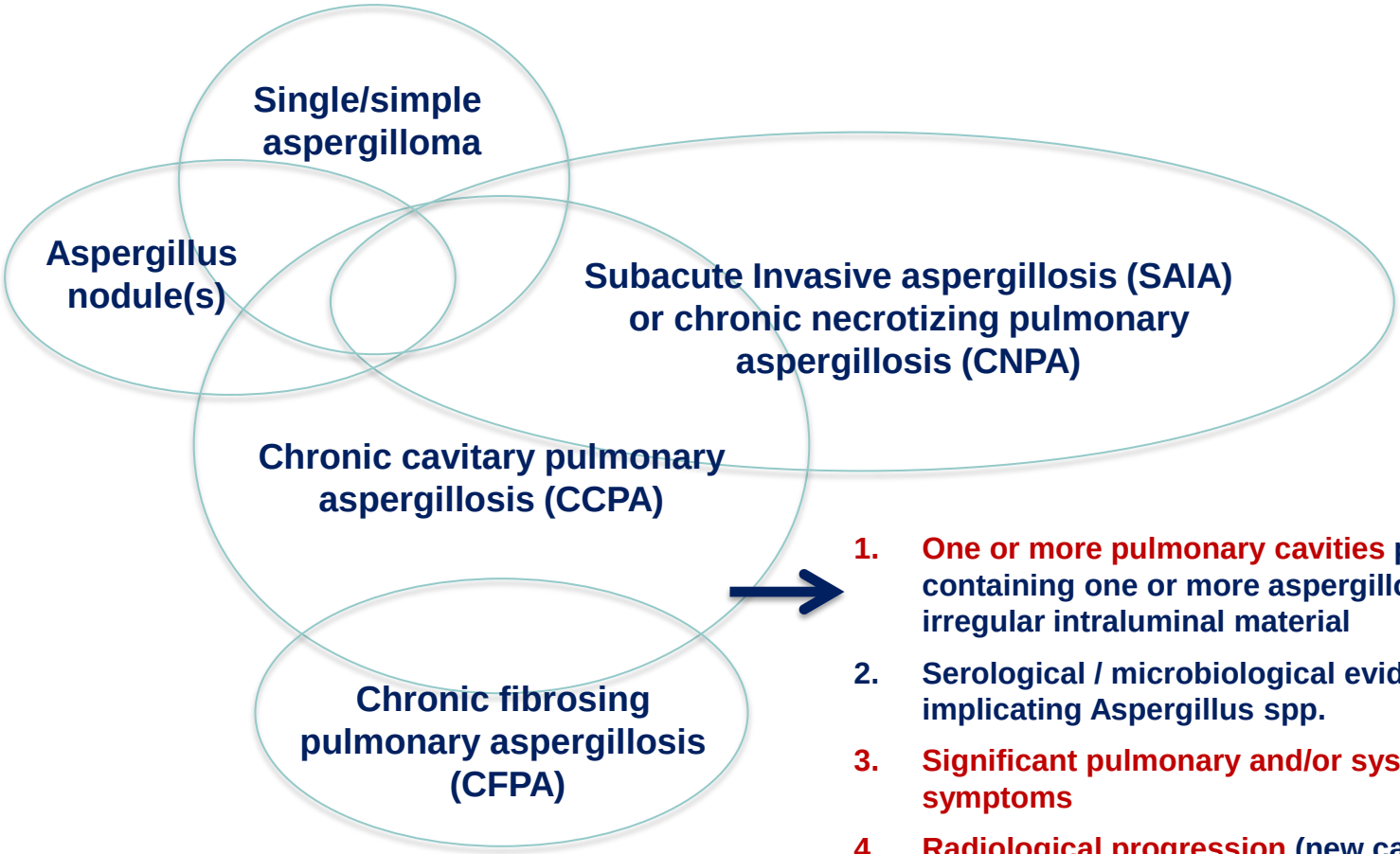
Definitions – SAIA



1. Invasive aspergillosis- **mildly immuno-compromised patients,** occurring over 1–3 months
2. Variable radiological features including cavitation, nodules, progressive consolidation with **"abscess formation".**
3. Biopsy- hyphae **in invading lung tissue**, ***Aspergillus*** GM antigen in blood (or respiratory fluids).

Chronic Pulmonary Aspergillosis (CPA)

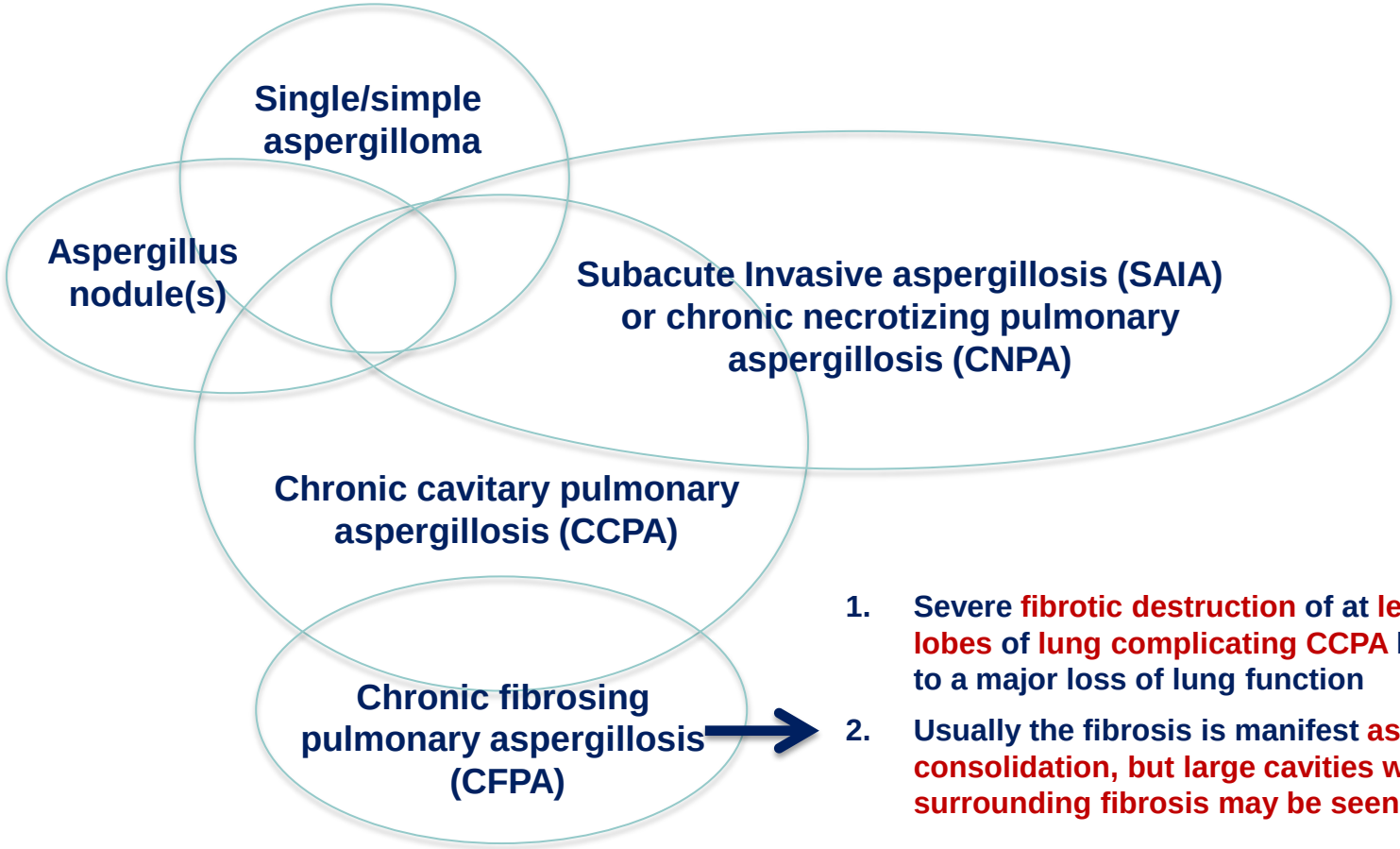
Definitions – CCPA



1. **One or more pulmonary cavities** possibly containing one or more aspergillomas or irregular intraluminal material
2. Serological / microbiological evidence implicating Aspergillus spp.
3. **Significant pulmonary and/or systemic symptoms**
4. **Radiological progression** (new cavities, increasing pericavitary infiltrates or increasing fibrosis) **over at least 3 months** of observation.

Chronic Pulmonary Aspergillosis (CPA)

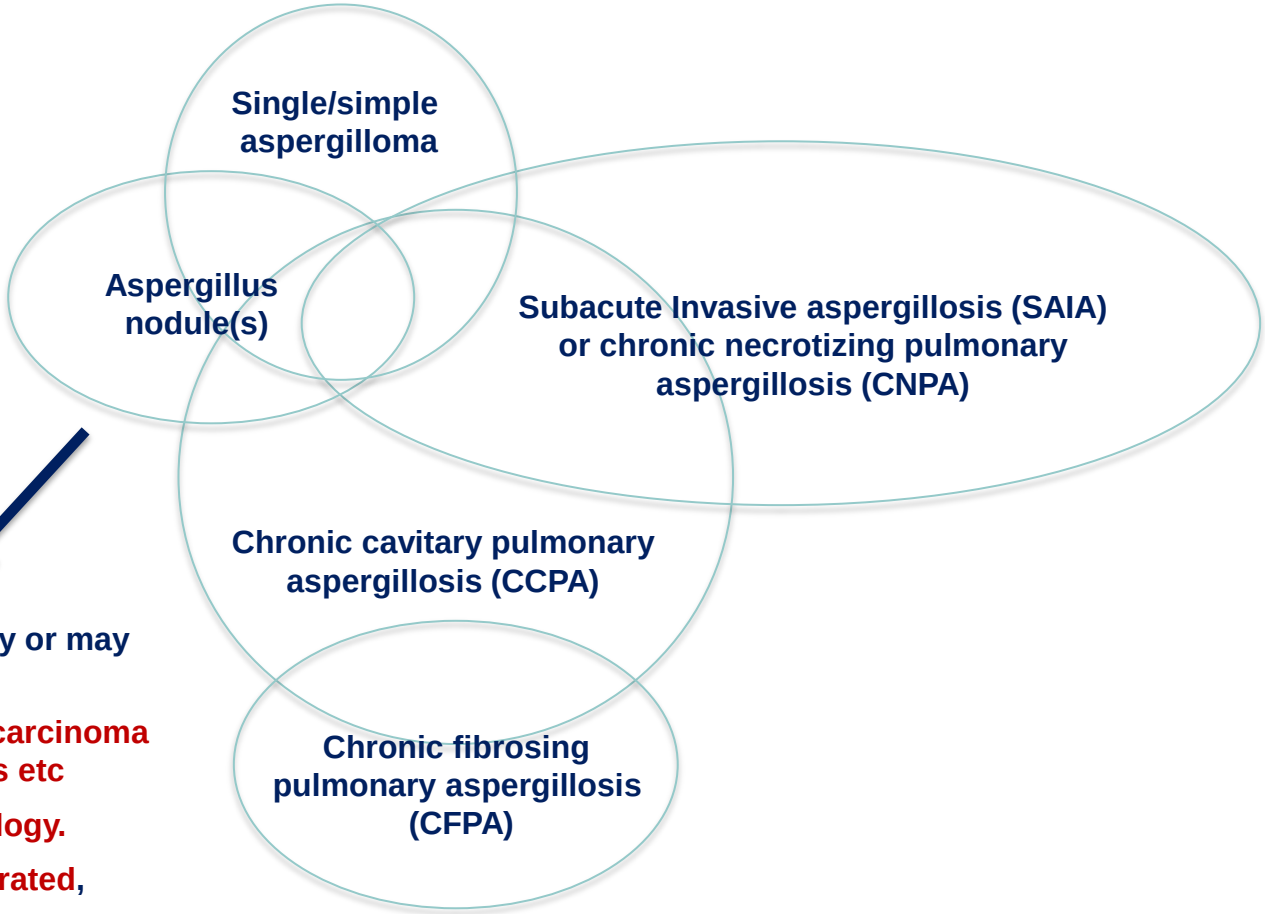
Definitions – CFPA



1. Severe fibrotic destruction of at least two lobes of lung complicating CCPA leading to a major loss of lung function
2. Usually the fibrosis is manifest as consolidation, but large cavities with surrounding fibrosis may be seen.

Chronic Pulmonary Aspergillosis (CPA)

Definitions – Aspergillus nodules



1. One or more nodules which may or may not cavitate
2. They may mimic tuberculoma, carcinoma of the lung, coccidioidomycosis etc
3. Definitively diagnosed on histology.
4. Tissue invasion is not demonstrated, although necrosis is frequent.

Chronic Pulmonary Aspergillosis (CPA)

CPA- Diagnosis

I. **Diagnosis of CPA = combination of characteristics**
   a. a consistent appearance in thoracic imaging (CT)
   b. direct evidence of *Aspergillus* infection or an immunological response to *Aspergillus* spp
   c. exclusion of alternative diagnoses

II. **The findings must be present for at least 3 months**

III. **Patients are usually not immunocompromised**

Chronic Pulmonary Aspergillosis (CPA)

CPA-Differential Diagnosis

1. **Tuberculosis**
   the diagnosis does not excude CPA
2. **Depending on geographical loacation**
   pulmonary histoplasmosis, paracoccidioidomycosis and coccidioidomycosis
3. **Conventional bacteria**
   Str. pneumoniae, *Haemophilus influenzae,* *Staphylococcus aureus, Pseudomonas aeruginosa,* anaerobic bacteria

Chronic Pulmonary Aspergillosis (CPA)

CPA- Key tests

Respiratory samples for patients with cavitary or nodular pulmonary infiltrate in non-immunocompromised patients

I. **Direct microscopy for hyphae**

II. **Fungal culture (sputum or BAL)**

III. **Histology**

IV. **Fungal cultures (transthoracic aspiration)**

V. ***Aspergillus* PCR (respiratory secretion)**

VI. **Bacterial cultures (sputum or BAL)**

Chronic Pulmonary Aspergillosis (CPA)

CPA- Microscopy, culture and PCR

1. ***Aspergillus spp***
   - in sputum : not diagnostic
   - in BAL : consistent with infection, including CPA
2. **Microscopy**
   - sputum or bronchoscopy specimens often reveals fungi, but has not been systematically studied
3. **Culture-positive rates** : 56–81%
4. **Respiratory samples** cultured on **media specific for fungi** have a higher yield than bacterial culture plates
5. **Positive cultures** during **antifungal therapy** are consistent with **azole resistance**
6. **Molecular detection** methods, such as PCR, are **more sensitive** than culture

Chronic Pulmonary Aspergillosis (CPA)

CPA- Antigens / Galactomannan (GM)

Study	Parameters	Sensitivity	Specificity
Izumikawa K et al *Med Mycol 2012; 50: 811–817.*	**BAL (**cut-off level of 0.4)	77.2%	77.0%
	Serum (cut-off level of 0.7)	66.7%	63.5%
Kono Y, et al *Respir Med 2013; 107:1094-1100*	**BAL (**cut-off level >0.5)	85.7%	76.3%
Shin B et al *J Infect 2014; 68: 494–499.* .	**Serum**	23%	

BAL and not serum GM should be used in diagnosis of CPA

Chronic Pulmonary Aspergillosis (CPA)

CPA- Galactomannan / better in BAL than in blood

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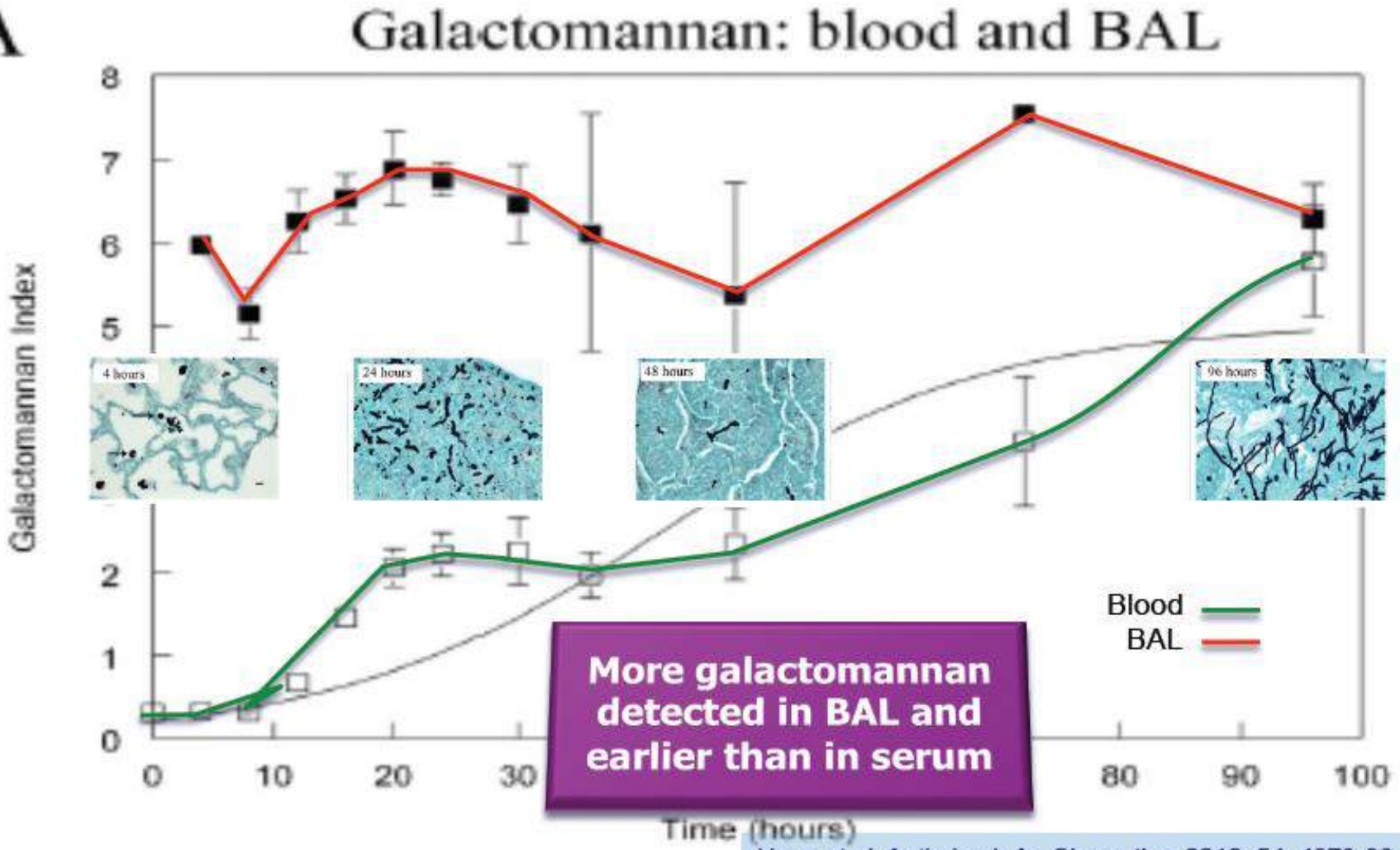


Hope et al Antimicrob Ag Chemother 2010: 54; 4879-86

Chronic Pulmonary Aspergillosis (CPA)

CPA- Antibodies

All patients suspected of having CPA should be tested for A. *fumigatus* IgG antibody or precipitins

- False negative results do occur
- If the clinical suspicion is high
  - ***Aspergillus fumigatus* IgE test** especially in asthmatic and cystic fibrosis patients and an alternative IgG test should be performed, with consideration given to other means of achieving the diagnosis (sputum culture and PCR, *Aspergillus* antigen, percutaneous biopsy/aspiration etc.)
- Antibody titres = **slowly fall** with successful therapy but **rarely** become undetectable
- **A sharply rising** antibody titre = sign of **therapeutic failure** or **relapse**
- **Cross-reactivity** with other fungi, such as *Histoplasma* or *Coccidioides* spp. may affect some tests

Chronic Pulmonary Aspergillosis (CPA)

CPA- Histology

Findings after biopsy or resection of lesions

1. **Definitive distinction** between (SAIA) subacute invasive aspergillosis and CCPA and better definition of the tissue response to *Aspergillus* infection
2. **Chronic inflammatory reaction**
   Septate hyphae may be found in a resected cavity, sometimes filling and obliterating it with
3. **Granuloma**
   Fibrosis surrounding or mixed with inflammatory infiltrate
4. **SAIA**
   Hyphae in lung parenchyma with **acute inflammatory or necrotic tissue response**

Chronic Pulmonary Aspergillosis (CPA)

CPA- Radiological diagnosis

I. **CxR**
   - the first imaging modality for the suspicion and diagnosis of CPA

II. **CT of the thorax**
   - provides better definition and location of imaging abnormalities as well as their distribution and extent

III. **CT- angiography**
   - is required at least for **the baseline CT scan** prior to therapy
   - is useful **to evaluate new haemoptysis**, and in failure treatment
   - use of average intensity projection post-processing of a CT could create slabs of variable thickness akin to a chest radiograph appearance

IV. **Positron emission tomography (PET)**
   - doesn’t appear to be useful

Chronic Pulmonary Aspergillosis (CPA)

CPA- Imaging findings

Combination of the findings

- related to underlying lung disorders
- and changes secondary to *Aspergillus* infection itself reflecting the chronic inflammatory and immune response to *Aspergillus* spp

CPA most commonly develops in…..

- a pre-existent bronchopulmonary or less usually pleural cavity

but also……

- directly causes the formation and expansion of new cavities or nodule and rarely alveolar consolidation

Changes secondary to the *Aspergillus* infection itself range from

a. the appearance of a fungus ball within a lung cavity (single or simple aspergilloma)
b. to complex pleuroparenchymal features related to a progressive destructive cavitary disease

Godet C et al. Chronic pulmonary aspergillosis: an update on diagnosis and treatment. Respiration 2014; 88: 162–174

Chronic Pulmonary Aspergillosis (CPA)

CPA- Imaging findings / distinctive hallmarks

a. **New and/or expanding cavities**
    1. variable wall thickness in the setting of chronic lung disease
    2. with or without intracavitary fungal ball formation
    3. with pleural thickening and
    4. marked parenchymal destruction and/ or fibrosis

b. ***Aspergillus*** **empyema may be seen**

c. Enlargement of bronchial or non-bronchial systemic arteries

d. Pseudo-aneurysms leading to sometimes fatal haemoptysis

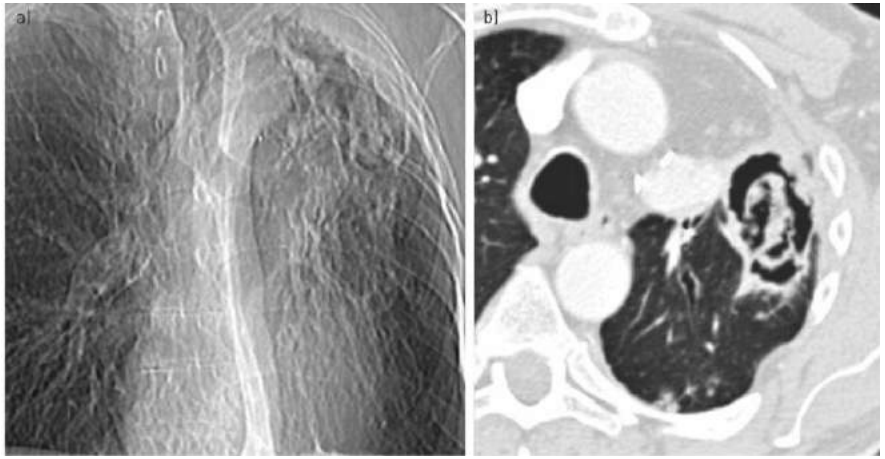
Chronic Pulmonary Aspergillosis (CPA)

CPA- Imaging findings / Aspergilloma

1. **Prior to Aspergilloma formation**
   - fungal growth on the interior surface of the cavity
   - a distinctive appearance of a bumpy or irregular interior cavity
2. **An aspergilloma typically starts as**
   a. a surface infection following colonisation in a lung cavity or a bronchiectasis
   b. an upper-lobe, solid, round or oval intracavitary mass, partially surrounded by a crescent of air, the “air-crescent” sign, mobile on prone position
   c. a fixed and immobile, irregular sponge-work filling the cavity and containing air spaces
   d. Calcification may be seen
3. **Fungus balls do not enhance after IV injection of contrast media**
4. **Adjacent pleural thickening is often observed**
   a. Aspergilloma may coexist with any underlying condition
   b. There are some mimics of aspergilloma including necrotic lung carcinoma

Chronic Pulmonary Aspergillosis (CPA)

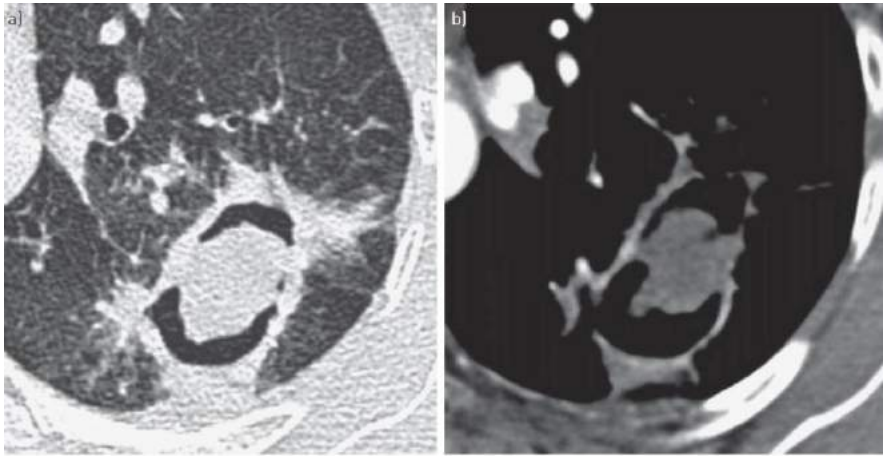
CPA- Imaging findings/ Aspergilloma



Cavity with irregular edge and aspergilloma

Apical pleural thickening bordering the cavity

Axial view with lung window at the level of the left upper lobe



Aspergilloma in CCPA

(a) “air-crescent” sign
(b) a thick-walled and slightly irregular cavity.