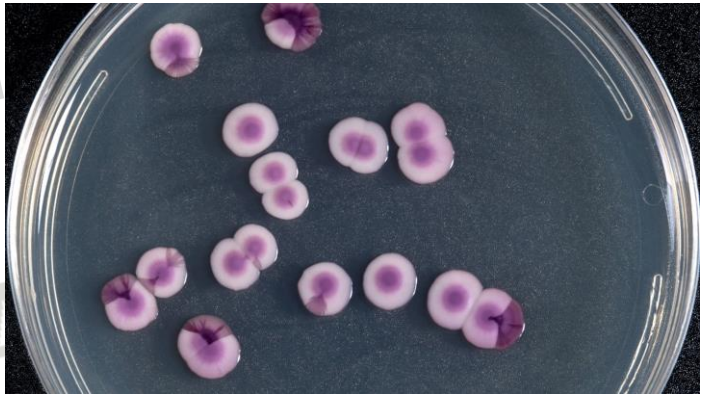
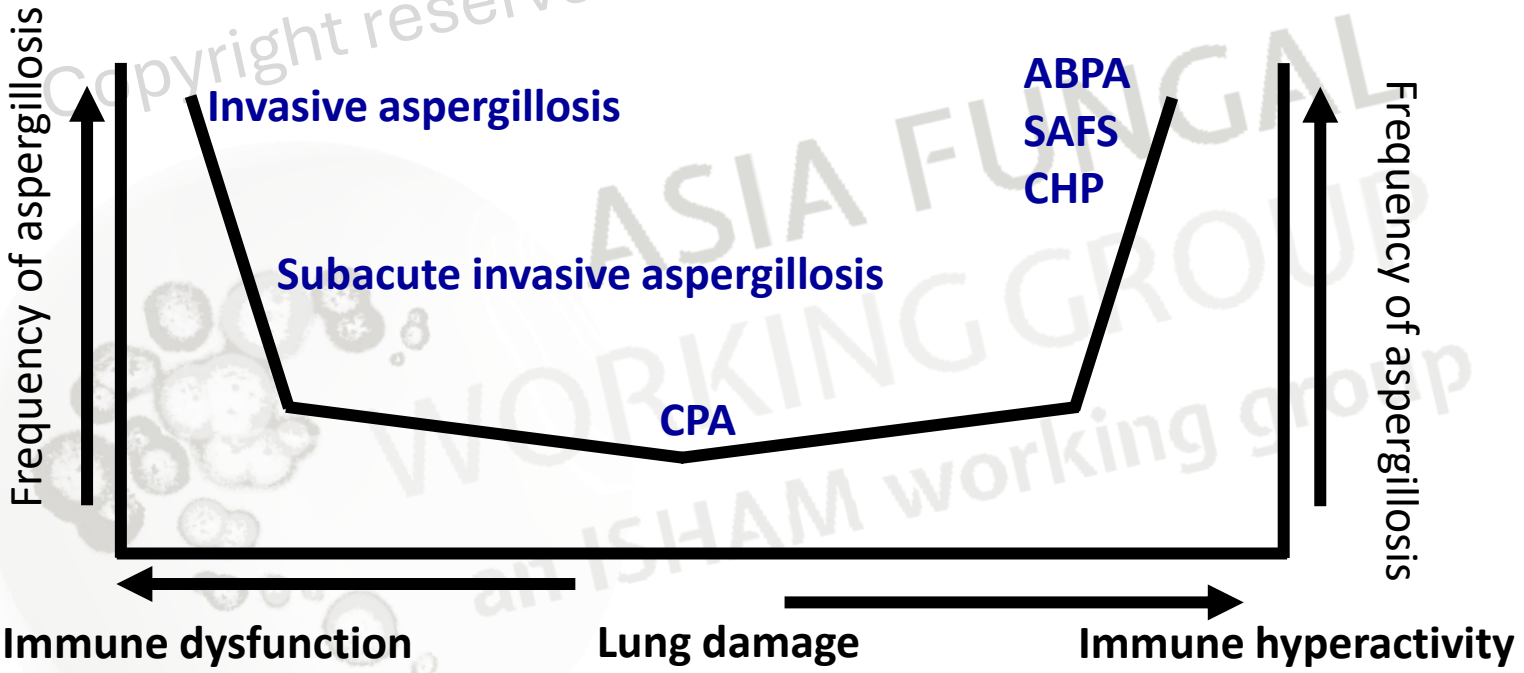


Diagnosis & treatment of chronic pulmonary aspergillosis

Arunaloke Chakrabarti

Director, Doodhdhari Burfani Hospital & Research Centre, Haridwar, India

Spectrum of Pulmonary Aspergillosis

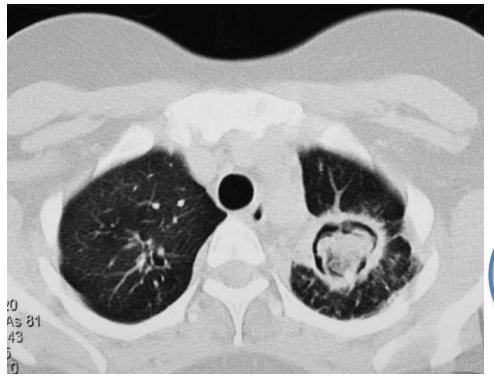


ABPA=allergic bronchopulmonary aspergillosis; SAFS=severe asthma with fungal hypersensitivity; CHP=chronic hypersensitivity pneumonitis; CPA=chronic pulmonary aspergillosis

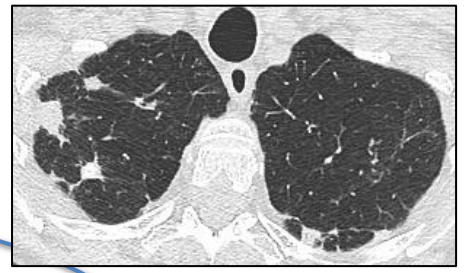
Kosmidis C, et al. Thorax 2015;70:270-277

What is chronic pulmonary aspergillosis?

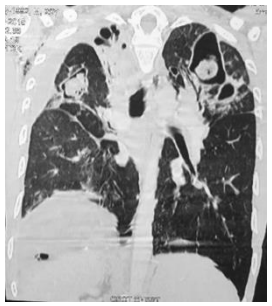
Chronic infection of the lung tissue caused by *Aspergillus* species (*A. fumigatus*) that **progressively destroys the lung tissue, usually in those with an underlying pulmonary condition**, including post-tuberculosis lung abnormality (PTLA), COPD, sarcoidosis, and others

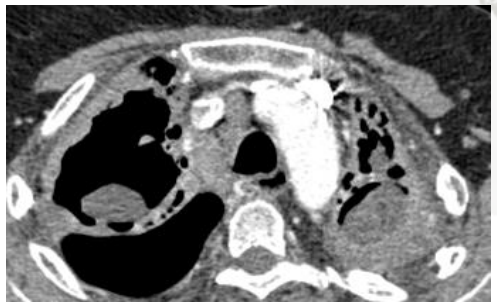


Aspergilloma

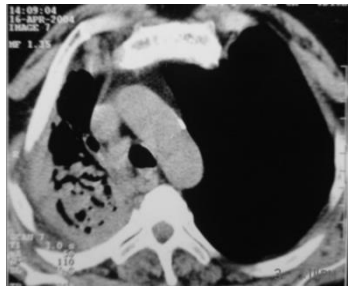


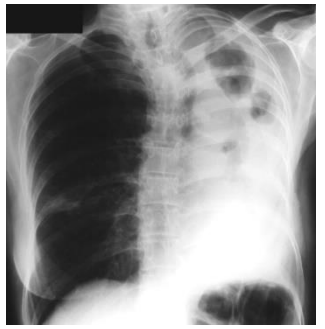
Aspergillus nodule





Chronic cavitary pulmonary aspergillosis





Chronic fibrosing pulmonary aspergillosis

Denning DW, et al. Eur Respir J 2016;47:45-68

Global CPA burden

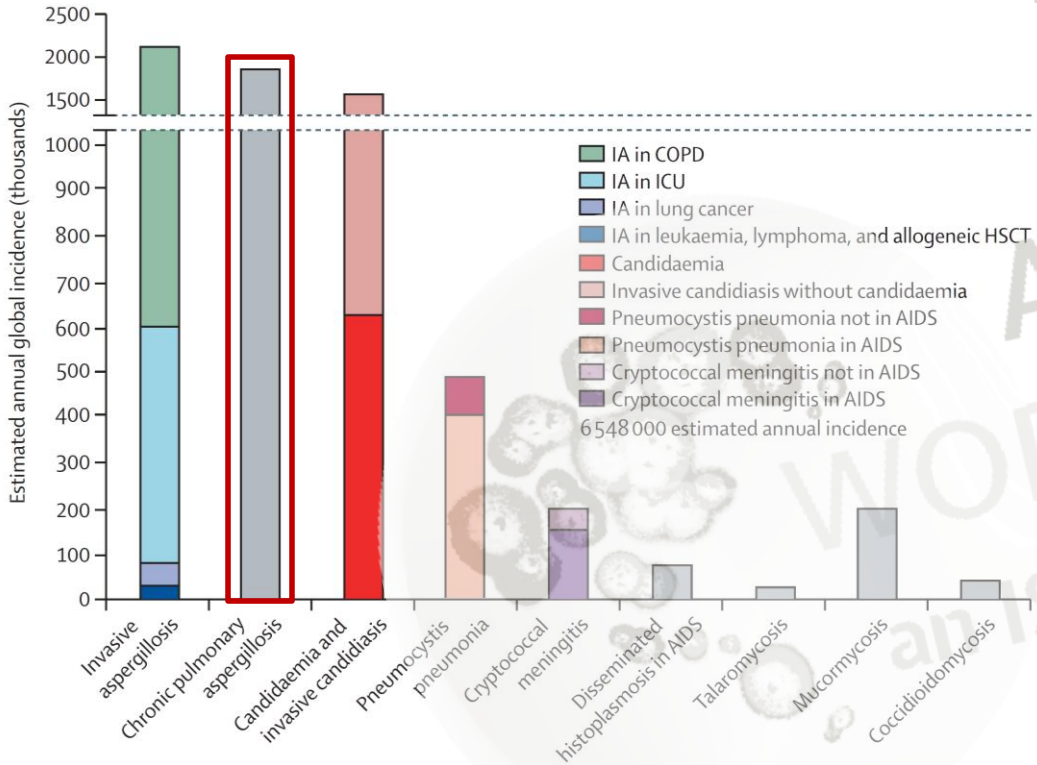


Figure 1: Estimated annual incidence of life-threatening invasive mycoses, together with chronic pulmonary aspergillosis

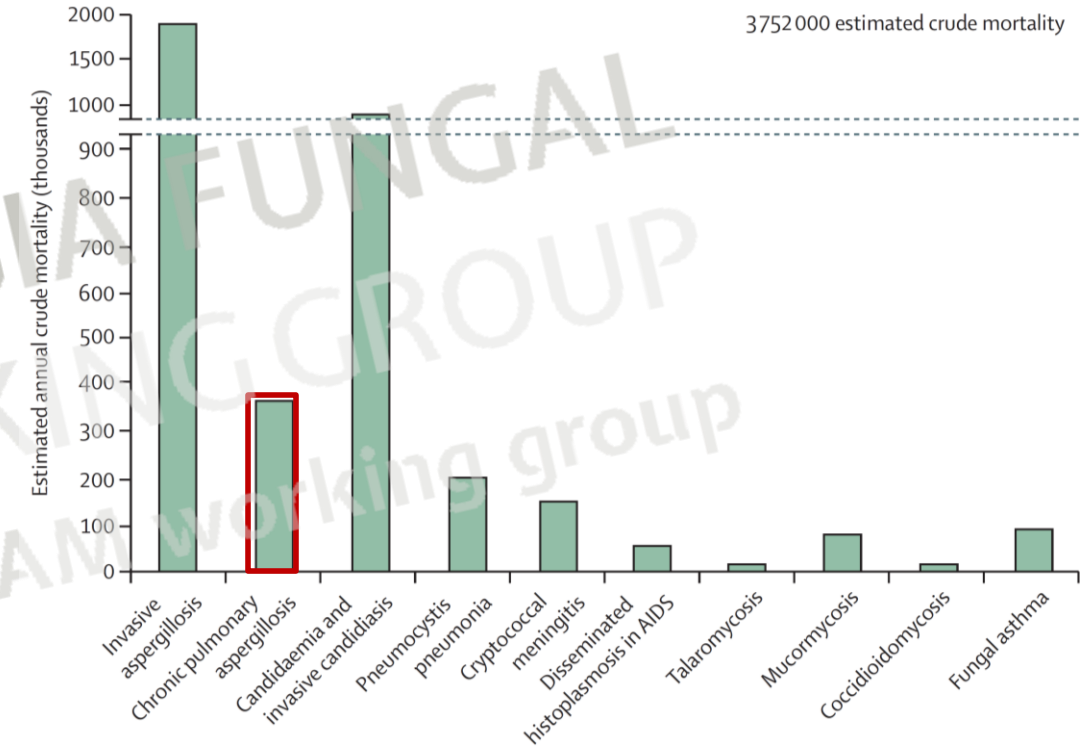


Figure 2: Estimated crude mortality of severe fungal disease, worldwide

>1,800,000 annual CPA cases globally

Denning D. Lancet Infect Dis 2024:S1473-3099(23)00692-8

Underlying lung disease

Manchester data (n=126)

Post TB	**20 (15.9%)**
NTM	**18 (14.3%)**
ABPA/asthma	**15 (11.9%)**
COPD	12 (9.5%)
Bullae	12 (9.5%)
Lung cancer	12 (9.5%)
None	1 (0.8%)
Pneumonia	10 (7.9%)
Sarcoidosis	9 (7.1%)
Thoracic surgery	6 (4.8%)
Rheumatoid arthritis	4 (3.2%)
Asthma	3 (2.4%)
SAFS/Bullae	4 (3.2%)

Smith et al Eur Respir J 2011; 37: 865-872

CPAnet Registry, international (n=74)

COPD	**29 (39%)**
Asthma	**19 (26%)**
Tuberculosis	**12 (16%)**
Thoracic surgery	**10 (14%)**
Bronchiectasis	**9 (12%)**
ABPA	**8 (11%)**

Laursen CB, et al J Fungi 2020; 6:96

Indonesia 216 patients proven/probable TB patients

CPA	percentage
Proven	6%
Probable	2%
Possible	7%
Total	**14.4%**

Setianingrum F, et al. Thorax 2022; 77: 821-8

French registry (n=2022)

COPD	**888 (44%)**
Bullae	**449 (22%)**
Bronchiectasis	**354 (18%)**
Lung cancer	**254 (13%)**
Thoracic surgery	**221 (11%)**
Post TB	163 (8%)
NTM	59 (3%)
Pneumonia	10 (8%)
Lung fibrosis	120 (6%)
Sarcoidosis	27 (1%)

Maitre T, *et al.* Eur Respir J 2021; 58: 2003345

PGI, Chandigarh data (n=137)

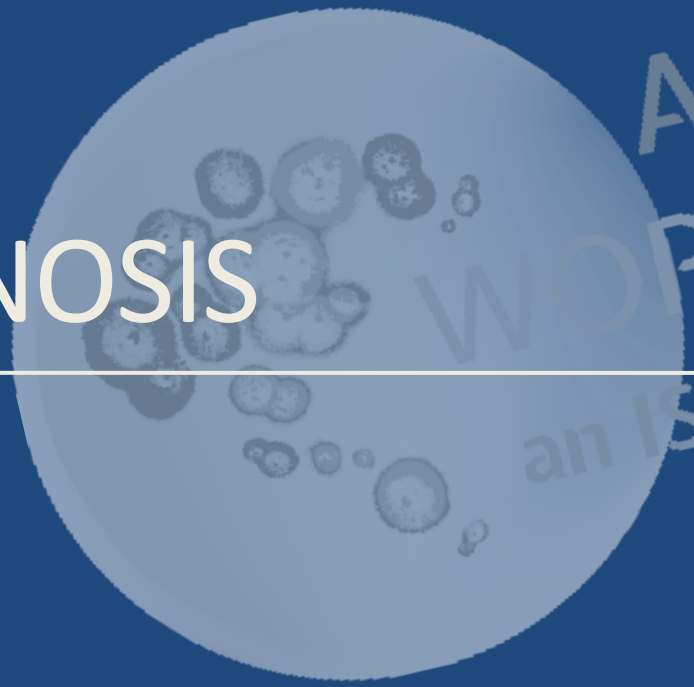
Post TB	**118 (86.1%)**
NTM	1 (<1%)
ABPA/asthma	1 (<1%)
COPD	1 (<1%)
None	10 (7.3%)
IPF	1 (<1%)
>1 risk factors	30 (21.9%)

Community prevalence of CPA in PTLA

- A cohort was identified from the records of the 12 tuberculosis treatment centers attached to the national program
- We performed CT of the thorax and measured serum *A.fumigatus*-specific IgG
- CPA prevalence: 10.3%
- CPA incidence rate: 4 per 100-person years

Soundappan K, et al. Mycoses; 2024;67(3):e13711

DIAGNOSIS



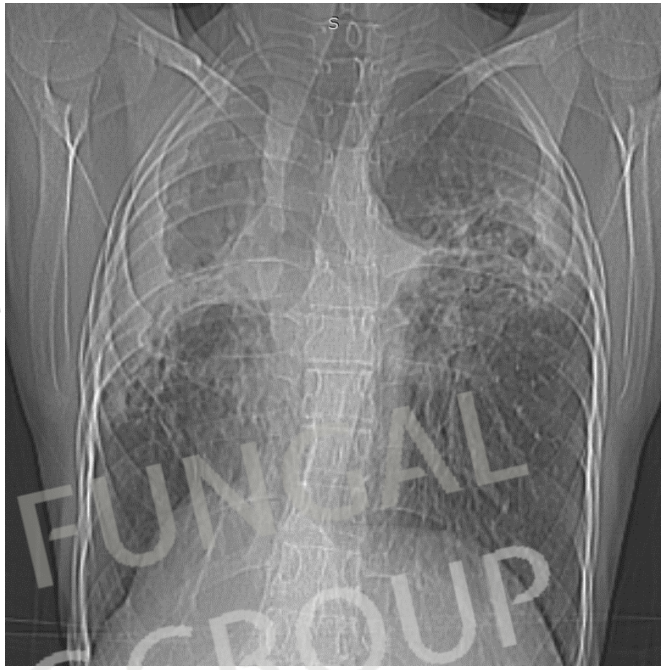
When to suspect CPA?

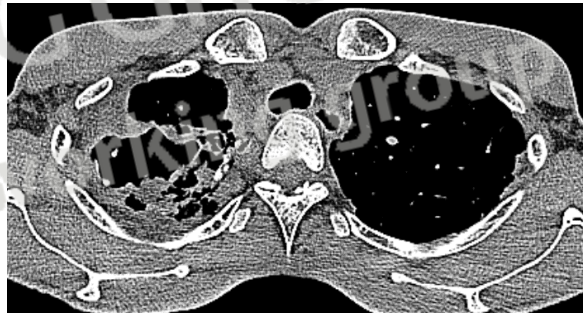
Post-TB (with cavities), sarcoidosis and Diffuse parenchymal lung disease with cystic areas, and COPD

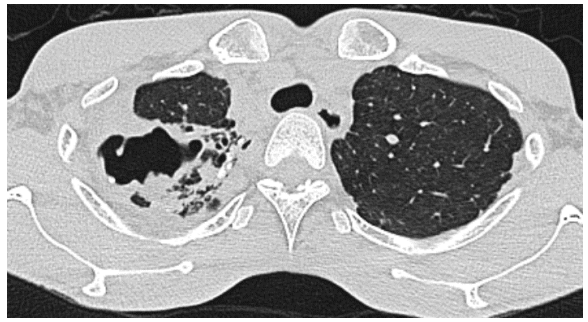
Chronic symptoms (systemic and respiratory)

- **Fever**
- **Hemoptysis**
- **Malaise**
- **Weight loss**

Repeated sputum workup for MTB negative







How to diagnose?

Clinical symptoms for ≥3 months

Consistent (cavities ± fungal ball) thoracic imaging (preferably by CT)

Evidence of *Aspergillus* infection

- **Direct: demonstration of *Aspergillus* species in respiratory secretions)**
- **Indirect: immunological response (precipitins, *A. fumigatus*-IgG, serum and BAL fluid galactomannan index) to *Aspergillus* spp.**

Exclusion of competing diagnoses (MTB, NTM, malignancy and others)

Sehgal IS, et al. Expert Rev Respir Med 2020;14:715-727

How to diagnose?

Clinical symptoms for ≥3 months

Consistent (cavities ± fungal ball) thoracic imaging (preferably by CT)

Evidence of *Aspergillus* infection

- **Direct: demonstration of *Aspergillus* species in respiratory secretions)**
- **Indirect: immunological response (precipitins, *A. fumigatus*-IgG, serum and BAL fluid galactomannan index) to *Aspergillus* spp.**

Exclusion of competing diagnoses (MTB, NTM, malignancy and others)

Symptoms

Clinical findings	
Duration of symptoms, in years	2.9±4.4
Cough	**235 (87.4%)**
Dyspnea	86 (32%)
mMRC grade I	49 (18.2%)
mMRC grade II	26 (9.6%)
mMRC grade III	11 (4.1%)
Recurrent hemoptysis	**191 (71%)**
Fever	83 (30.9%)
Malaise	62 (23%)
Weight loss	**150 (55.8%)**

Sehgal IS, et al. J Allergy Clin Immunol Pract 2019;7:969-974

How to diagnose?

Clinical symptoms for ≥3 months

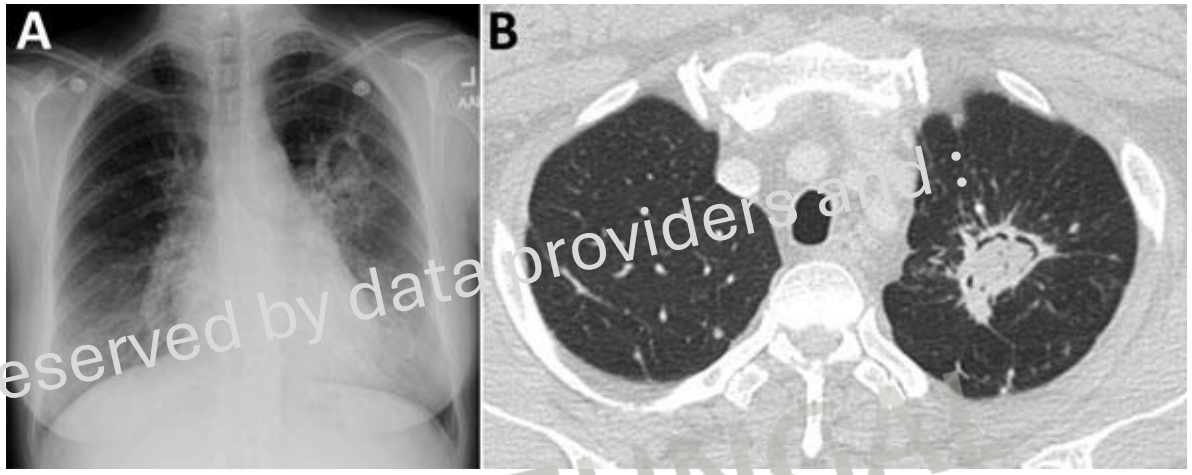
Consistent (cavities ± fungal ball) thoracic imaging (preferably by CT)

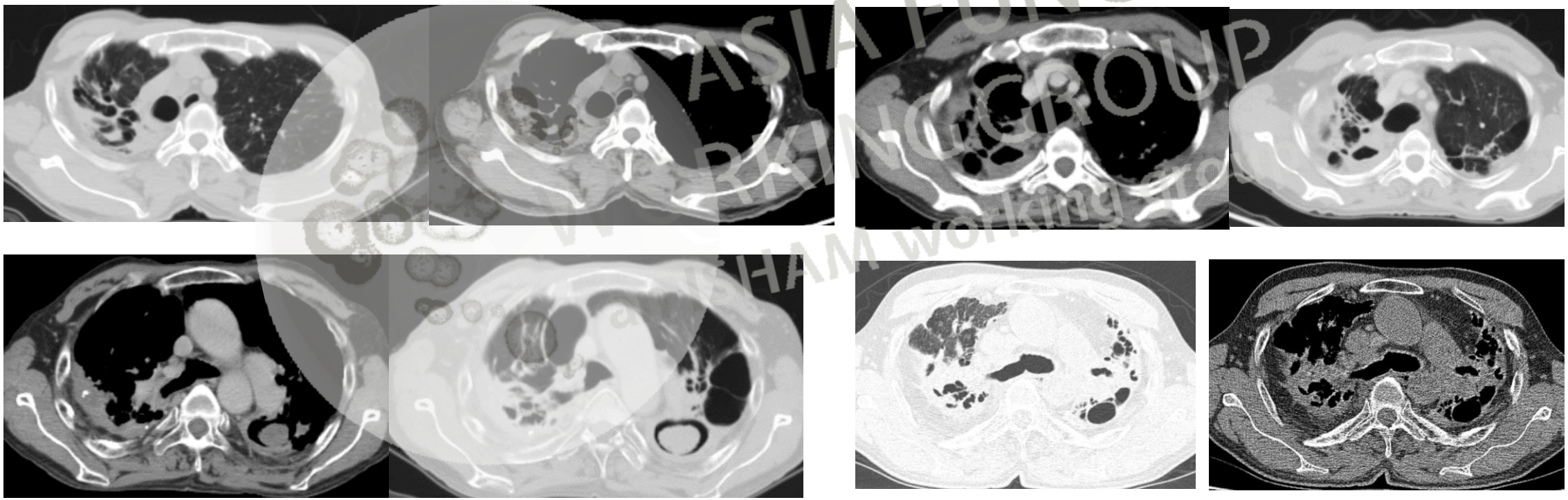
Evidence of *Aspergillus* infection

- **Direct: demonstration of *Aspergillus* species in respiratory secretions)**
- **Indirect: immunological response (precipitins, *A. fumigatus*-IgG, serum and BAL fluid galactomannan index) to *Aspergillus* spp.**

Exclusion of competing diagnoses (MTB, NTM, malignancy and others)

Radiology





Denning DW, et al. Emerg Infect Dis 2018 August, DOI: 10.3201/eid2408.171312

How to diagnose?

Clinical symptoms for ≥3 months

Consistent (cavities ± fungal ball) thoracic imaging (preferably by CT)

Evidence of *Aspergillus* infection

- **Direct: demonstration of *Aspergillus* species in respiratory secretions)**
- **Indirect: immunological response (precipitins, *A. fumigatus*-IgG, serum and BAL fluid galactomannan index) to *Aspergillus* spp.**

Exclusion of competing diagnoses (MTB, NTM, malignancy and others)

Direct evidence of Aspergillus infection

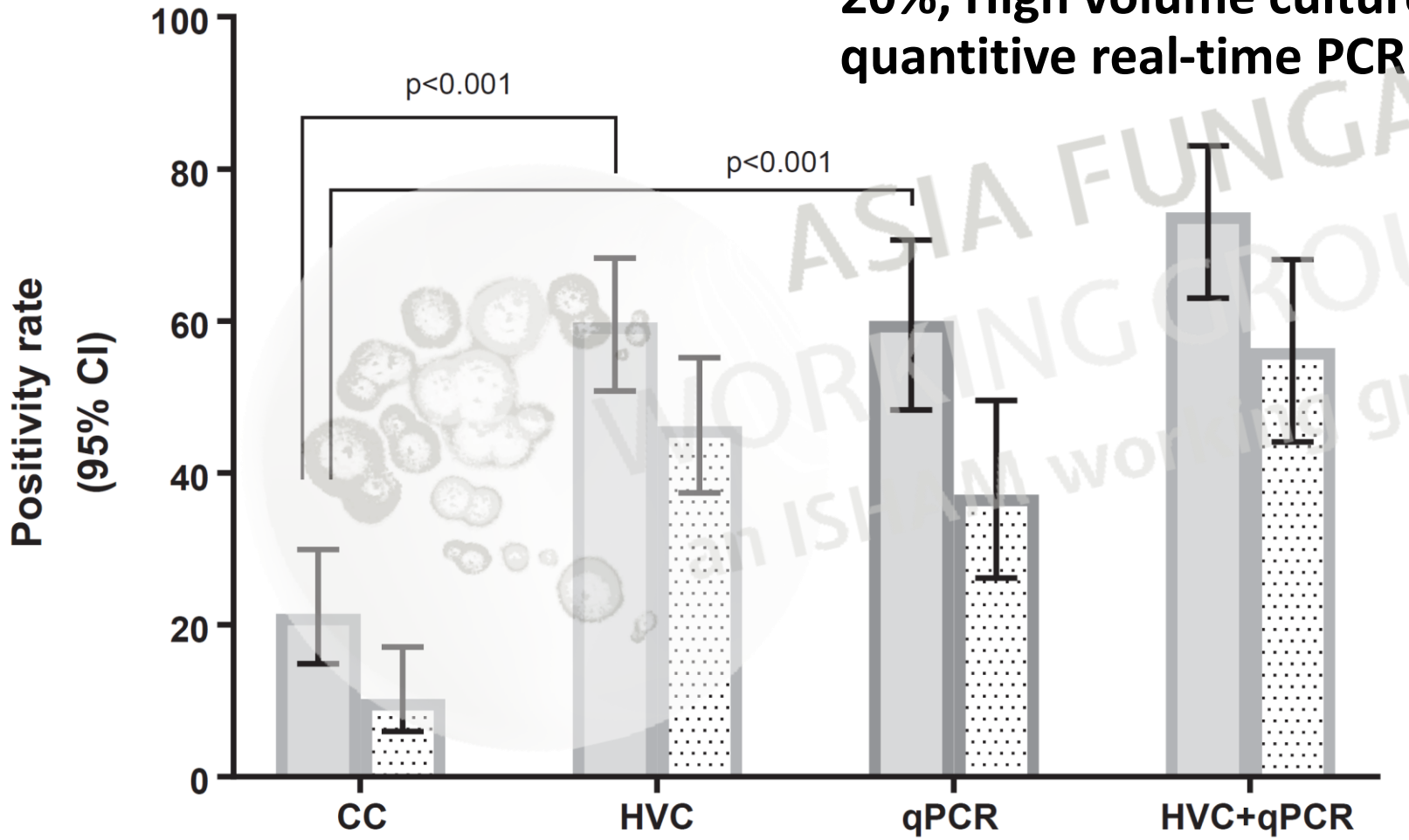
- **Almost all cases of CPA are caused by *A. fumigatus*,** although patients have been described with *A. niger* or *A. flavus* infection
- **Sensitivity of sputum and BALF culture is 13.2% and 35.5%, respectively**

Sputum fungal culture (n=243)	
A. fumigatus	17 (7)
A. flavus	14 (5.8)
A. terreus	1 (0.4)
BAL fungal culture (n=126)	
A. fumigatus	24 (19)
A. flavus	17 (13.5)

Sehgal IS, et al. J Clin Microbiol. 2019;57(3): pii: e01821-18
Sehgal IS, et al. Expert Rev Respir Med 2020;14:715-727

High-volume culture and real-time PCR may improve sensitivity

The positivity rate of conventional culture was 20%, High volume culture was 60% and quantitive real-time PCR was 66% in CPA



Vergidis P, et al. Clin Microbiol Infect. 2020;26:935-940

How to diagnose?

Clinical symptoms for ≥3 months

Consistent (cavities ± fungal ball) thoracic imaging (preferably by CT)

Evidence of *Aspergillus* infection

- **Direct: demonstration of *Aspergillus* species in respiratory secretions)**
- **Indirect: immunological response (precipitins, *A. fumigatus*-IgG, serum and BAL fluid galactomannan index) to *Aspergillus* spp.**

Exclusion of competing diagnoses (MTB, NTM, malignancy and others)

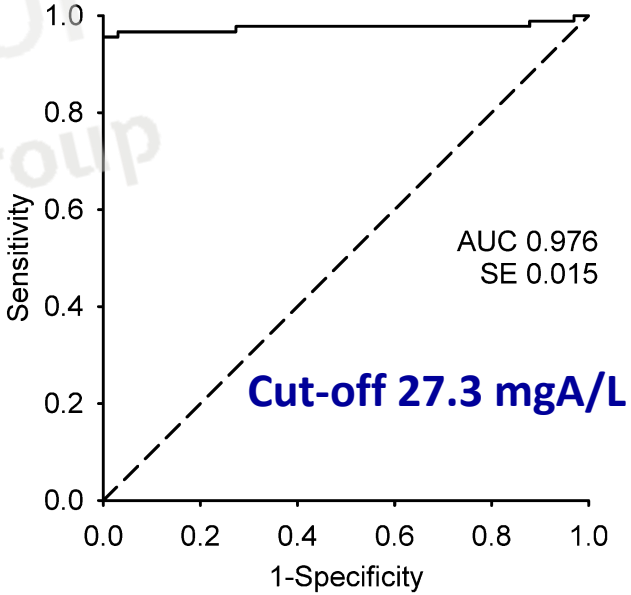
ORIGINAL ARTICLE

WILEY mycoses Diagnosis, Therapy and Prophylaxis of Fungal Diseases

Diagnostic cut-off of *Aspergillus fumigatus*-specific IgG in the diagnosis of chronic pulmonary aspergillosis

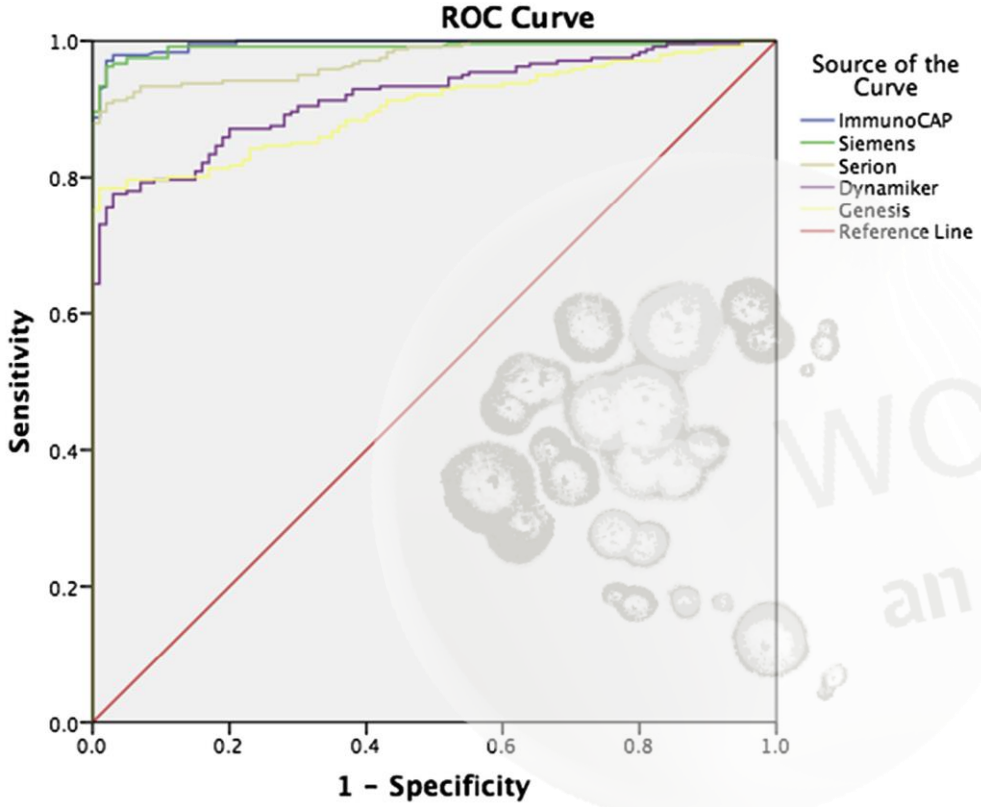
Inderpaul Singh Sehgal[1] | Hansraj Choudhary[2] | Sahajal Dhooria[1] | Ashutosh Nath Aggarwal[1] | Mandeep Garg[3] | Arunaloke Chakrabarti[2] | Ritesh Agarwal[1]

- 187 subjects [137 Chronic cavitary pulmonary aspergillosis (CCPA), 50 diseased controls]
- Derivation cohort of 124 subjects
- **Serum precipitins had a sensitivity of 26%**
- ***A. fumigatus*-specific IgG [Phadia, ImmunoCAP system, Thermo Fisher Scientific, Uppsala, Sweden] had a sensitivity of 91% & specificity of 100%**



Mycoses 2018; 61: 770-776

Comparison of six *Aspergillus*-specific IgG assays for the diagnosis of chronic pulmonary aspergillosis (CPA)



Healthy Ugandan controls

Assay (unit)	Diagnostic cut-off	Sensitivity	Specificity
ImmunoCap (mg/L)	**20**	**96%**	**98%**
Immulite (mg/L)	**10**	**96%**	**98%**
Serion (U/mL)	**35**	**90%**	**98%**
Dynamiker (AU/mL)	65	77%	97%
Genesis (U/mL)	20	75%	99%
Precipitins	-	59%	100%

Page et al. J Infect 2016;72:240-9

Contents lists available at ScienceDirect

Indian Journal of Medical Microbiology

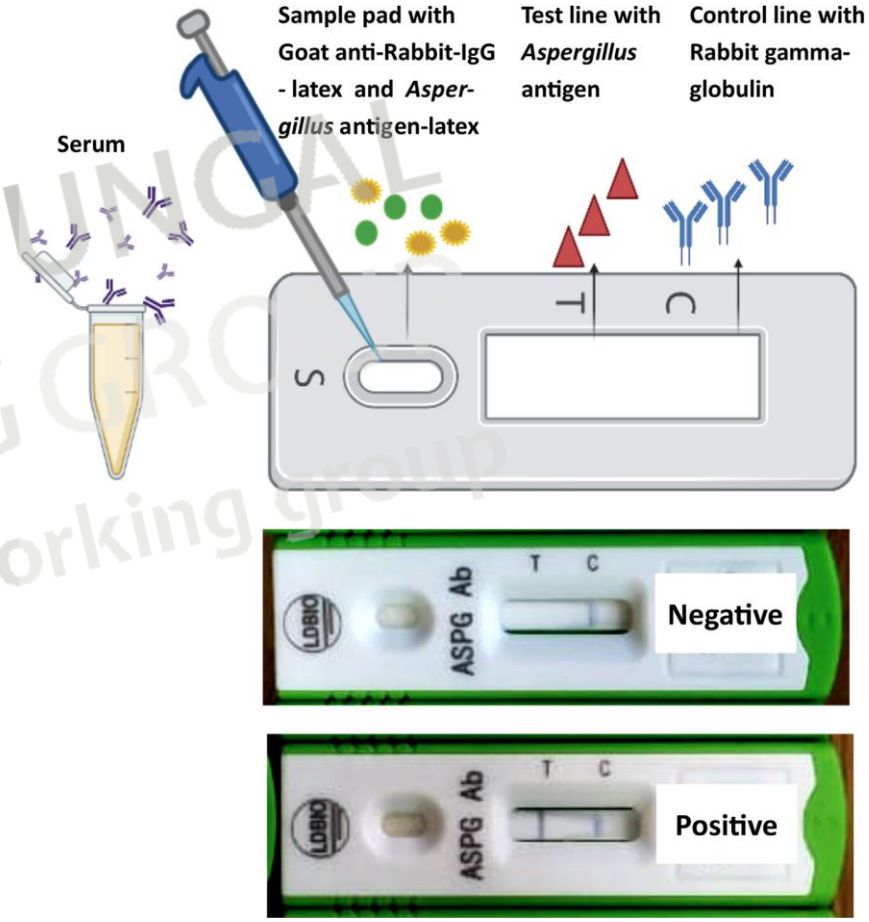
journal homepage: www.journals.elsevier.com/indian-journal-of-medical-microbiology

Original Research Article

LDBio Aspergillus immunochromatographic test lateral flow assay for IgG/IgM antibody detection in chronic pulmonary aspergillosis: Single-centre evaluation and meta-analysis

Shreya Singh [a], Hansraj Choudhary [a], Sourav Agnihotri [a], Inderpaul Singh Sehgal [b], Ritesh Agarwal [b], Harsimran Kaur [a], Anup Ghosh [a], Arunaloke Chakrabarti [a], Shivaprakash M. Rudramurthy [a,*]

- 60 serum samples (30 CPA & 30 controls)
- ***Aspergillus*** **immunochromatographic test IgG/IgM LFA - sensitivity and specificity of 87% and 90%, respectively**
- **4 more studies – pooled sensitivity 90% & specificity 91%**



Indian J Med Microbiol 2022; 40: 204-210

Role of LDBio Aspergillus LFA

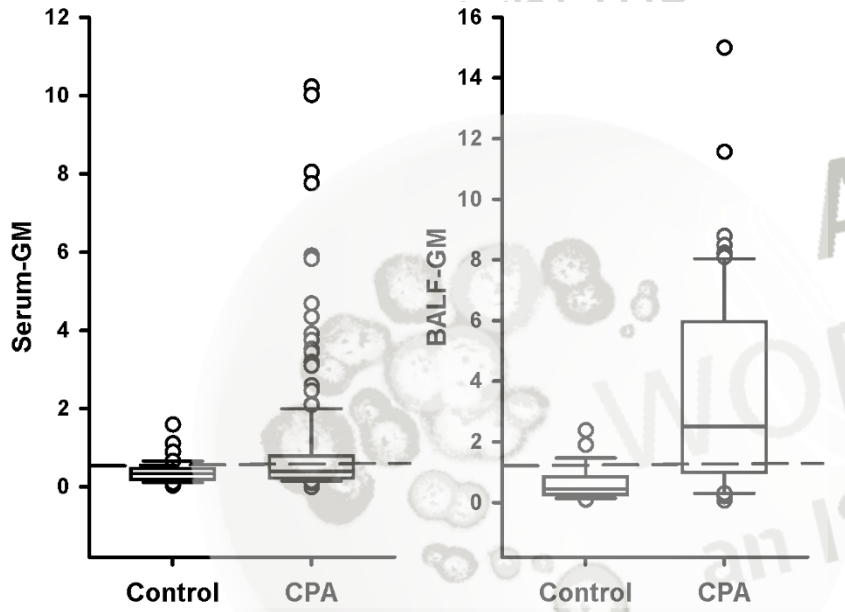
- We enrolled 508 patients with post-tuberculosis with lung symptoms
- 122 field cohort and 386 hospital cohort
- The sensitivity and specificity of LDBio-ALFA was 82.2% and 85.3%
- In field cohort the sensitivity and specificity was 83.3% and 93.9%
- In the hospital cohort the sensitivity and specificity was 81.1% and 75.3%
- Can be done by finger prick test also

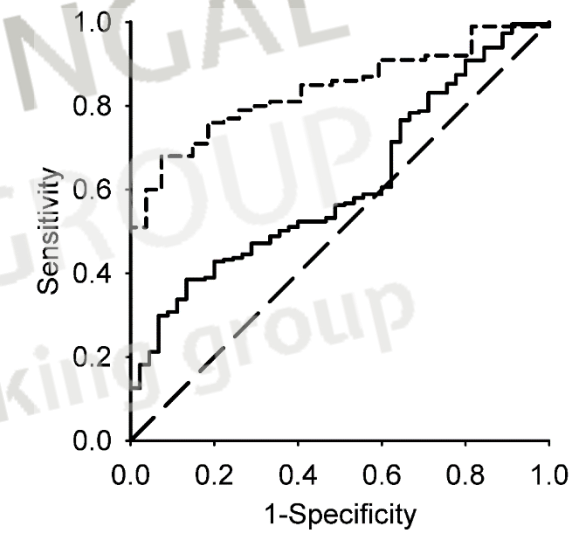
Sehgal IS, et al. Mycopathologia 2025;190(1):9
Sehgal IS, et al. Clin Microbiol Infect 2023;29:404-405

Utility of Serum and Bronchoalveolar Lavage Fluid Galactomannan in Diagnosis of Chronic Pulmonary Aspergillosis

J Clin Microbiol 2019;57: e01821-18

Inderpaul Singh Sehgal [1], Sahajal Dhooria [1], Hansraj Choudhary [2], Ashutosh Nath Aggarwal [1], Mandeep Garg [3], Arunaloke Chakrabarti [2], Ritesh Agarwal [4]





The best cut-off value of **serum GM was 0.55** (sensitivity: 38%, specificity: 87%)

The best cut-off value of **BALF-GM was 1.375** (sensitivity: 68%, specificity: 93%)

Serum-GM > 1.55 and BALF-GM >2.5 had 100% specificity (rule-in test)

Usefulness of Two *Aspergillus* PCR Assays and *Aspergillus* Galactomannan and β-D-Glucan Testing of Bronchoalveolar Lavage Fluid for Diagnosis of Chronic Pulmonary Aspergillosis

Naohisa Urabe,[a] Susumu Sakamoto,[a] Go Sano,[a] Junko Suzuki,[b] Akira Hebisawa,[c] Yasuhiko Nakamura,[a] Kazuya Koyama,[a] Yoshikazu Ishii,[d] Kazuhiro Tateda,[d] Sakae Homma[a]

- **Sensitivity and specificity of in-house Aspergillus PCR 1 was 86.7% and 84.2%**
- **Sensitivity and specificity of in-house Aspergillus PCR 2 was 66.7% and 94.2%**

J Clin Microbiol 2017;55:1738-1746

The Utility of Galactomannan and Polymerase Chain Reaction Assays in Bronchoalveolar Lavage for Diagnosis of Chronic Pulmonary Aspergillosis

Mohit Chowdhury · Gagandeep Singh · Mragnayani Pandey · Himanshu Mishra · Ved Prakash Meena · Prayas Sethi · Amandeep Singh · Bindu Prakash · Ashish Datt Upadhyay · Anant Mohan · Sanjeev Sinha · Immaculata Xess · Naveet Wig · Sushil Kumar Kabra · Animesh Ray

- **Sensitivity and specificity of in-house Aspergillus PCR was 36% and 39%**
- **Sensitivity and specificity of commercially available Aspergillus PCR** (AsperGenius®) **was 52% and 34%**

Mycopathologia 2023;188:1041-1053

Which investigation?

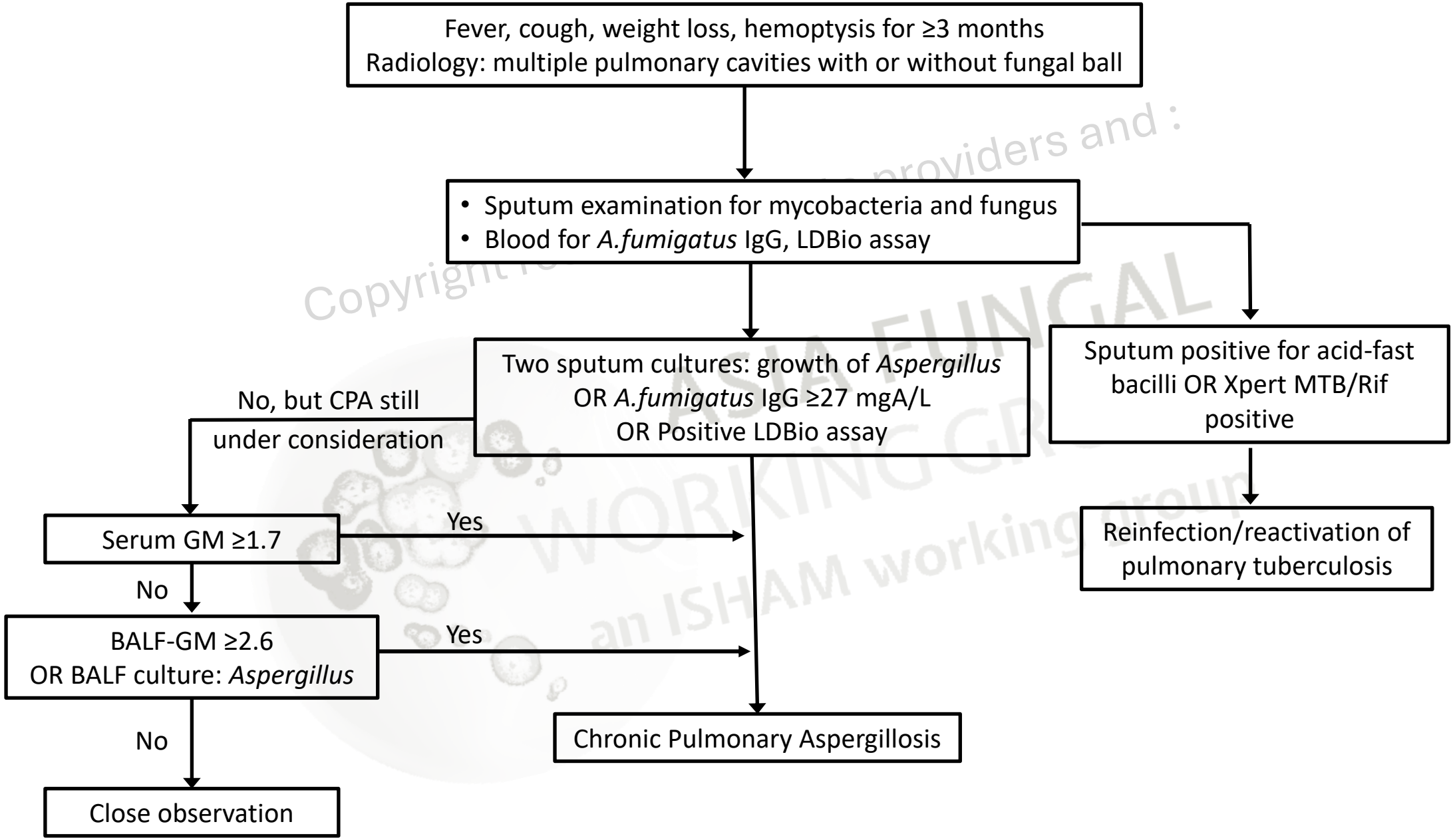
Detection of *A. fumigatus*-IgG is the most sensitive & specific test for diagnosing CPA

Investigation	Sensitivity
Aspergillus species in respiratory secretions	15-60%
Serum galactomannan index	30-40%
BAL fluid galactomannan index	40-65%
Aspergillus PCR	36-87%
Precipitins	15-60%
LDBio-ALFA	82-85%
***A. fumigatus*-IgG**	**85-92%**

What if we combine the tests?

Cut off	Sensitivity	Specificity
Af. IgG ≥27 mgA/L or serum GM ≥1.7 or BALF-GM ≥2.6	**98 (96.4-99.7)**	**100 (92.1-100)**

Sehgal IS, et al. Mycoses 2018;61:770-776
Sehgal IS, et al. J Clin Microbiol 2019;57: e01821-18
Sehgal IS, et al. Expert Rev Respir Med 2020;14:715-727

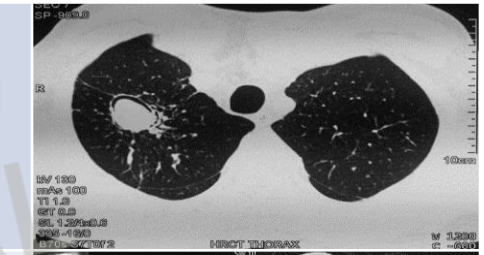
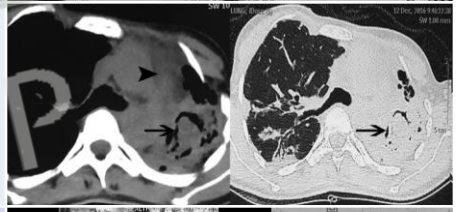
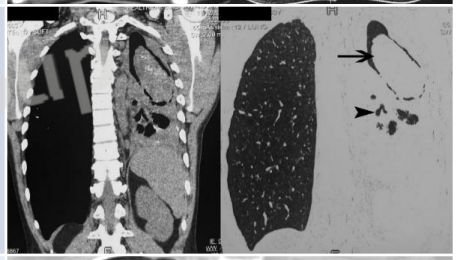
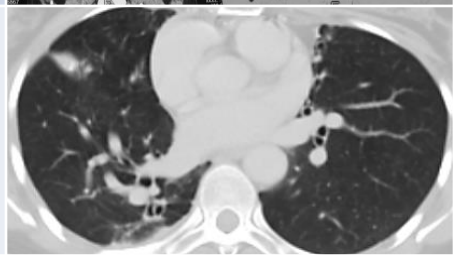

Fever, cough, weight loss, hemoptysis for ≥3 months
Radiology: multiple pulmonary cavities with or without fungal ball
• Sputum examination for mycobacteria and fungus
• Blood for A.fumigatus IgG, LDBio assay
Two sputum cultures: growth of Aspergillus
OR A.fumigatus IgG ≥27 mgA/L
OR Positive LDBio assay
Sputum positive for acid-fast bacilli OR Xpert MTB/Rif positive
Reinfection/reactivation of pulmonary tuberculosis
No, but CPA still under consideration
Serum GM ≥1.7
Yes
No
BALF-GM ≥2.6
OR BALF culture: Aspergillus
Yes
No
Chronic Pulmonary Aspergillosis
Close observation

Recommendation for low resource setting

Required criteria	Details
Symptoms for ≥3 months	Hemoptysis &/or persistent cough &/or weight loss
Radiological features	Progressive cavitation &/or intra-cavitary fungal ball &/or pleural thickening or peri-cavitary fibrosis or infiltrates adjacent to cavities
Microbiological evidence of *Aspergillus* infection	Positive *Aspergillus* specific IgG &/or hyphae consistent with *Aspergillus* in sputum &/or *Aspergillus* growth on ≥2 sputum or other respiratory samples
Mycobacterial infection ruled out with smear, GeneXpert, &/or Mycobacterial culture	Mycobacterial infection & CPA can be present concurrently, but then diagnosis requires characteristic findings on CT scan including pleural thickening, a fungal ball or other intra-cavitary material, or marked peri-cavitary infiltrates + positive *Aspergillus* IgG antibody test

Denning DW, et al. Emerg Infect Dis 2018 August, DOI: 10.3201/eid2408.171312

Subtypes of CPA

CPA type	Presenting symptoms	Investigations	Imaging
Simple aspergilloma	Hemoptysis, occasionally life threatening	Serum *A. fumigatus*-IgG may or may not be elevated	
Chronic cavitary pulmonary aspergillosis (CCPA)	Fever, malaise, hemoptysis, weight loss, chest pain, dyspnea, frail	Serum *A. fumigatus*-IgG is elevated in >92%	
Chronic fibrosing pulmonary aspergillosis (CFPA)	Fever, malaise, hemoptysis, weight loss, chest pain, dyspnea, cor pulmonale, frail	Serum *A. fumigatus*-IgG is elevated in >92%	
Aspergillus nodule	Hemoptysis, incidental	Serum *A. fumigatus*-IgG may or may not be elevated. Diagnosis on histopathology	

Denning et al. Eur Respir J 2016;47:45-68
Sehgal IS, et al. Expert Rev Respir Med 2020;14:715-727

Goal of treatment

- Prevent progression
- Achieve remission
- Prevent or prolong time of relapse
- Prevent treatment emergent adverse events

Should everyone be treated?

Which agent?

How long?

How to monitor?

Should minimally symptomatic CPA patients be treated?

- SA (n=17), CCPA (n=28), CFPA (n=4) with minimal symptoms
- Followed for a mean followup duration of 46.9 months
- Treatment initiated in 11/49 (22.4%) due to clinical or radiological worsening after a mean of 33.3 months
- 5/49 (10.2%) died during follow-up after a mean of 56.2 months
- About one-fifth of patients require treatment during follow-up

- **Close observation is required without the need for universal treatment in minimally symptomatic patients**

Unpublished data

Should symptomatic patients with CPA be treated?

Randomized 31 symptomatic subjects to itraconazole (n=17) vs. supportive care (n=14)

Better overall response in the itraconazole group (76.5% vs. 35.7%, p=0.02)

Significantly better clinical and radiological response with itraconazole

All symptomatic patients require treatment

Agarwal R, et al. Mycoses 2013; 56: 559-70

Treatment of CPA

- Non-specific
  - Tranexamic acid, ethamsylate
  - Bronchodilator for those with obstruction on spirometry
  - Nutritional support
  - Mucoactive therapy (nebulized saline, airway clearance techniques)
  - Vaccination for influenza, pneumococcus, COVID-19
- Fungus specific therapy

Antifungals used in CPA

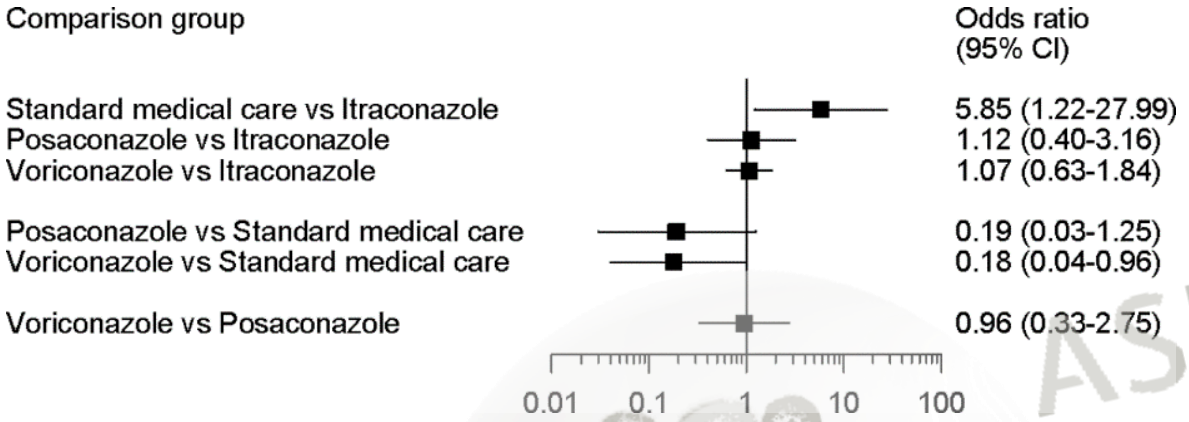
- **Oral**
  - **Terbinafine**
  - **Itraconazole**
  - **Voriconazole**
  - **Posaconazole**
  - **Isavuconazole**
- **Intravenous**
  - **Amphotericin B deoxycholate**
  - **Liposomal amphotericin B**
  - **Voriconazole**
  - **Echinocandins**

No head-to-head comparison of oral antifungal agents in CPA

Comparison of antifungal agents in treatment of CPA: network meta-analysis

10 studies (718 patients)

Oral



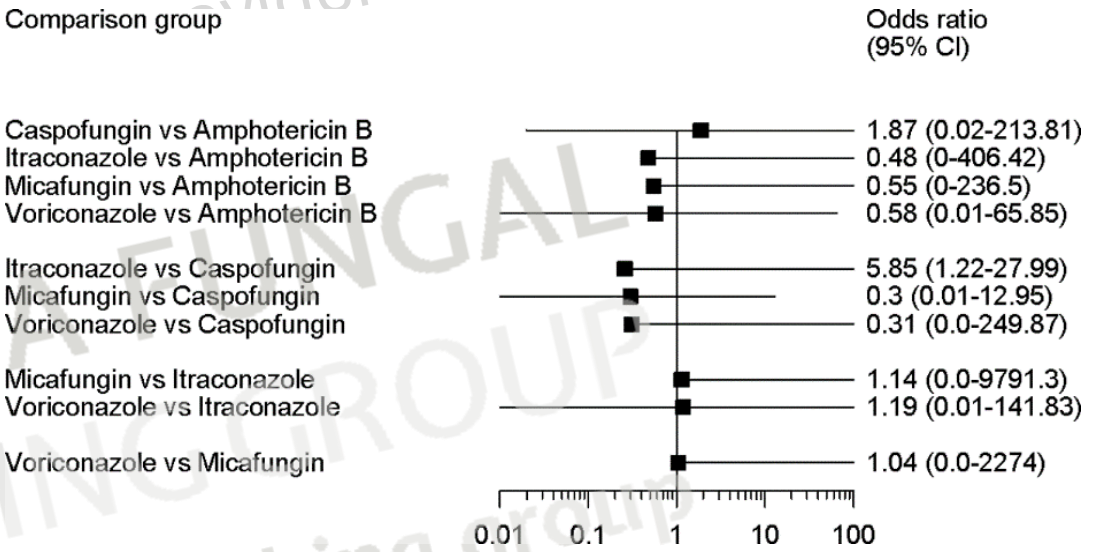
Network rank

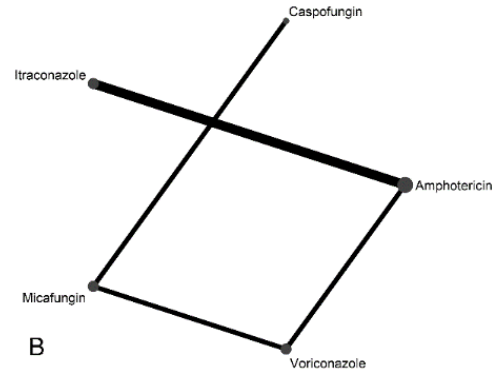
1. Itraconazole

2. Voriconazole

3. Posaconazole

Intravenous





Network rank

1. Echinocandins

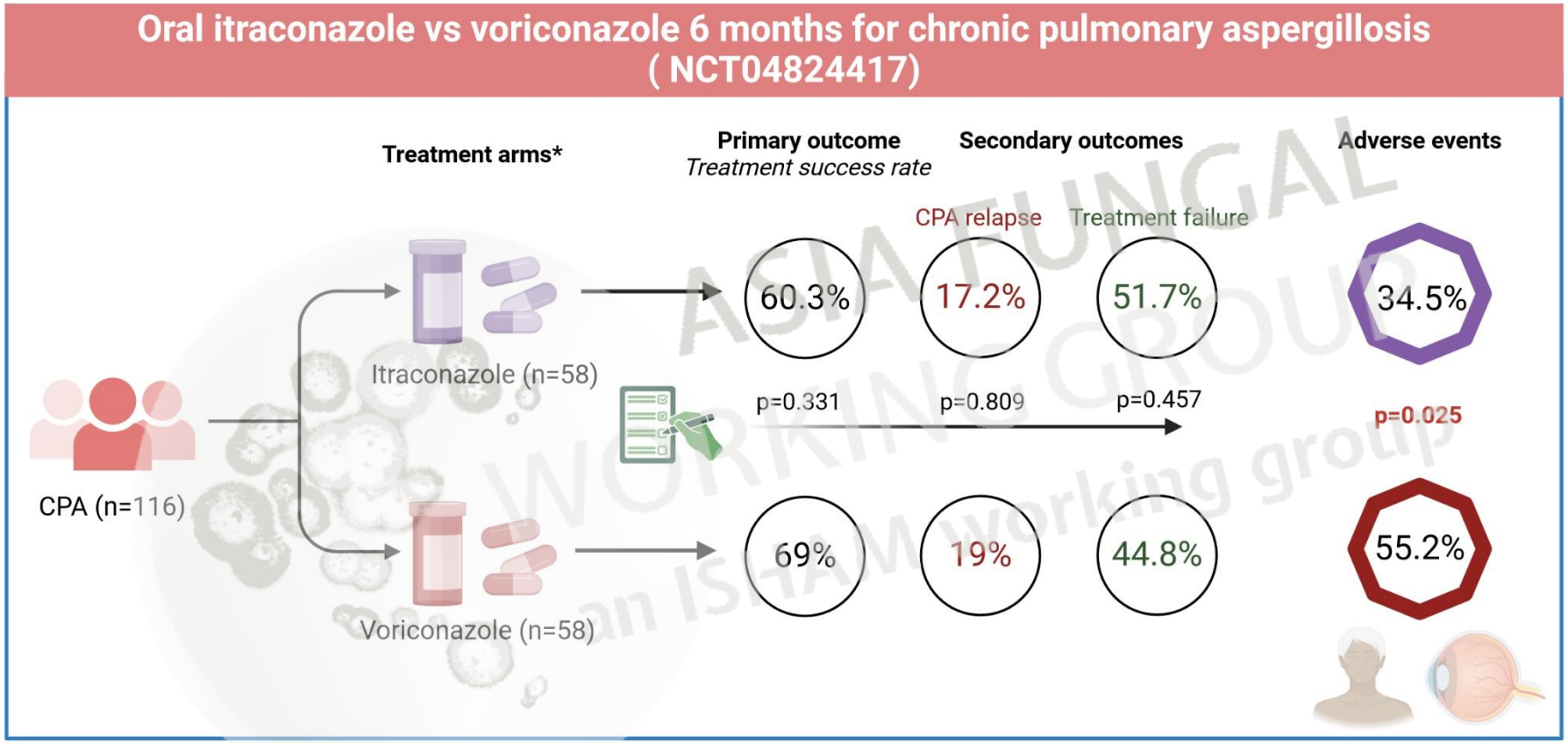
2. Voriconazole

3. Amphotericin

Oral itraconazole may be preferred over other azoles as the initial therapy for CPA. Amongst the intravenous agents, echinocandins & voriconazole may be preferred over amphotericin B.

Sehgal IS et al. Mycoses 2021;64(9):1053-1061

Comparison of six months of oral itraconazole vs. oral voriconazole in CPA



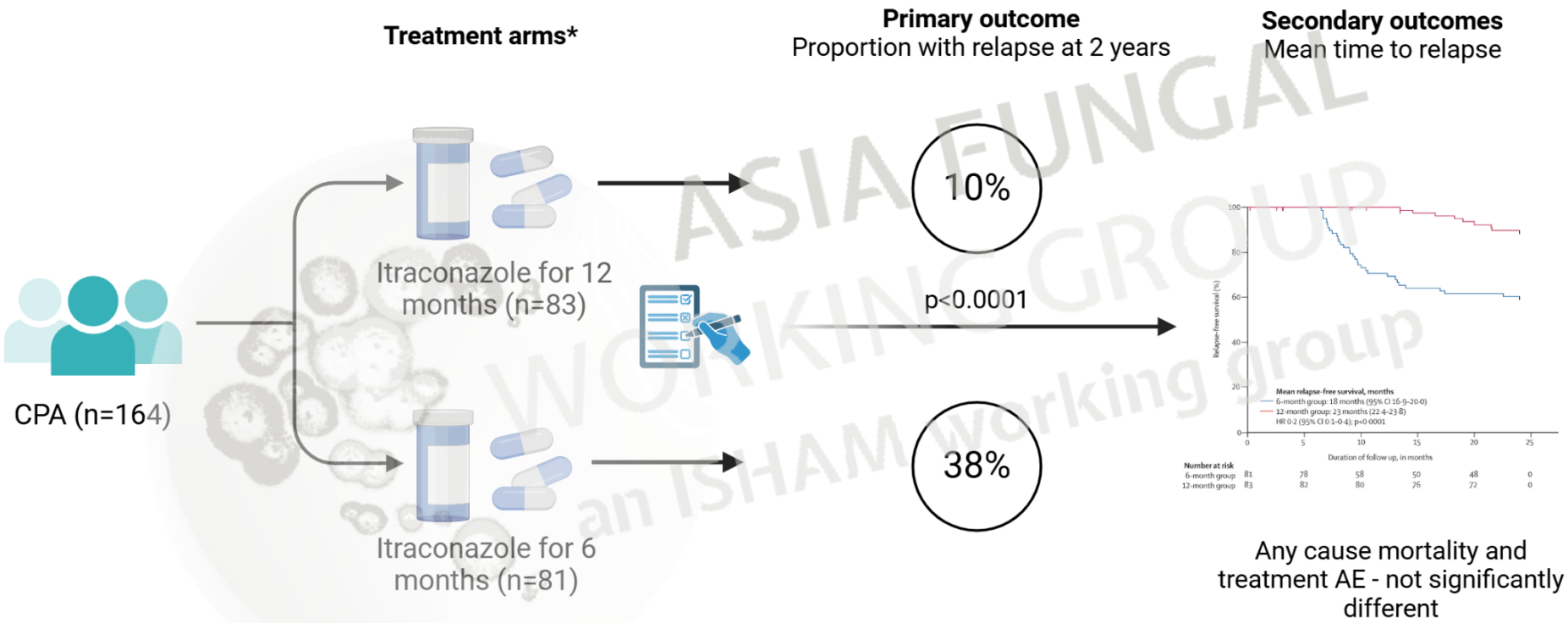
***Itraconazole and voriconazole**: 400 mg/day with therapeutic drug monitoring

Voriconazole is not superior to itraconazole in treating CPA

Unpublished data

Is 12 months of oral itraconazole better than six months?

Oral itraconazole 6 vs 12 months for chronic pulmonary aspergillosis (NCT03920527)



***Itraconazole**: 400 mg/day with therapeutic drug monitoring with a target trough level of at least 0·5 mg/L

All symptomatic patients require treatment for at least 12 months

Sehgal IS, et al. Lancet Infect Dis 2022;22(7):1052-1061

What is the current role of nebulized amphotericin B

- Our experience of 43 (32 CCPA, 11 CFPA) patients
- Used as initial therapy (n=8), maintenance therapy (n=33), and as salvage (n=1)
- Amphotericin B deoxycholate 10 mg twice daily (median duration, 6 months)
  - Alternate days (n=20), six times a week (n=22)
- Treatment outcome
  - Stable or improved: 29 (67.4%)
  - Worsened or did not tolerate: 14 (32.6%)
    - Bronchospasm (n=7), hemoptysis (n=1)

Unpublished data

When should we use intravenous therapy

- As salvage therapy
- Intolerance to oral antifungal drugs
- Poor response to antifungal drugs
- Drug interactions, specially with anti tuberculosis therapy

CPA Clusters

- **Low Th-1 response**
  - Low IFN-Y
  - Low CD4 T lymphocytes
  - Dysfunctional neutrophil oxidative burst

Interferon-gamma as Adjunctive Therapy in Chronic Pulmonary Aspergillosis: a Randomised Feasibility Study (INCAS)(NCT05653193)

- **Type 2 dominant cluster**
  - Higher serum total IgE, blood eosinophil count, and *A. fumigatus*-IgE and IgG
  - More fungal balls on CT
  - Lower FEV1:FVC ratio

Oral Itraconazole Versus Combination of Systemic Glucorticoids and Oral Itraconazole in CPA-ABPA Overlap Syndrome (GLITZ)(NCT05444946)

Sehgal IS, et al. Mycoses 2023;66:299-303
Colombo SAP, et al. J Infect Dis 2022;225:1822-1831
Kumar N, et al. Mycoses 2024;67:e13746

Role of surgery in CPA

Primary therapy in simple aspergilloma

Life-threatening hemoptysis, or inadequate response to anti-fungal agents

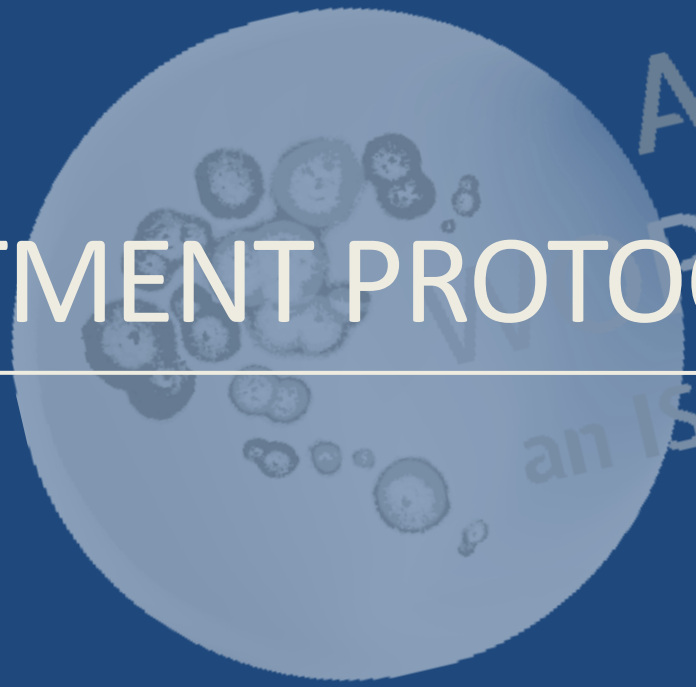
Lobectomy, sub-lobar resection, and occasionally pneumonectomy

Complication rates: none to 30%

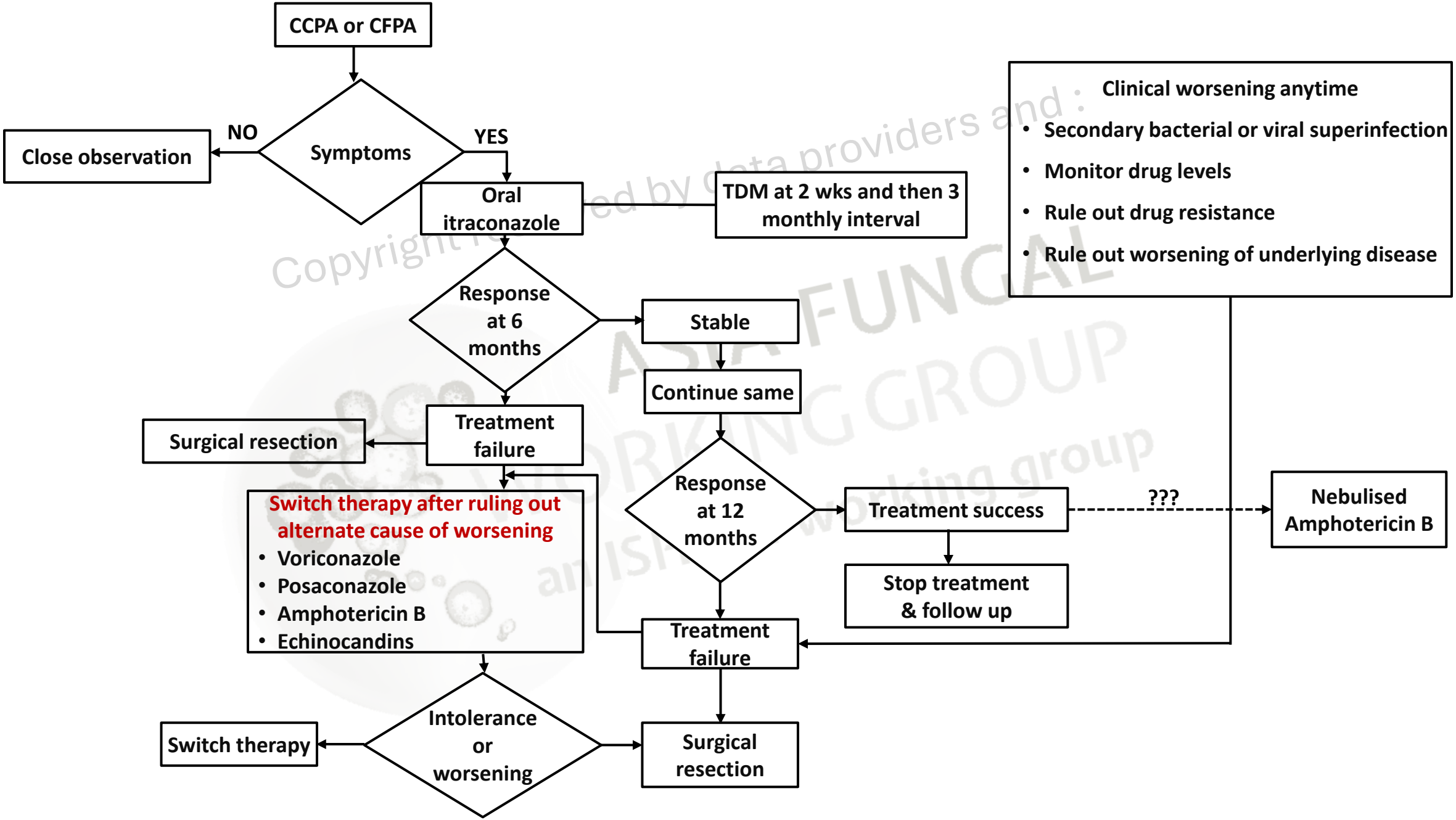
- Prolonged air leak
- Pleural spillage
- Empyema
- Death

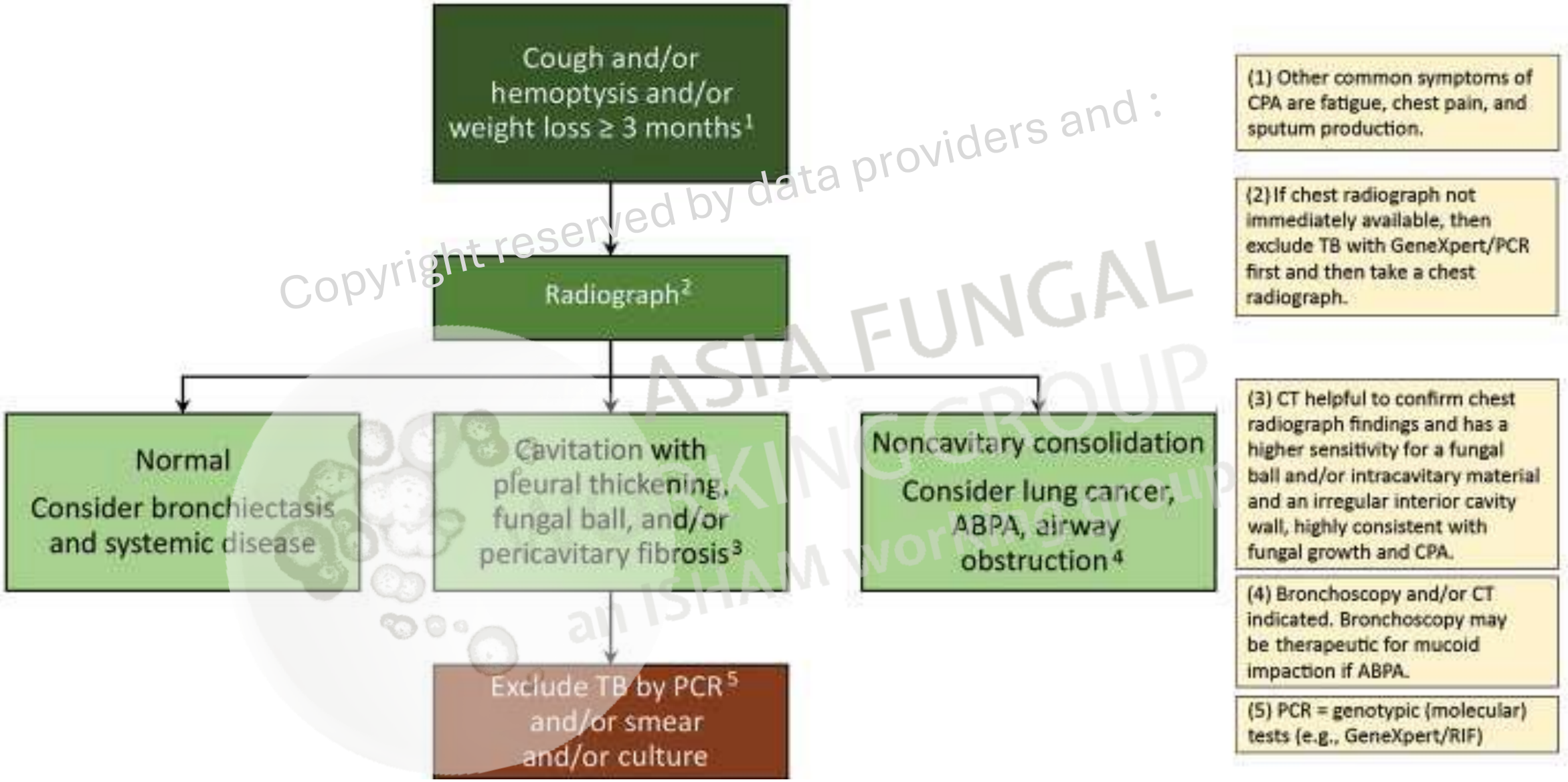
Recurrence of CCPA can occur in 25-30% of subjects during follow up after surgery

Denning et al. Eur Respir J 2016;47:45-68
Sehgal IS, et al. Expert Rev Respir Med 2020;14:715-727

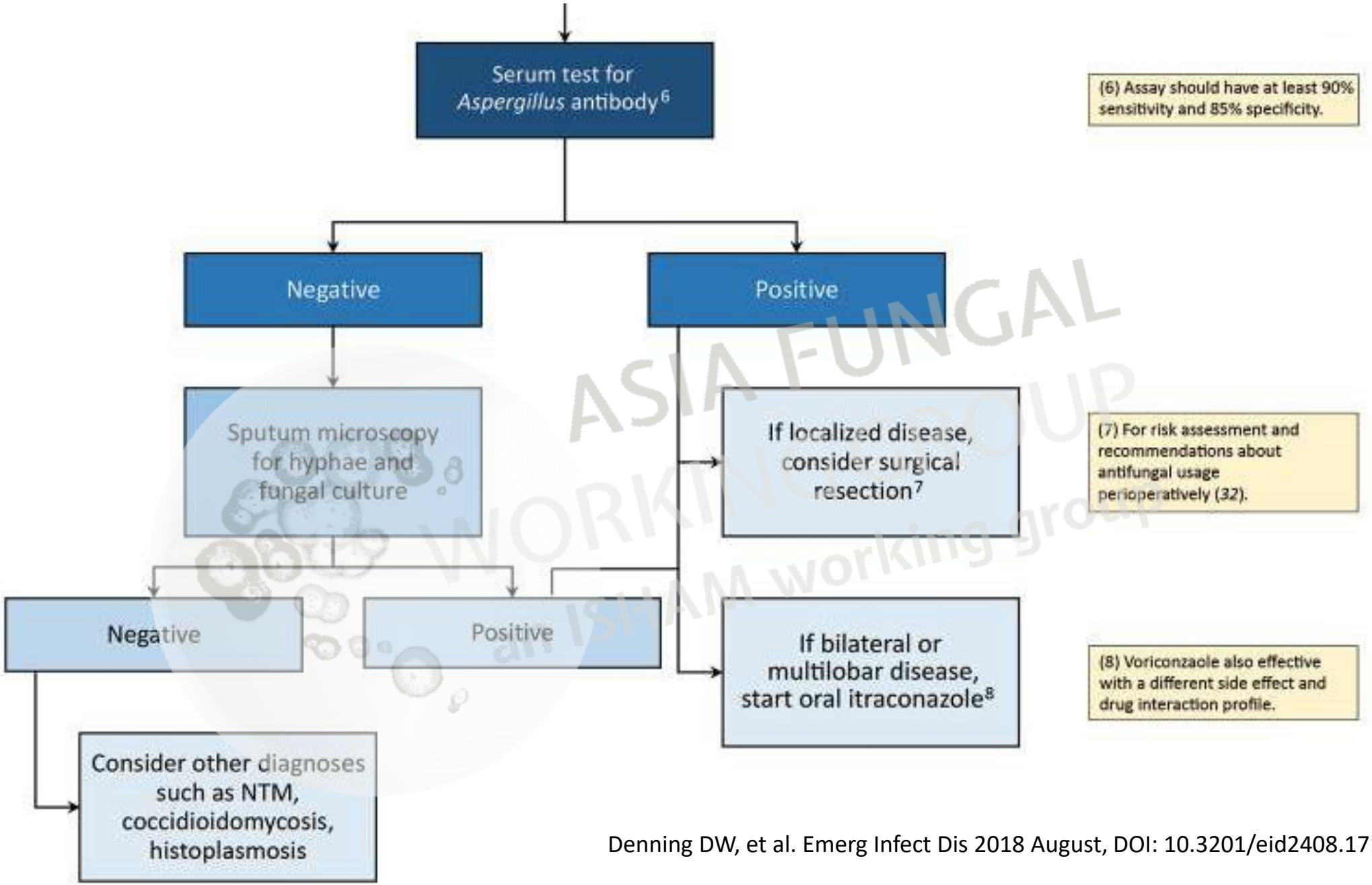


TREATMENT PROTOCOL


CCPA or CFPA
Symptoms
NO
Close observation
YES
Oral itraconazole
TDM at 2 wks and then 3 monthly interval
Clinical worsening anytime
• Secondary bacterial or viral superinfection
• Monitor drug levels
• Rule out drug resistance
• Rule out worsening of underlying disease
Response at 6 months
Stable
Continue same
Treatment failure
Surgical resection
Switch therapy after ruling out alternate cause of worsening
• Voriconazole
• Posaconazole
• Amphotericin B
• Echinocandins
Response at 12 months
Treatment success
???
Nebulised Amphotericin B
Stop treatment & follow up
Treatment failure
Intolerance or worsening
Switch therapy
Surgical resection



Denning DW, et al. Emerg Infect Dis 2018 August, DOI: 10.3201/eid2408.171312



Denning DW, et al. Emerg Infect Dis 2018 August, DOI: 10.3201/eid2408.171312

TREATMENT RESPONSE AND MONITORING IN CPA

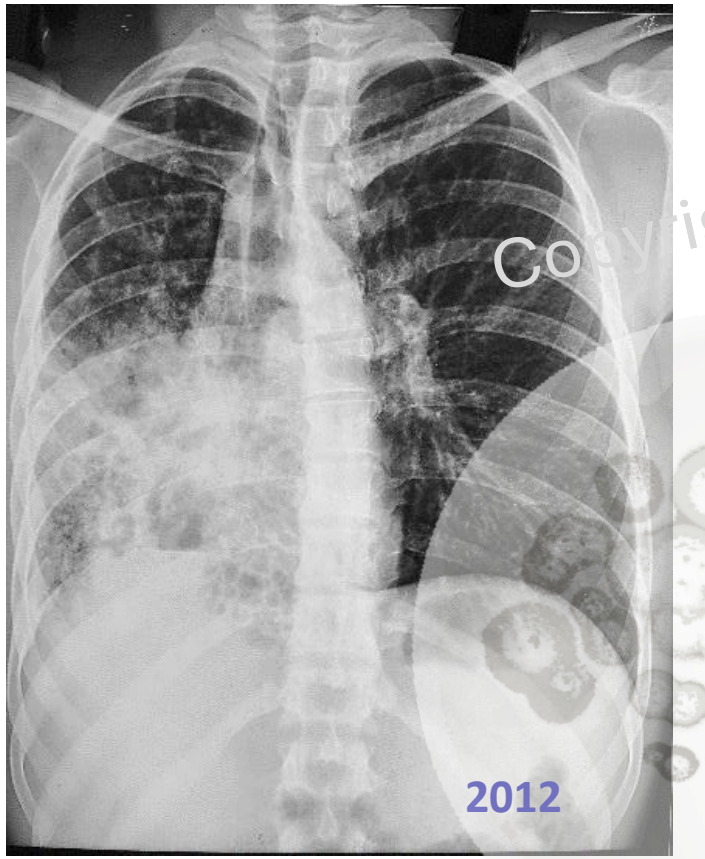
Treatment response and monitoring

- **Clinical**: pulmonary symptoms (cough, sputum production, dyspnea, hemoptysis) and systemic symptoms
- **Serological**: falling *Aspergillus* antibody (IgG, or precipitins)
- **Microbiological**: Sputum culture conversion
- **Inflammatory markers**, such as C-reactive protein and/or erythrocyte sedimentation rate
- **Radiological**: Stabilization or response (decrease in size of fungal ball, cavity size, resolution of pericavitary infiltrates)

- **Progressive worsening**
- **Remission**
- **Relapse**

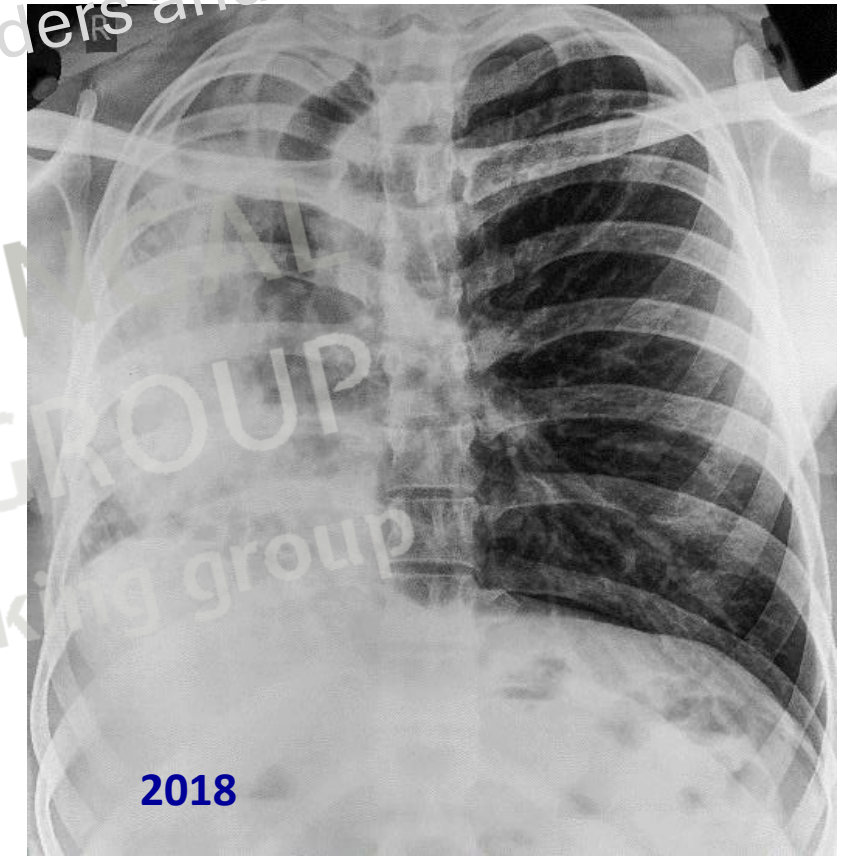
Denning DW et al. Eur Respir J 2016;47:45-68

Progressive worsening



2012

2014

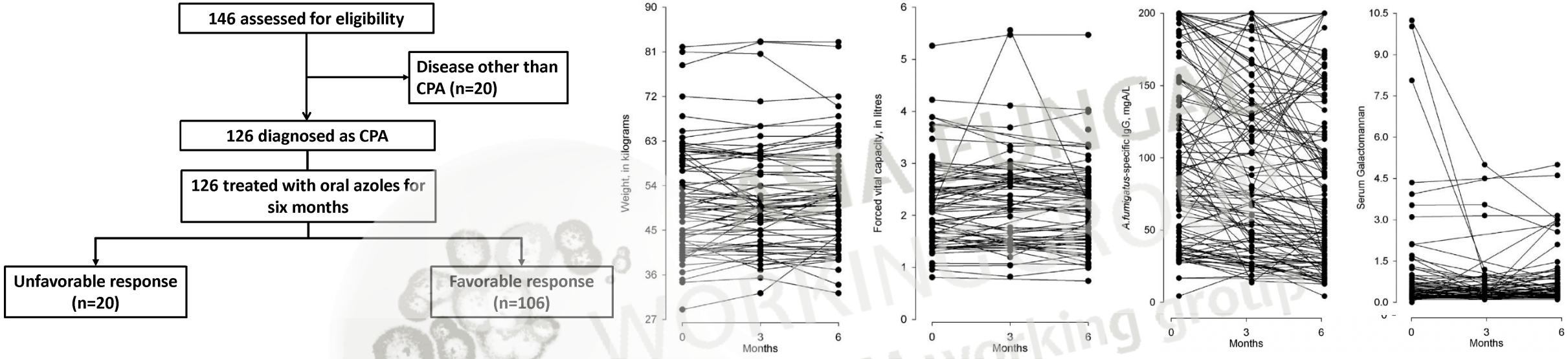


2018

Monitoring treatment response in chronic pulmonary aspergillosis: role of clinical, spirometric and immunological markers

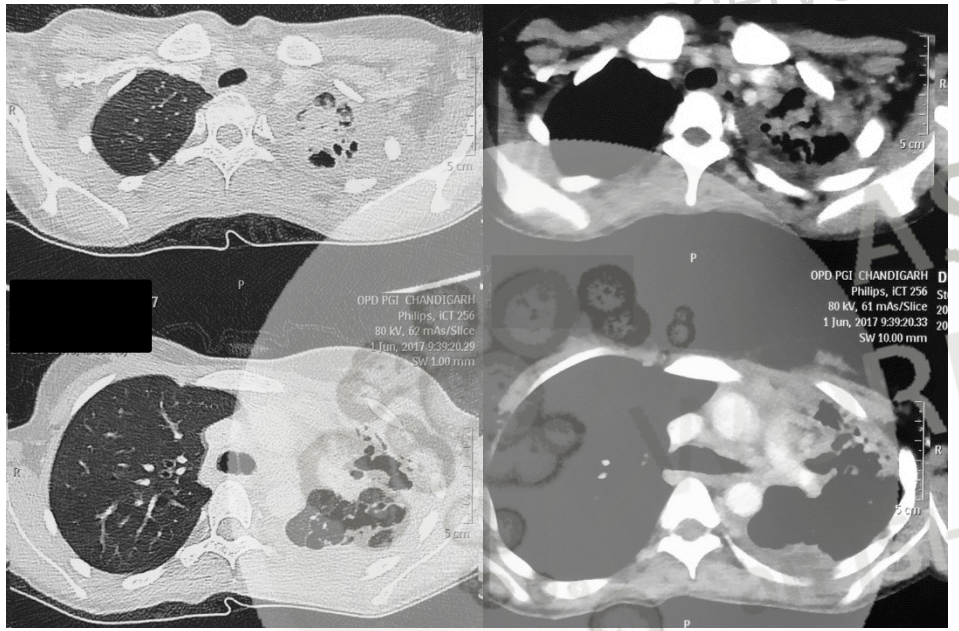
Clinical Microbiology and Infection 25 (2019) 1157.e1–1157.e7

I.S. Sehgal [1], S. Dhooria [1], H. Choudhary [2], A.N. Aggarwal [1], M. Garg [3], A. Chakrabarti [2], R. Agarwal [1,*]

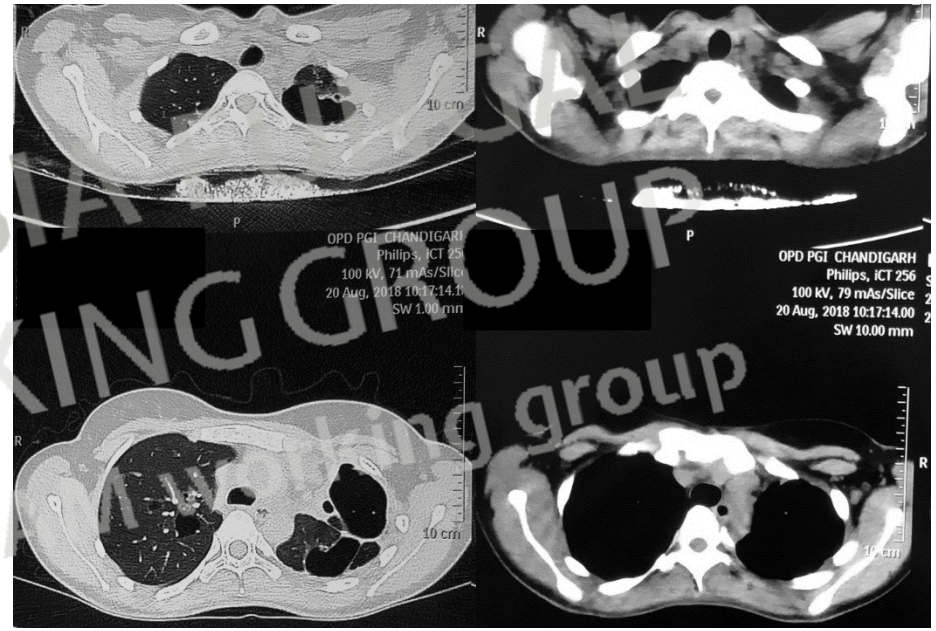


- **After 6 months of treatment, the decline in serum *A. fumigatus*-specific IgG was similar in those with favourable or unfavourable response**
- **No significant change in the serum galactomannan or FEV1 favourable vs. unfavourable)**
- **There was significant loss of weight (mean ± SD, e2.5 ± 4.5 kg) in subjects with unfavourable response**
- **Gain in body weight is seen in those with favourable response**

Radiological response



Baseline



1 year

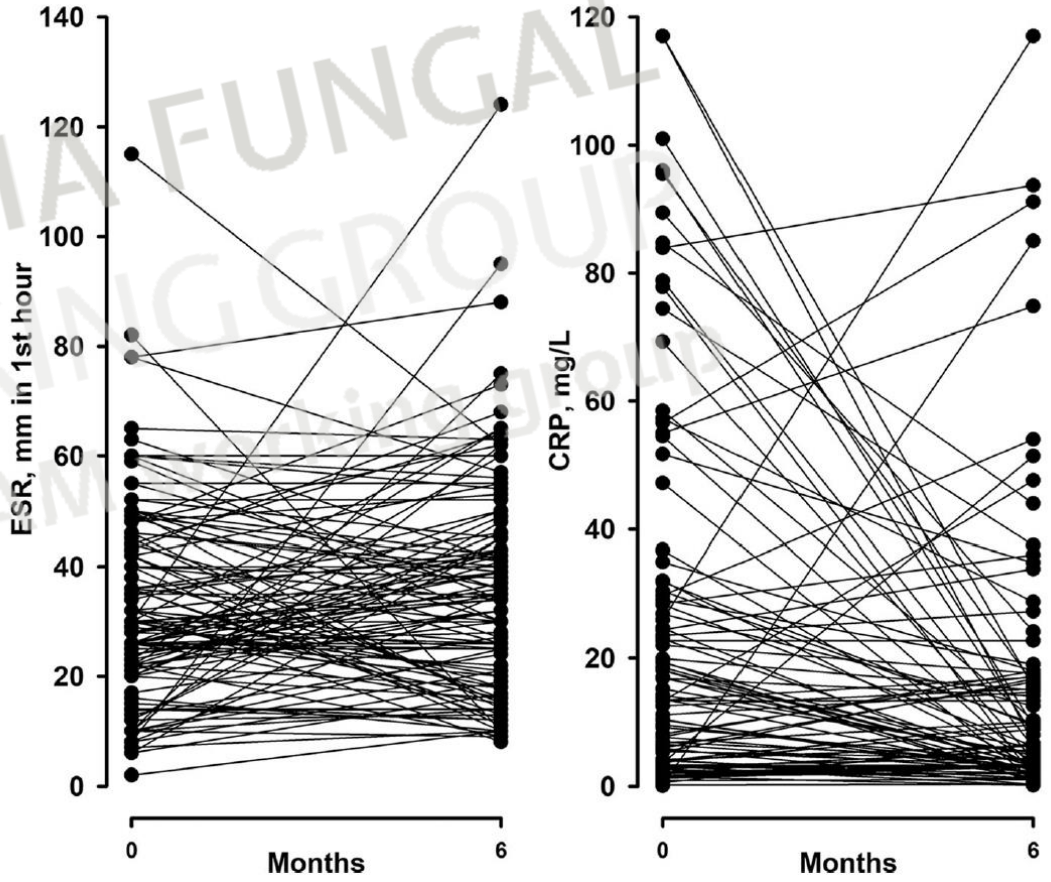
Role of C-Reactive Protein and Erythrocyte Sedimentation Rate in the Diagnosis and Monitoring of Treatment Response in Treatment Naïve Subjects with Chronic Pulmonary Aspergillosis

Mycopathologia (2023) 188:705–711

Inderpaul Singh Sehgal · Sahajal Dhooria · Shivaprakash M. Rudramurthy · Kuruswamy Thurai Prasad · Valliappan Muthu · Ashutosh Nath Aggarwal · Mandeep Garg · Pulkit Rastogi · Ritesh Agarwal

Both ESR and CRP had erratic trend following treatment. ESR and CRP declined or remained stable in approximately 60% of subjects but increased in approximately 40% of the subjects despite treatment.

Serum CRP and ESR have limited utility in diagnosing and following subjects with CPA



Treatment response and monitoring

- **Clinical**: pulmonary symptoms (cough, sputum production, dyspnea, hemoptysis) and systemic symptoms
- **Serological**: falling *Aspergillus* antibody (IgG, or precipitins)
- **Microbiological**: Sputum culture conversion
- **Inflammatory markers**, such as C-reactive protein and/or erythrocyte sedimentation rate
- **Radiological**: Stabilization or response (decrease in size of fungal ball, cavity size, resolution of pericavitary infiltrates)

- **Treatment success**
  - Clinical and radiological stability or improvement
- **Treatment failure**
  - Clinical or radiological worsening

Denning DW et al. Eur Respir J 2016;47:45-68

Failure of therapy

- Low serum concentration of azole
- Antifungal drug resistance
- Co-infection with bacterial (viral) pathogen
- Worsening due to underlying disease (reactivation of PTB)

Sehgal IS, et al. Expert Rev Respir Med 2020;14:715-727
Sehgal IS, et al. Mycoses 2023;66:576-584

CPA remission

- Sustained (> 6 months) clinical and radiological stability off CPA therapy

CPA relapse

- Any subject with persistent worsening (>2 weeks) of symptoms (systemic or respiratory) and imaging, with or without microbiological evidence of *Aspergillus* on culture > 3 months after stopping treatment
- Exclusion of other cause for clinical or radiological deterioration, including (myco)bacterial super-infection

Sehgal IS, et al. Expert Rev Respir Med 2020;14:715-727
Van Braeckel E, et al. Eur Respir J. 2022;59:2102950
Sehgal IS, et al. Mycopathologia 2023;188(5):721-730

Conclusion

- The diagnosis of CPA is made using a composite of clinical, radiological, and microbiological findings
- Sputum or BALF fungal culture have poor sensitivity in diagnosing CPA
- At a threshold of 27 mgA/L serum *A. fumigatus*-IgG is the most useful test for diagnosing CPA
- LDBio-ALFA has reasonable performance for diagnosing CPA
- As a stand-alone test serum and BALF GM should not be used for diagnosing CPA

Conclusion

- Close observation is required without the need for universal treatment in minimally symptomatic patients
- All symptomatic patients with CPA should be treated
- Treatment with itraconazole should be given for at least 12 months
- Voriconazole is not superior to itraconazole in treating CPA
- The current treatment response criteria for CPA is imperfect

I acknowledge Dr. Inderpaul Singh of PGIMER, Chandigarh, India for providing leadership in most of the studies