CG- CS Raipur- 2025

ABPA : *State of Art 2025*

Deepak Talwar

Director & Chair, Metro Centre for Respiratory Diseases

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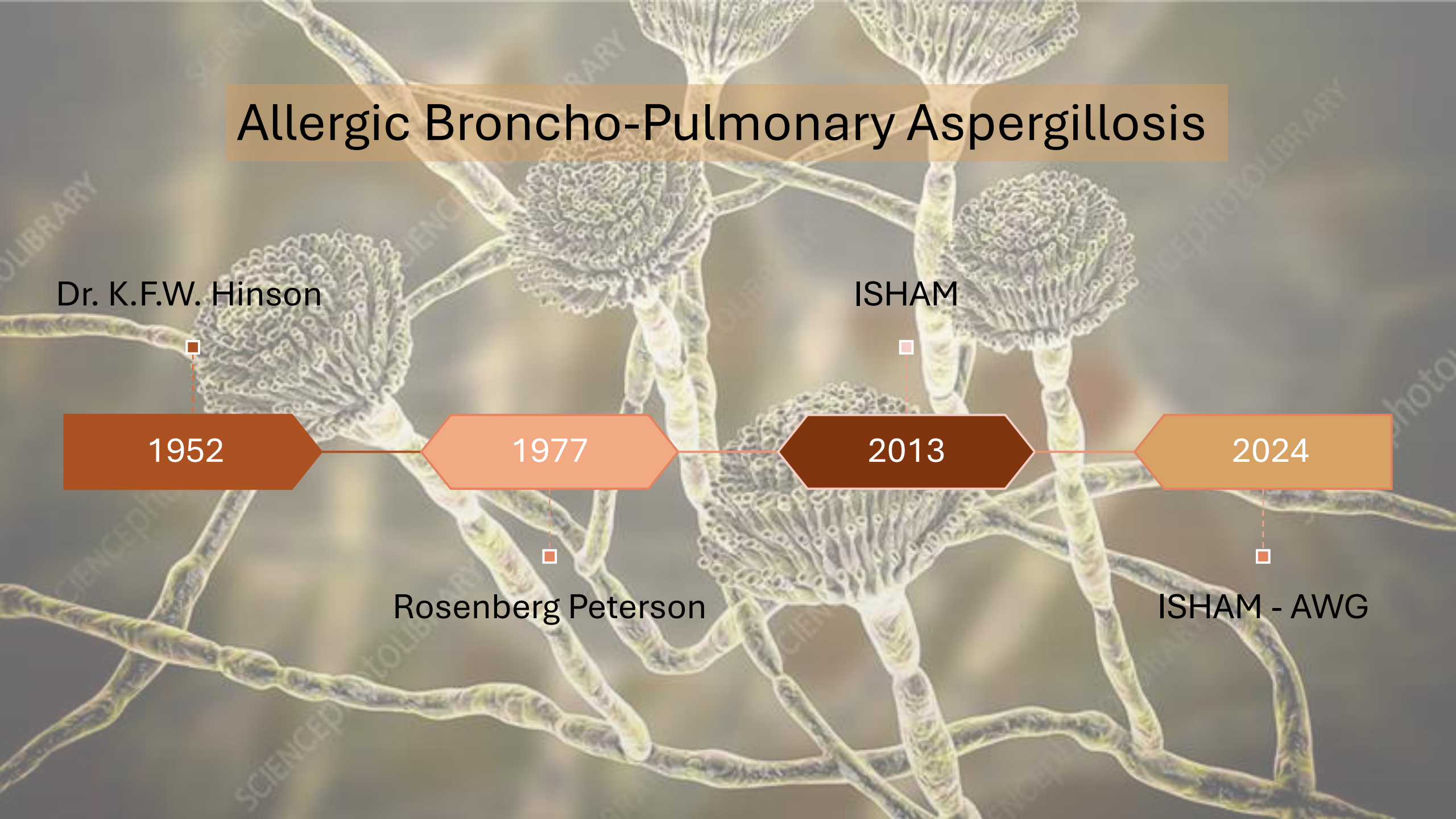
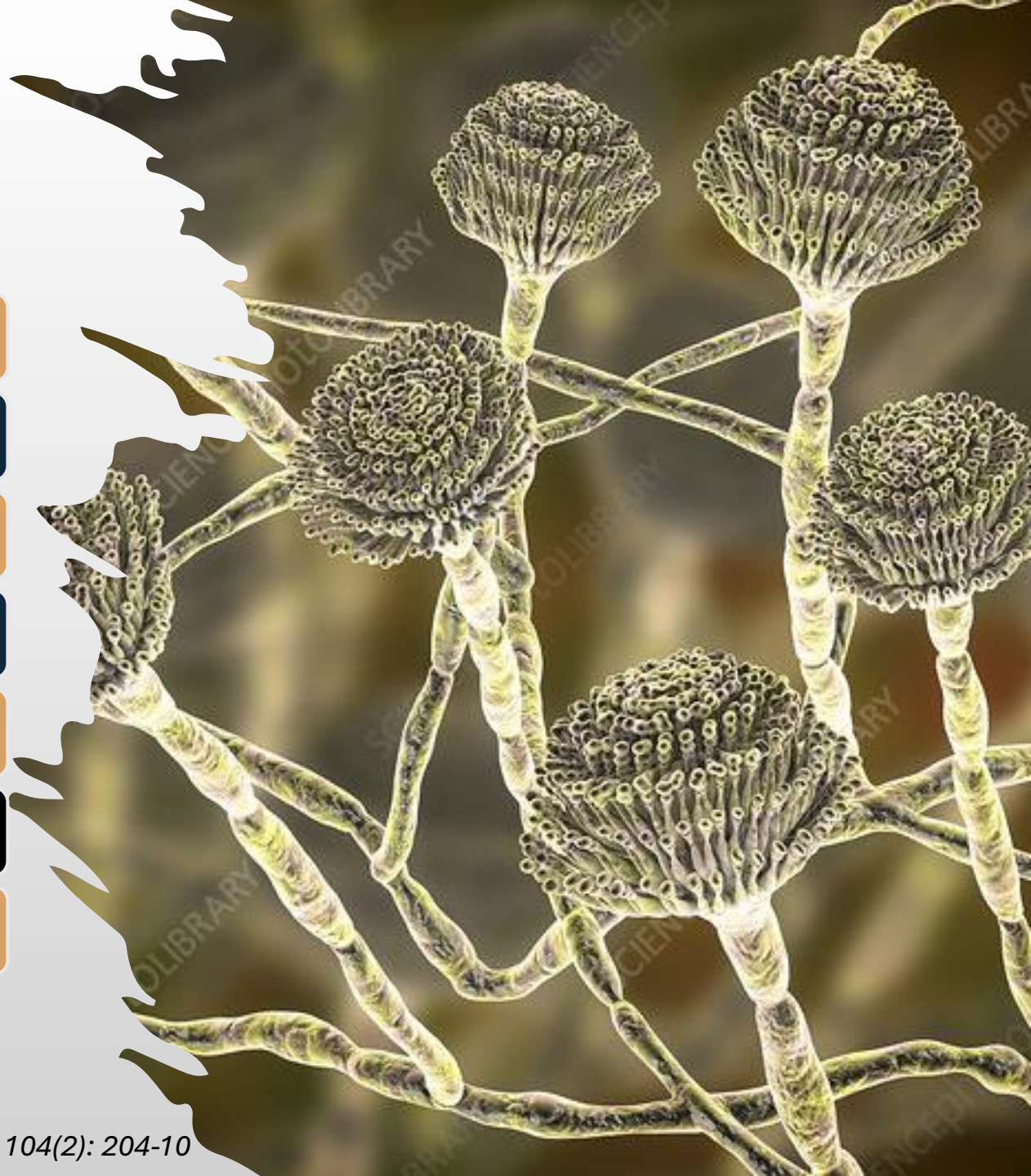
Allergic Broncho-Pulmonary Aspergillosis



ABPA

- Aspergillus colonize airways
- IgE mediated hypersensitivity disease
- 4% of asthmatics have ABPA
- 38% asthmatics ~ Aspergillus sensitization
- Present as ‘Difficult to Treat Asthma’
- India has 2X burden of ABPA vs World
- 1/5th gets tuberculsis treatment - misdiagnosis



Agarwal R, et al. Chest 2007; 132(4): 1183-90 Agarwal R, et al. Respir Med 2010; 104(2): 204-10

Underlying Conditions :

- Asthma
- Cystic Fibrosis
- ↘ COPD
- ↘ Bronchiectasis

Agarwal R: Revised ISHAM-ABPA. Eur Respir J 2024;63:2400061.

DIAGNOSIS

Predisposing Condition

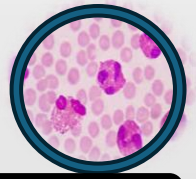
Asthma / CF/COPD/ Bronchiectasis

Clinical

Aspergillus Hyphae

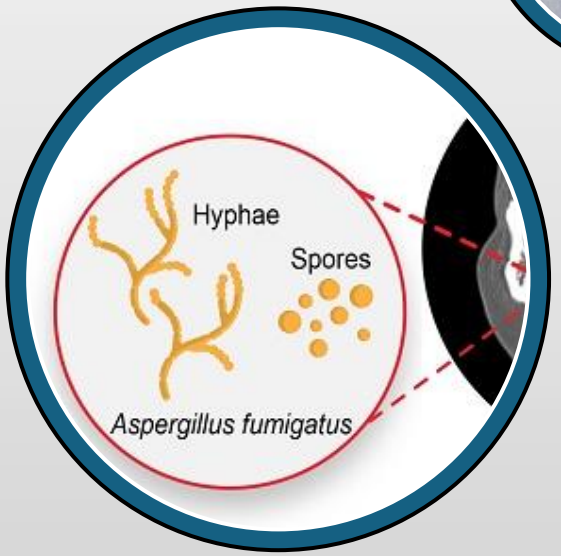
Hemoptysis

Biochemical



AEC > 500

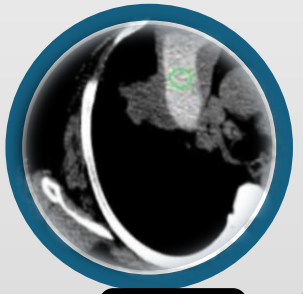
Total IgE ≥ 500



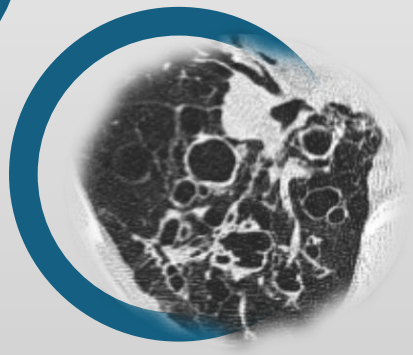
Aspergillus Specific IgE ≥ 0.35

Aspergillus Specific IgG > 27

Radiological



HAM



Bronchiectasis

2024 ISHAM-AWG guidelines

Algorithm For ABPA Diagnosis

Asthma
Cystic Fibrosis
COPD
Bronchiectasis

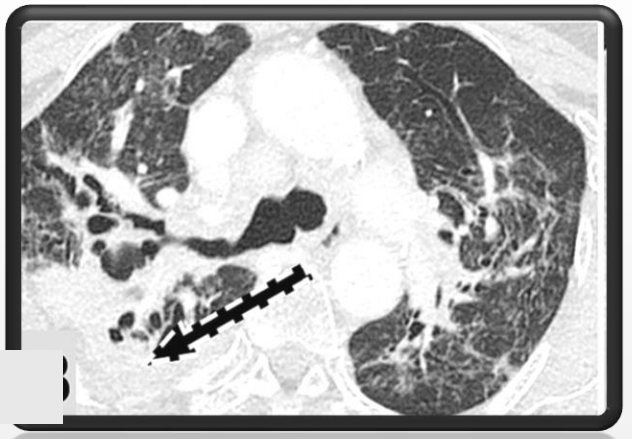
Aspergillus IgE > 0.35 / SPT + to Aspergillus

Total IgE > 500 IU/ml

AEC> 500cells/uL
Aspergillus IgG > 27 mgA/L

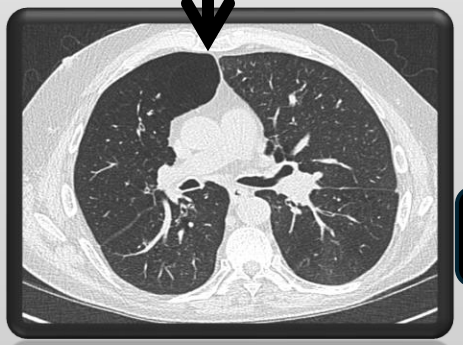
HRCT Chest

ABPA -S

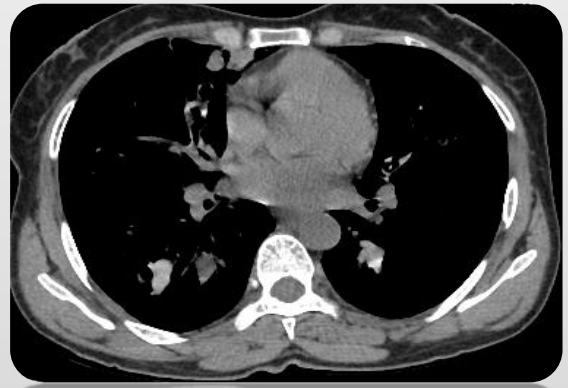


ABPA -CPF

ABPA -B



ABPA - MP



ABPA - HAM

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Algorithm For ABPM Diagnosis

Asthma
Cystic Fibrosis
COPD
Bronchiectasis

OR

Compatible Clinical Picture

Elevated Serum Fungus Specific IgE HIGH

Total IgE ≥ 500 IU/ml

Any 2 of 3

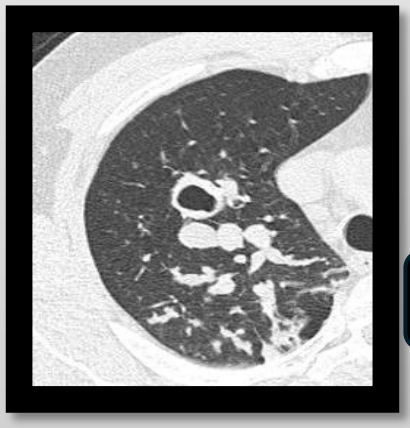
1. AEC> 500cells/u
2. Fungus specific IgG HIGH
3. 2 Sputum OR 1 BAL Fungus Culture +ve

HRCT Chest

ABPM

ABPM -B

ABPM - MP



ABPM - HAM

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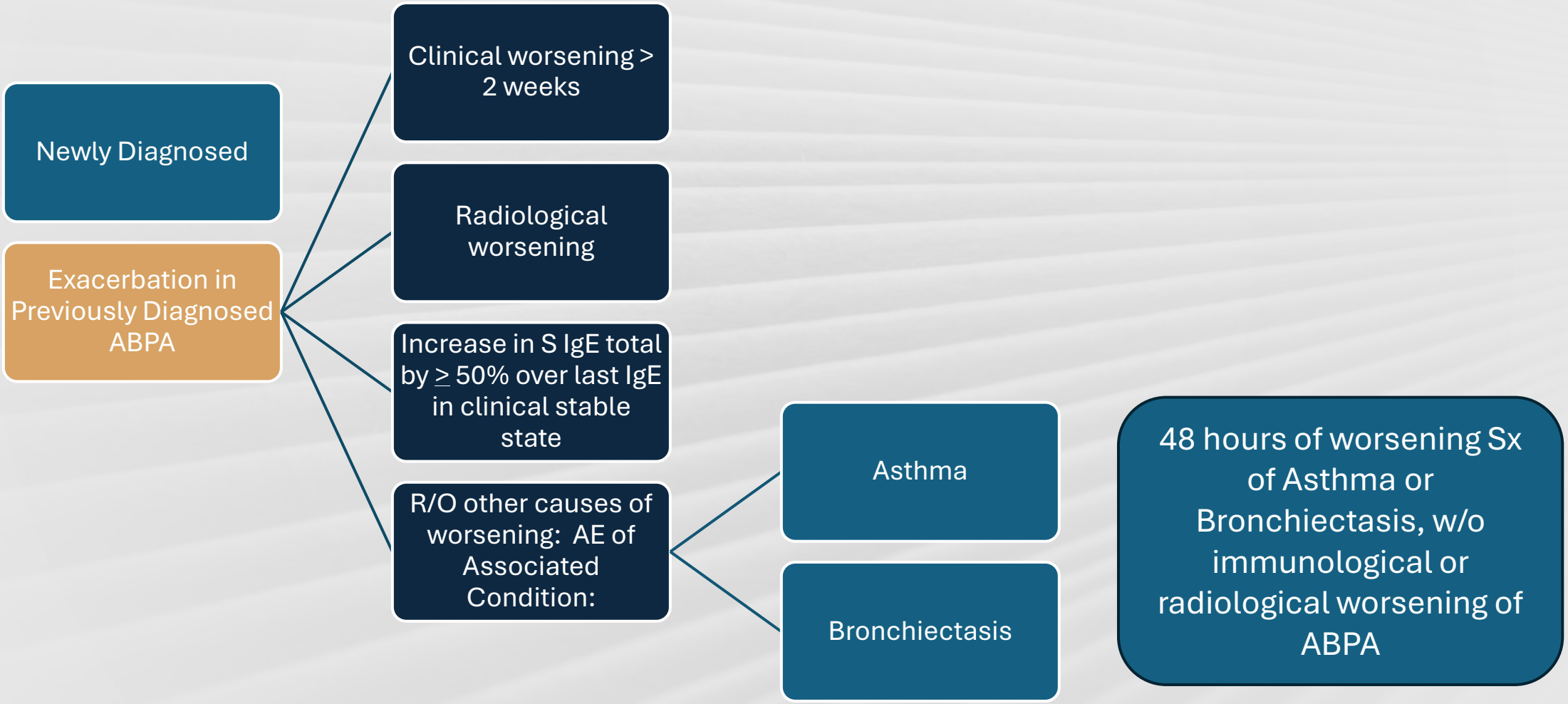
Clinico-Radiological Stages of ABPA : *Acute ABPA*



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Clinico-Radiological Stages of ABPA : *Response*

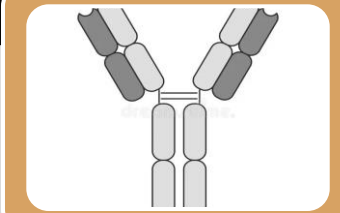
Improvement
@
8 weeks

Symptoms

- ≥ 50% in Visual Analogue Scale

Imaging

- ≥ 50% reduction in radiological opacities



Immunological

- Decrease in IgE Total ≥20%

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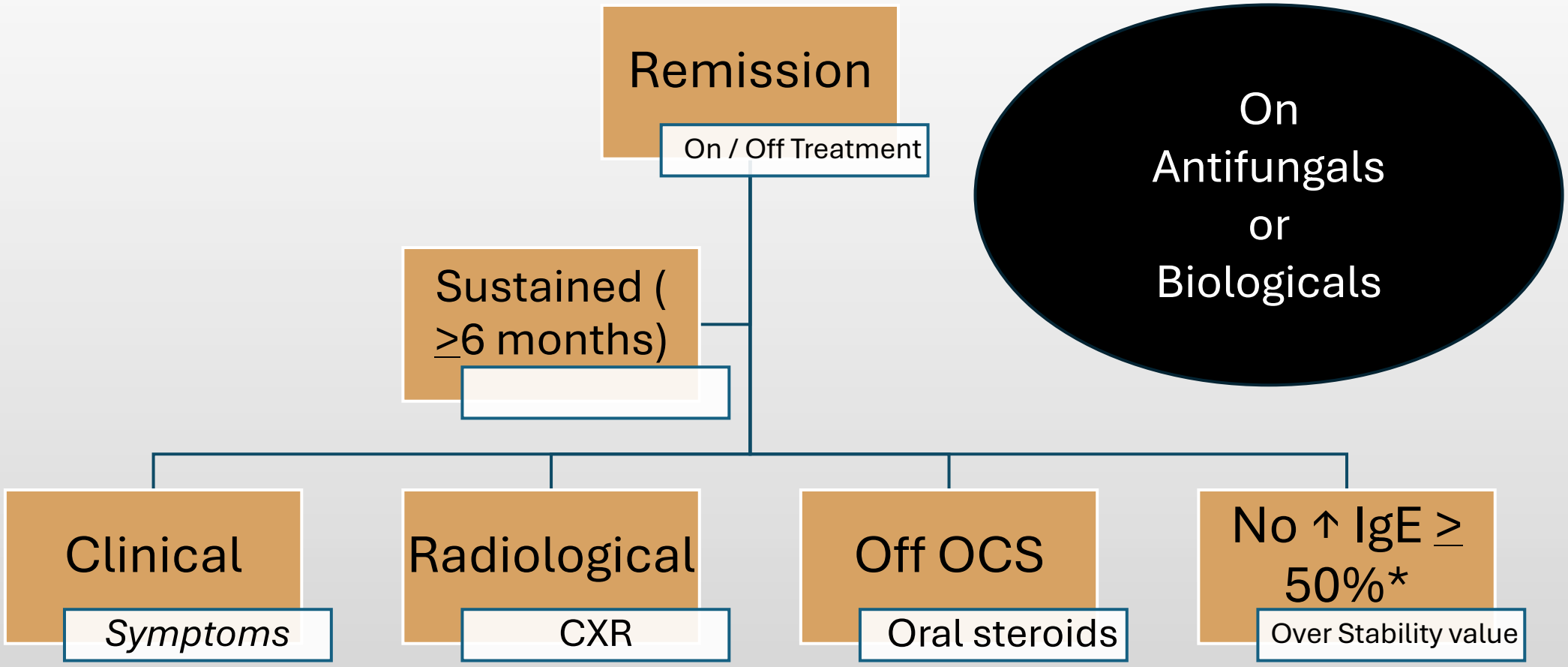
Clinico-Radiological Stages of ABPA : *Remission*



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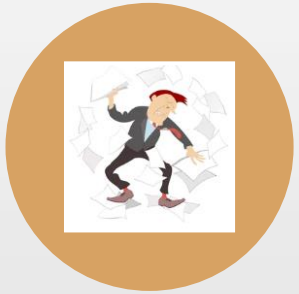
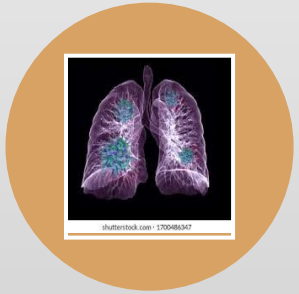
Clinico-Radiological Stages of ABPA :

Treatment Dependent



≥ 2 consecutive ABPA exacerbations, within 3 months of stopping OCS

+



Worsening imaging

OR

Worsening respiratory symptoms

AND

Rise in serum total IgE by 50% within 4 weeks of tapering OCS on 2 separate occasions

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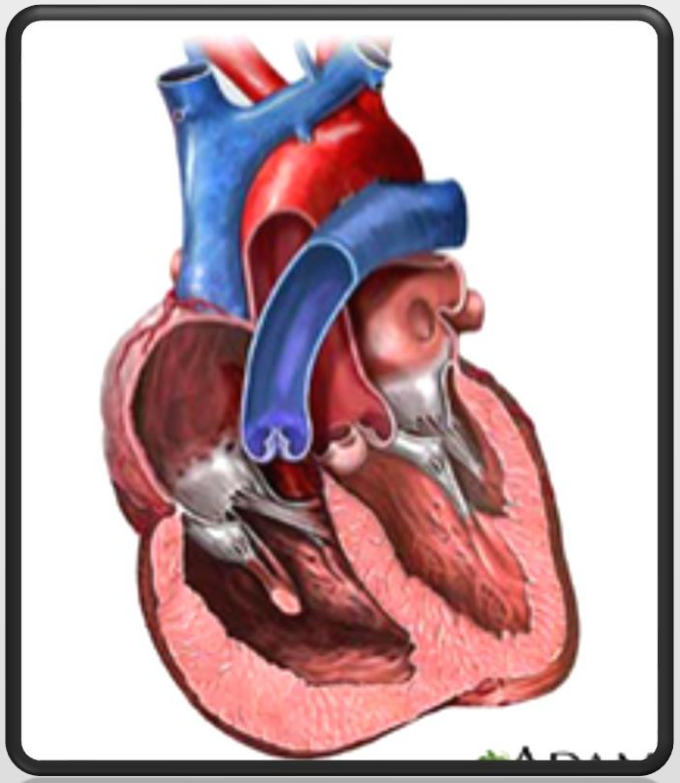
Advanced ABPA

- Extensive bronchiectasis (≥10 segments) due to ABPA on imaging



AND

- Cor pulmonale

OR

- Type 2 Respiratory Failure

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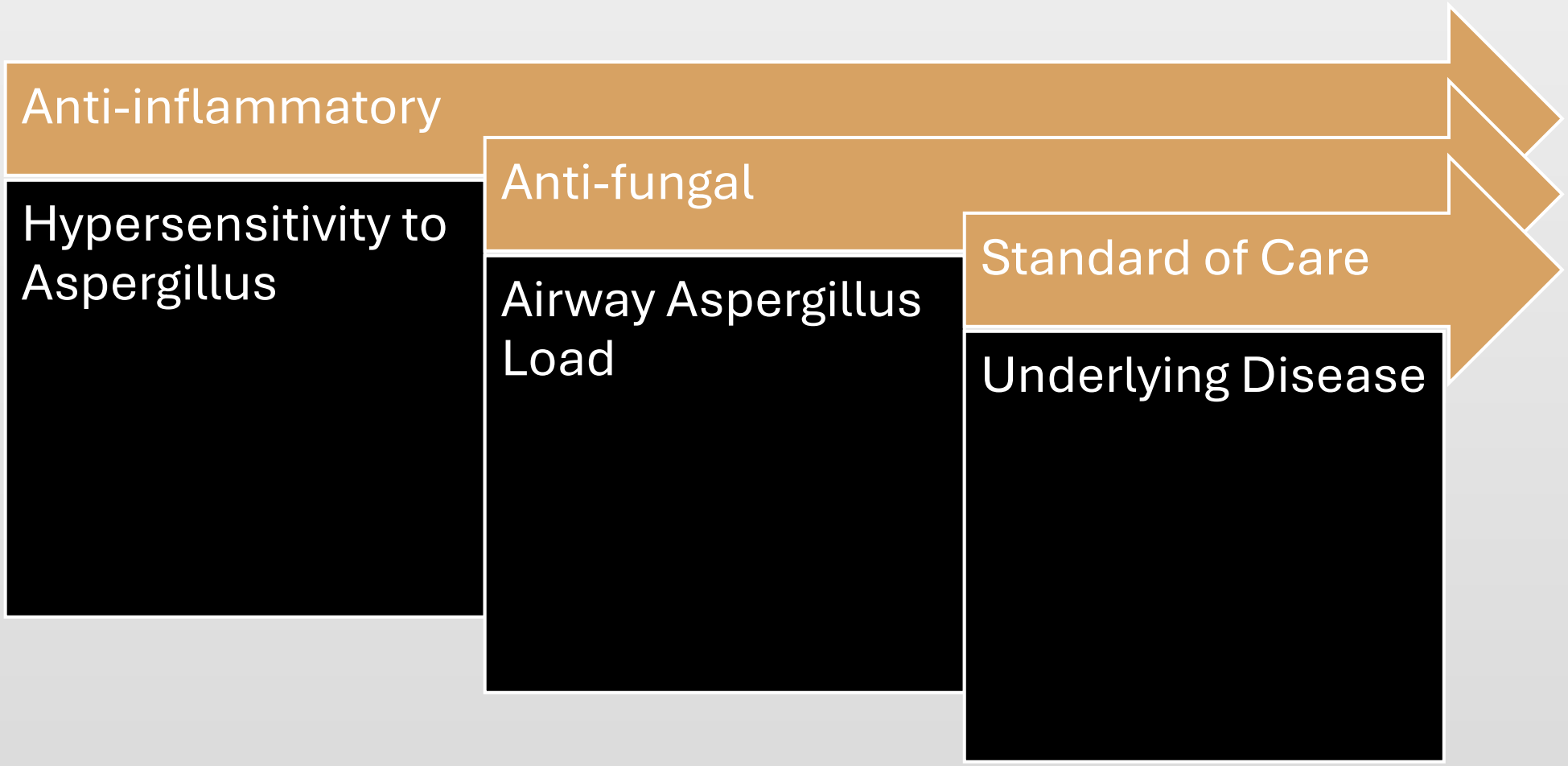
Treatment of ABPA : Principles



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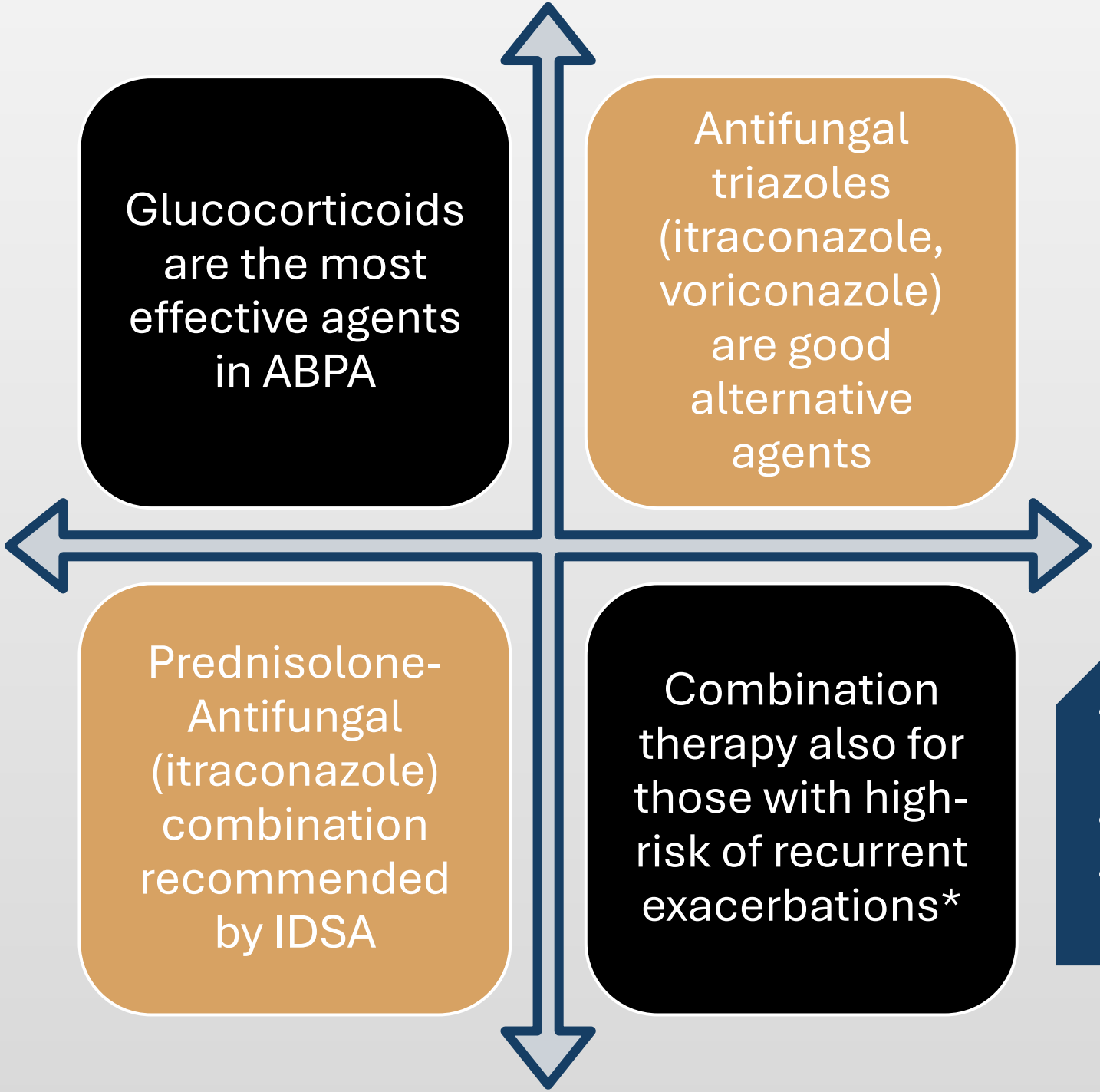

ABPA Treatment

*

- First exacerbation of ABPA (to maintain remission)
- Glucocorticoid-dependent ABPA
- Alternative therapy in acute-stage ABPA

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Steroids in ABPA : *1st Line Therapy*

Dose : 0.5mg/kg/day – 2 weeks, decrease dose by 5 mg every 2 weeks till maintenance dose 10 mg /day for ~ 6 months

Relapses -13.5–45% and can become OCS-dependent

Steroid induced side effects : Total OCS dose dependent

Agarwal R, et al. Clin Chest Med 2022; 43(1): 99-125

Azoles in ABPA : *Add on 1st Line or 2nd Line Therapy*

As 1st line when OCS can't, be used *

* Poorly controlled DM or Severe OCS related side effects threatening life or organ or chronic infections

Issues

- Drug interactions
- Hepatotoxicity
- Bioavailability

Delayed Response

2nd line or as combined therapy

Adding Azoles to OCS – Adrenal suppression

- Itraconazole : need monitoring of serum drug levels
- Voriconazole : less affected bioavailability
- Posaconazole : used in resistance to other azoles

Agarwal R, et al. Clin Chest Med 2022; 43(1): 99-1

Goals of Treatment & Drugs in ABPA

Goals For Treatment	Acute ABPA Newly Diagnosed	ABPA in Remission Improvement for ≥ 6 months without OCS	Treatment Dependent ABPA ; Exacerbation or worsening after tapering OCS	Advanced ABPA Extensive Brx or Respiratory Failure
Relief of Symptoms	✓ # ^	✓	✓#^	✓
Prevent Bronchiectasis	✓#^	^	^	
Reduce Adverse Effects	✓^		✓^	✓^
Prevent Reoccurrences	✓#^	✓^	✓#^	

✓ Biologicals # Steroids ^ Antifungals

Biologicals in ABPA : Omalizumab

2.09 % LESS EXACERBATIONS

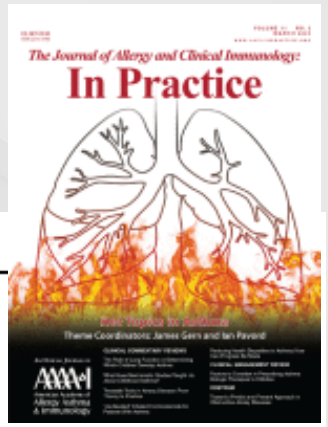
65 % REDUCTION IN OCS USE

53 % OCS TERMINATION

15 % REDUCTION IN OCS MG/DAY

12 % FEV_1 IMPROVEMENT

8 % BETTER ASTHMA CONTROL

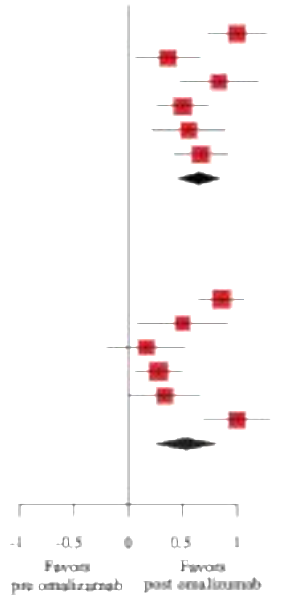


Original Article

Omalizumab in Allergic Bronchopulmonary Aspergillosis: A Systematic Review and Meta-Analysis

Meiling Jin, MD[a], Jo A. Douglass, MD[b], J. Stuart Elborn, MD[c], Ritesh Agarwal, MD[d], William J. Calhoun, MD[e], Slawomir Lazarewicz, MD[f], Xavier Jaumont, MD[f], and Meng Yan, MD[f] *Shanghai, China; Melbourne, Victoria, Australia; Belfast, United Kingdom; Chandigarh, India; Galveston, Texas; and Basel, Switzerland*

Study or Subgroup	Treatment Duration	Post omalizumab Event	Total (n)	Weight	Risk Difference MH, Random, 95% CI
Reduction in Oral Corticosteroid					
Emiralioglu 2016	1-3 months	6	6	17.3%	1.00 [0.73; 1.27]
Koutsokera 2020*	12 months	4	11	16.5%	0.36 [0.07; 0.66]
Lehmann 2014	19.7 months	5	6	14.6%	0.83 [0.47; 1.19]
Nové-Josserand 2017	6-12 months	9	18	18.4%	0.50 [0.26; 0.74]
Tillie-Leblond 2011*	12 months	5	9	15.2%	0.56 [0.22; 0.89]
Totomatsu 2020*	3.7 months	10	15	18.0%	0.67 [0.42; 0.91]
Total (95% CI)			**65**	**100.0%**	**0.65 [0.46; 0.84]**
Heterogeneity: $Tau^2 = 0.0333$; $Chi^2 = 12.92$, df = 5 ($P = 0.02$); $I^2 = 61\%$					
Test for overall effect: $Z = 6.79$ ($P < 0.01$)					
Oral Corticosteroid Use Stopped					
Aydin 2015	54 months	12	14	19.7%	0.86 [0.65; 1.07]
Emiralioglu 2016	12.5 months	3	6	13.3%	0.50 [0.08; 0.92]
Lehmann 2014	19.7 months	1	6	15.0%	0.17 [-0.19; 0.53]
Nové-Josserand 2017	6-12 months	5	18	19.5%	0.28 [0.06; 0.49]
Tillie-Leblond 2011	12 months	3	9	16.0%	0.33 [0.01; 0.66]
Unal 2019	36 months	5	5	16.4%	1.00 [0.69; 1.31]
Total (95% CI)			**58**	**100.0%**	**0.53 [0.26; 0.80]**
Heterogeneity: $Tau^2 = 0.0627$; $Chi^2 = 28.44$, df = 5 ($P < 0.01$); $I^2 = 82\%$					
Test for overall effect: $Z = 3.79$ ($P < 0.01$)					



Average dose 375 mg/ twice a month

Biologicals in ABPA : Anti IL-5 Mabs

Mepolizumab :

- Reduction in :
  - Exacerbations
  - OCS dose
- Improvement in:
  - Asthma control
  - Lung functions

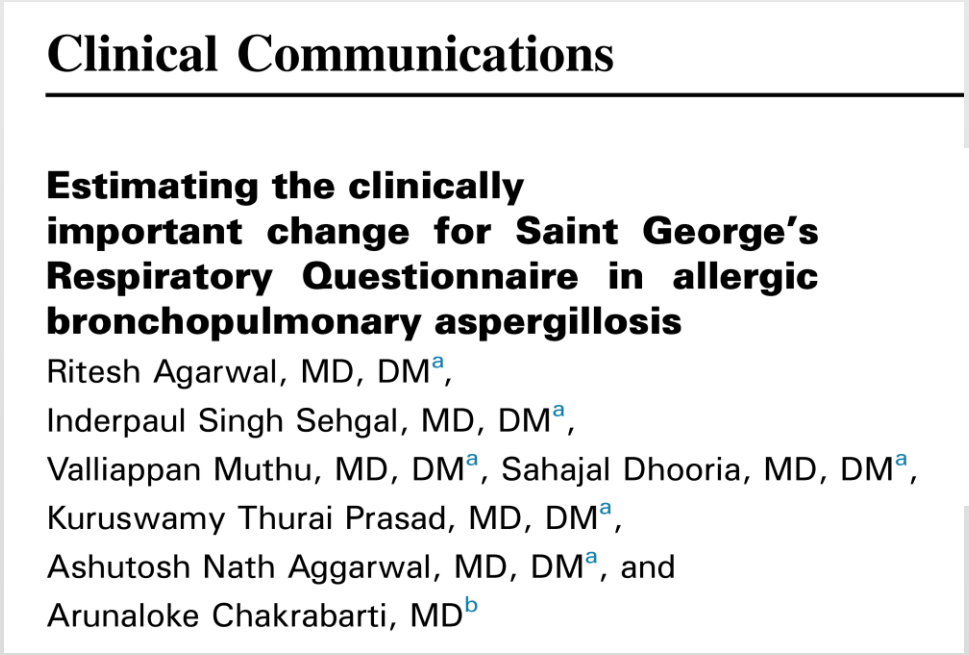
Benralizumab :

- May be more effective in ABPA patients with mucus plugging

Small studies mostly failed on antifungals or omalizumab

Follow-up and monitoring

- Clinical examination, chest radiograph, Total IgE levels (25% (35%)) decline; **not specific IgE or IgG**) every 8 weeks



Clinical Communications

Estimating the clinically important change for Saint George's Respiratory Questionnaire in allergic bronchopulmonary aspergillosis

Ritesh Agarwal, MD, DM[a],
Inderpaul Singh Sehgal, MD, DM[a],
Valliappan Muthu, MD, DM[a], Sahajal Dhooria, MD, DM[a],
Kuruswamy Thurai Prasad, MD, DM[a],
Ashutosh Nath Aggarwal, MD, DM[a], and
Arunaloke Chakrabarti, MD[b]

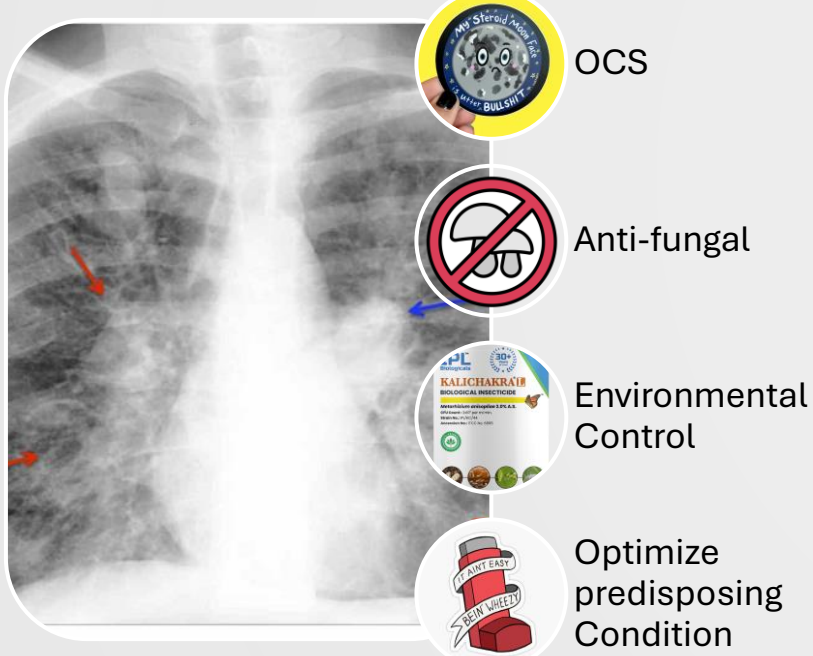
EUROPEAN RESPIRATORY *journal*
OFFICIAL SCIENTIFIC JOURNAL OF THE ERS

Estimating the minimal important difference for FEV1 in patients with allergic bronchopulmonary aspergillosis

Agarwal R, et al. Respir Med 2010; 104(2): 204-10
Agarwal R, et al. Mycoses 2016; 59(1): 1-6
Agarwal R, et al. Mycoses 2017; 60(1): 33-9
Agarwal R, et al. J Allergy Clin Immunol Pract 2022; In press
Agarwal R, et al. Eur Respir J 2022; In press

Treatment of ABPA : *Summary*

2024 ISHAM-AWG & NICE guidelines



OCS

Anti-fungal

Environmental Control

Optimize predisposing Condition

Acute/ Exacerbation

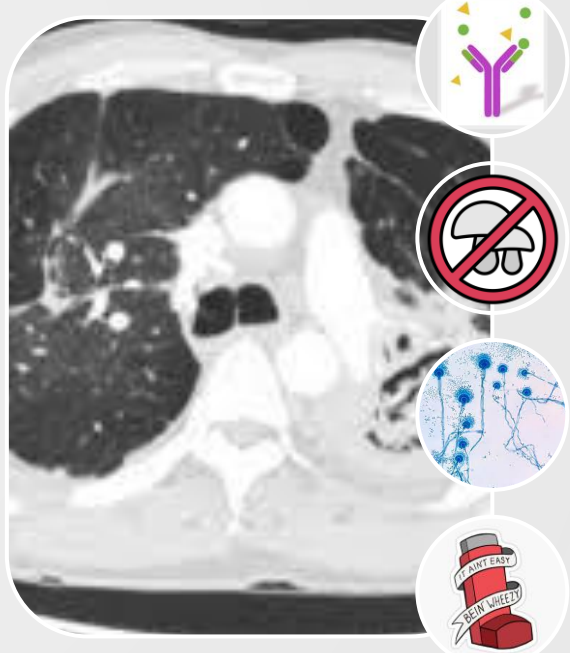
OCS

Anti-fungal

Environmental Control

Optimize predisposing Condition

OCS Dependent



Biologicals

Anti-fungal

Environmental Control

Optimize predisposing Condition

Advanced End Stage

Conclusions:

- ABPA & ABPM are now defined with 4 underlying conditions
- Clinical + Serological + Radiological criteria refined
- Imaging subtypes ABPA variants
- Acute / Exacerbations / Relapse defined as serological vs disease
- Treatment dependent needs careful approach – side effects
- Advanced ABPA needs management of underlying conditions
- Upfront Treatment is dual therapy (OCS+ Azoles)
- Monitoring every 2 months – serology & imaging
- Biologicals to use if OCS or antifungals are giving side effects

Foundation for Pulmonary Allergy Critical Care & Sleep Medicine In India

Thank You

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