

The spectrum of aspergillosis

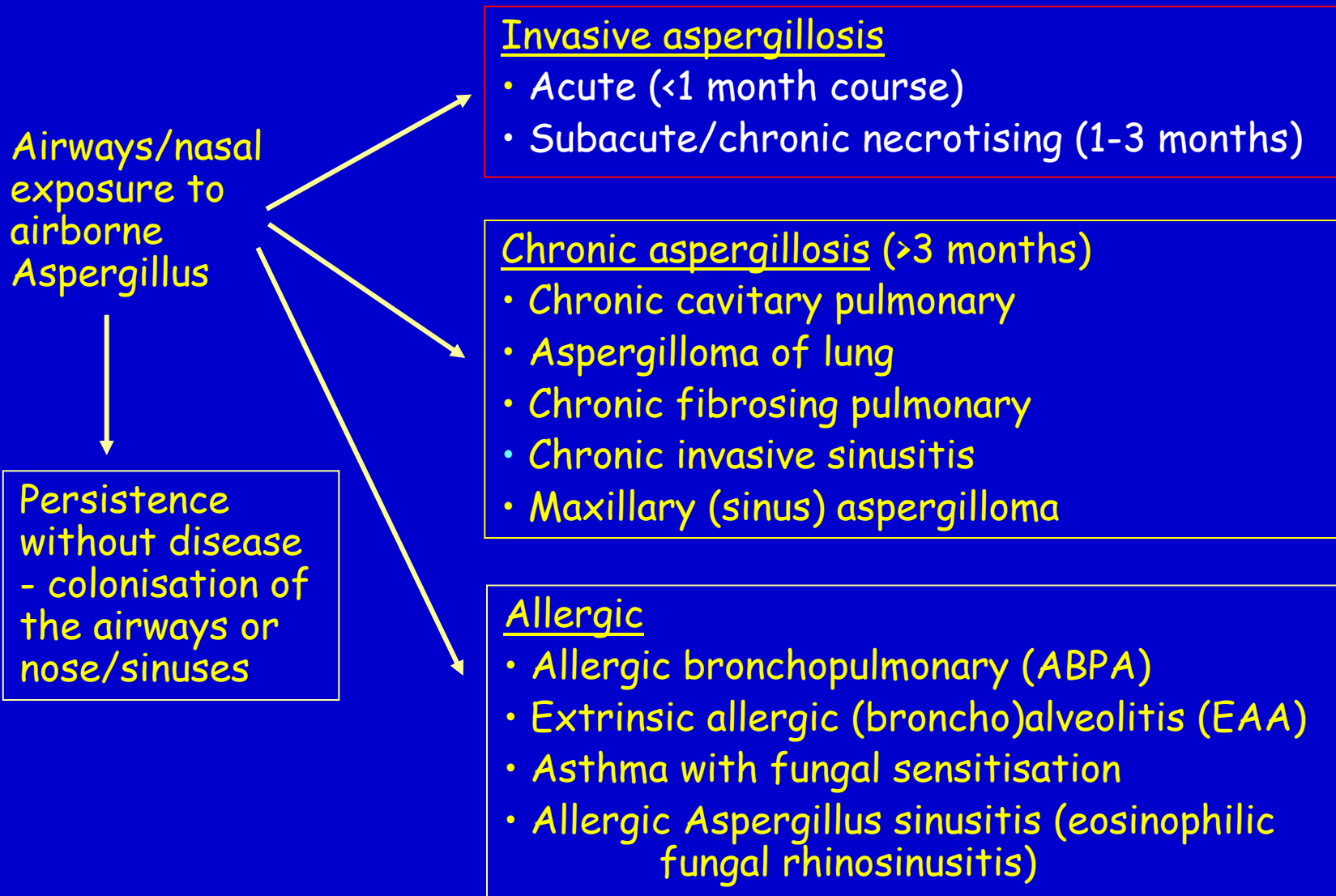
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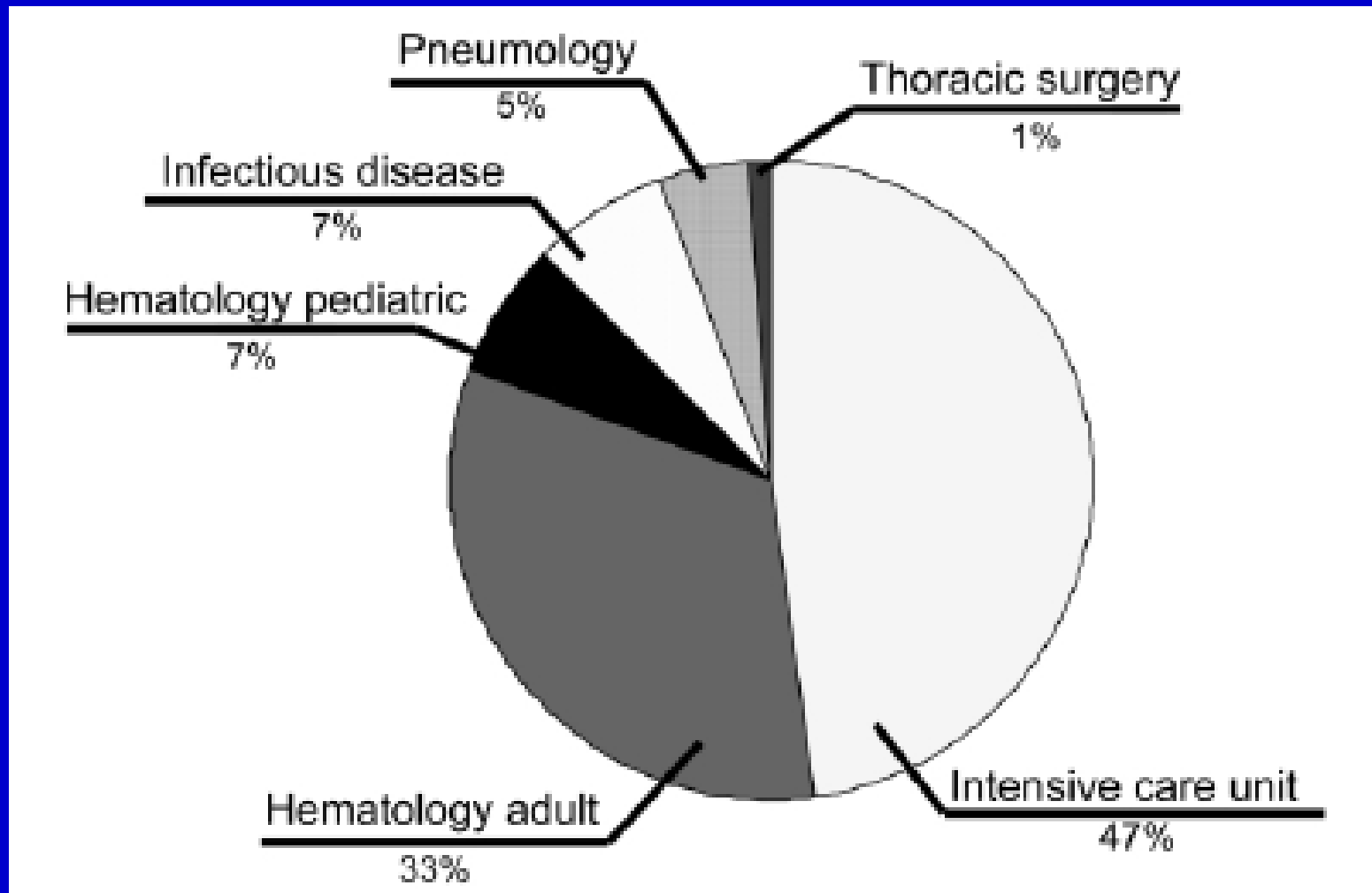
The University of Manchester

Myconostica Ltd

CLASSIFICATION OF ASPERGILLOSIS



Where in the hospital does invasive aspergillosis occur?



Risk factors for invasive aspergillosis

Major

- Neutropenia (+ monocytopenia)
- Corticosteroid treatment

Minor

- CD4penia
- Inherited immunodeficiency (ie CGD)
- Lung or sinus damage/disease
- Severe liver disease
- Exposure to high inocula

Risk factors for invasive aspergillosis in ICU

Table 2. Risk of invasive aspergillosis among patients admitted to the intensive care unit (ICU; medical, mixed or surgical).

High-risk category

Neutropenia (neutrophil count, <500 neutrophils/mm³)

Hematological malignancy

Allogeneic bone marrow transplantation

Intermediate-risk category

Prolonged treatment with corticosteroids before admission to the ICU

Autologous bone marrow transplantation

Chronic obstructive pulmonary disease

Liver cirrhosis with a duration of stay in the ICU >7 days

Solid-organ cancer

HIV infection

Lung transplantation

Systemic diseases requiring immunosuppressive therapy

Low-risk category

Severe burns

Other solid-organ transplant recipients (e.g., heart, kidney, or liver transplant recipients)

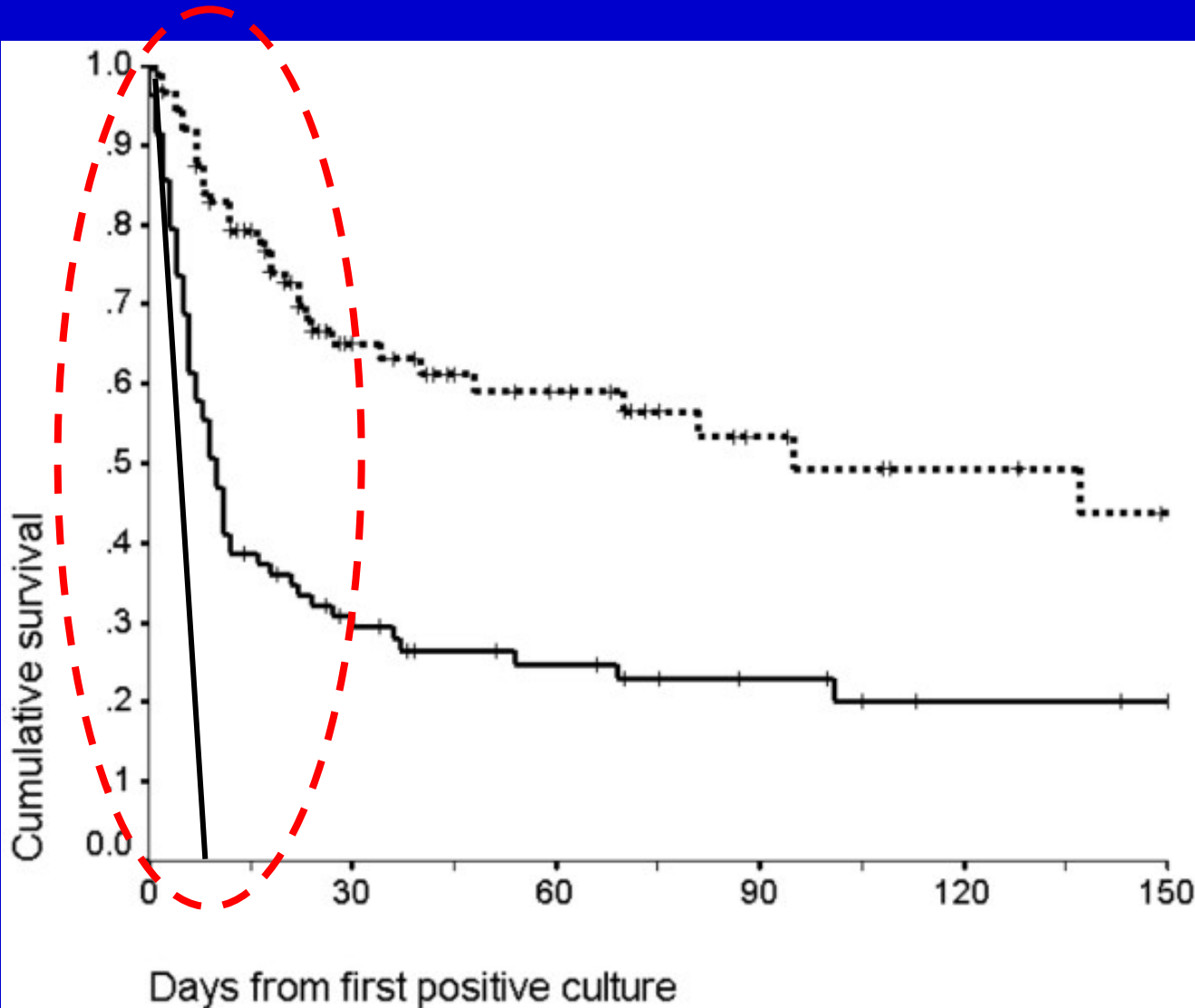
Steroid treatment with a duration of ≤ 7 days

Prolonged stay in the ICU (>21 days)

Malnutrition

Post-cardiac surgery status

Invasive aspergillosis in ICU

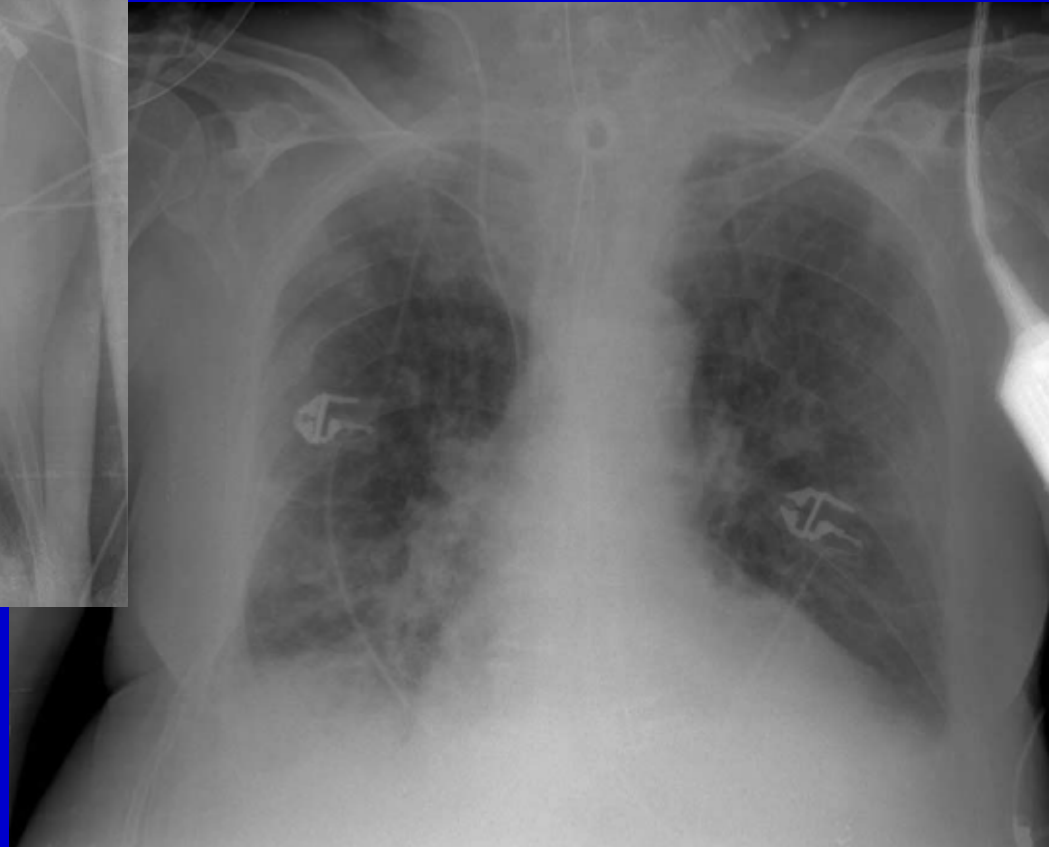


Aspergillus detected,
no infection
N = 89

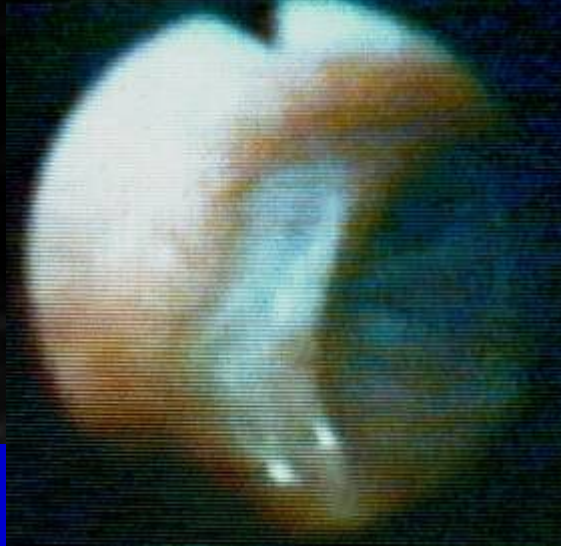
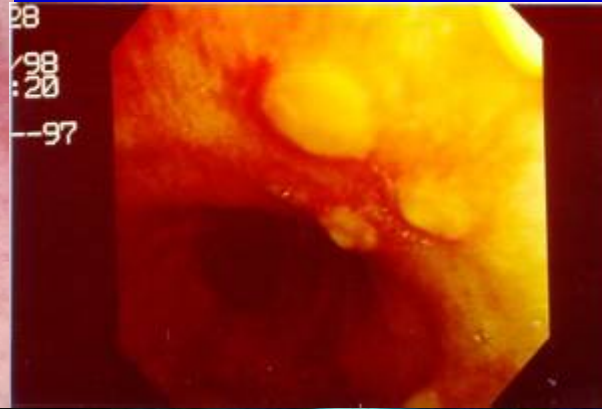
Invasive aspergillosis
+ treatment
N = 73

Invasive aspergillosis
no treatment
N = 12

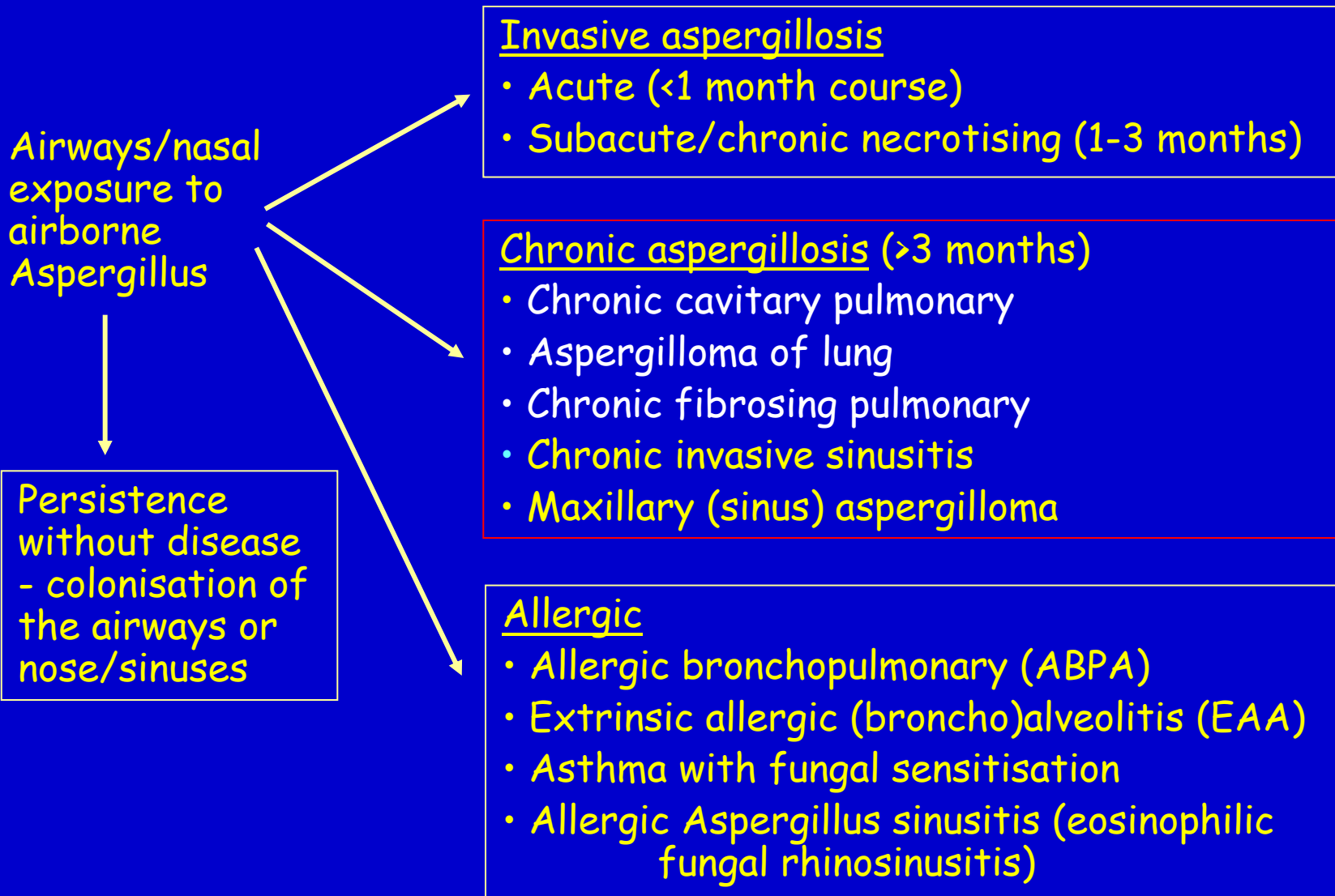
Radiology completely unhelpful in suspecting the diagnosis



Airways aspergillosis - spectrum

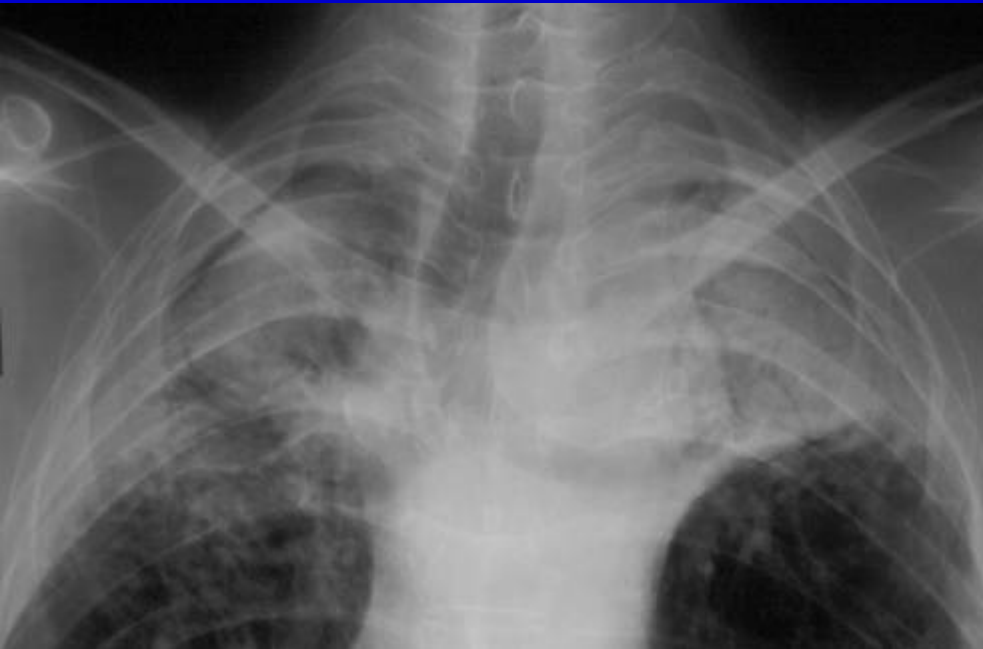


CLASSIFICATION OF ASPERGILLOSIS



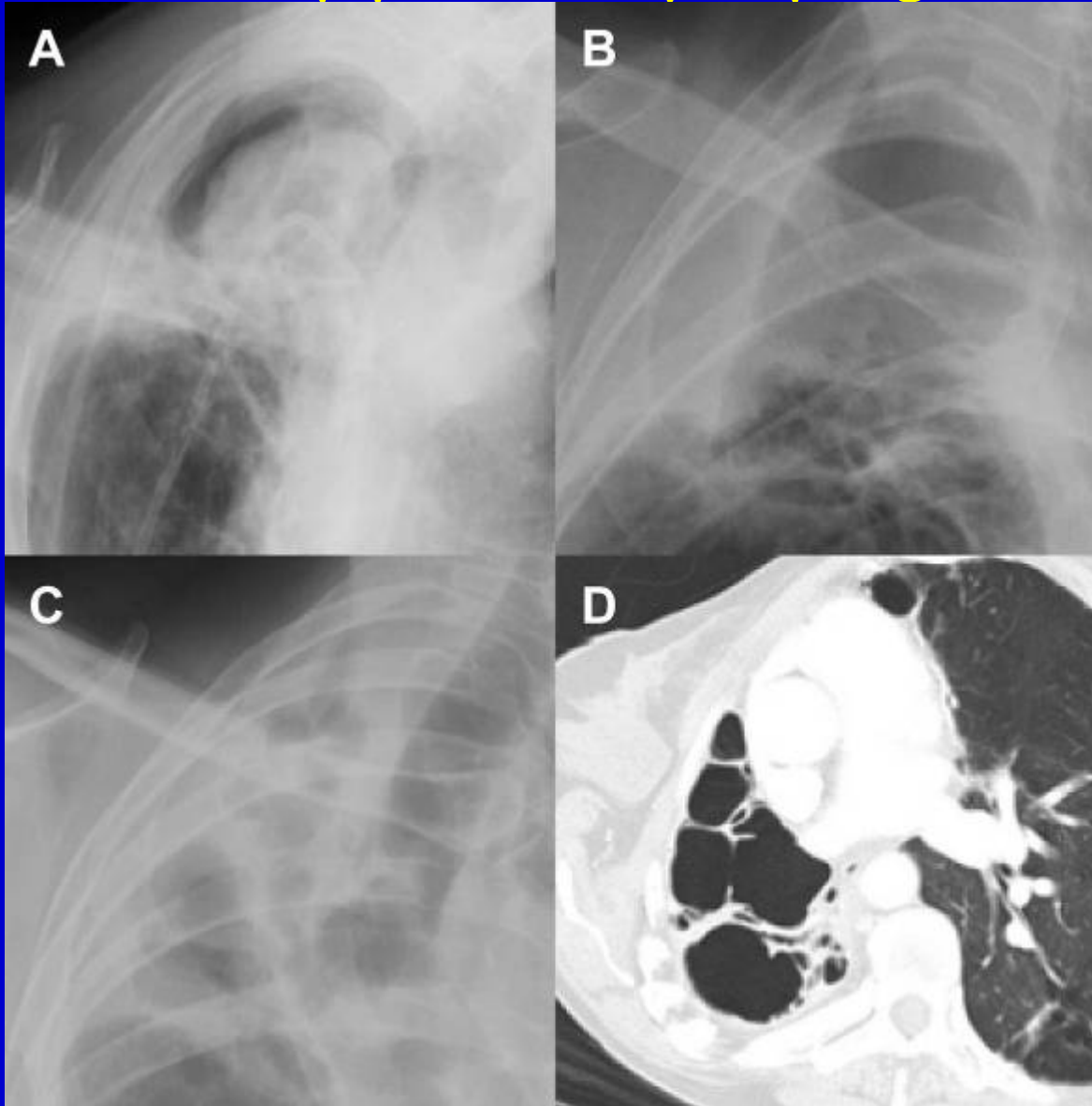
Chronic pulmonary aspergillosis

Chronic cavitory
pulmonary
aspergillosis
complicating ABPA



Chronic cavitory pulmonary
aspergillosis with bilateral
aspergillomas complicating
sarcoidosis

'Multicavity' disease is the hallmark of chronic cavitary pulmonary aspergillosis (CCPA)



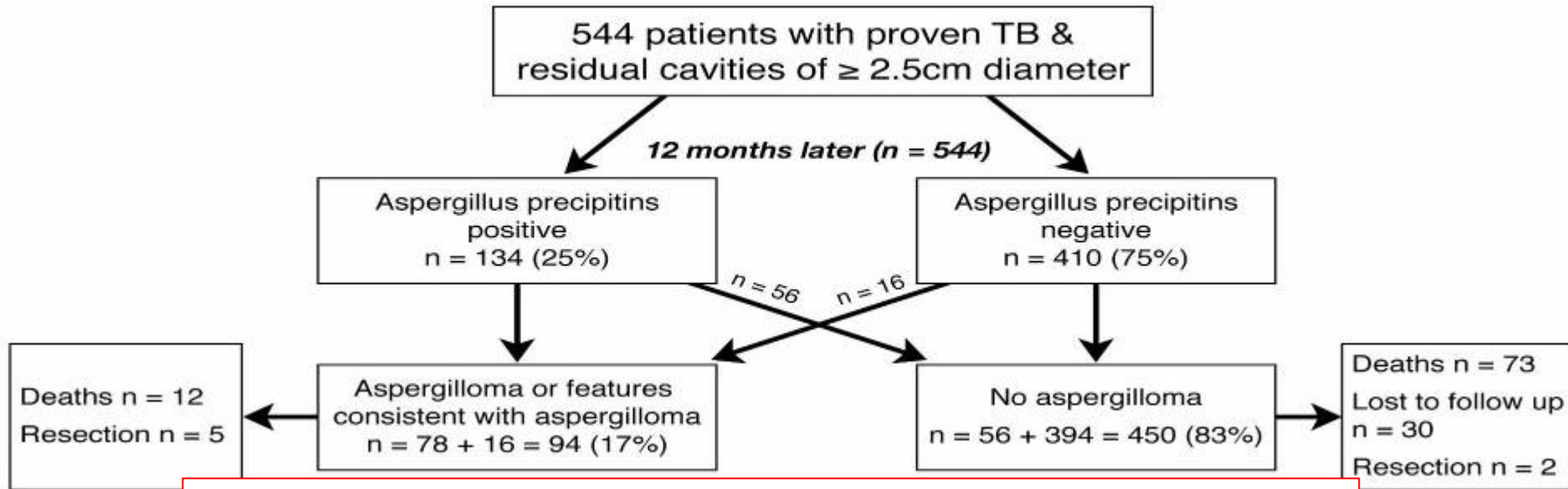
+ *Aspergillus* IgG antibodies
(precipitins)

+ symptoms

Underlying diseases in patients with CPA (%)

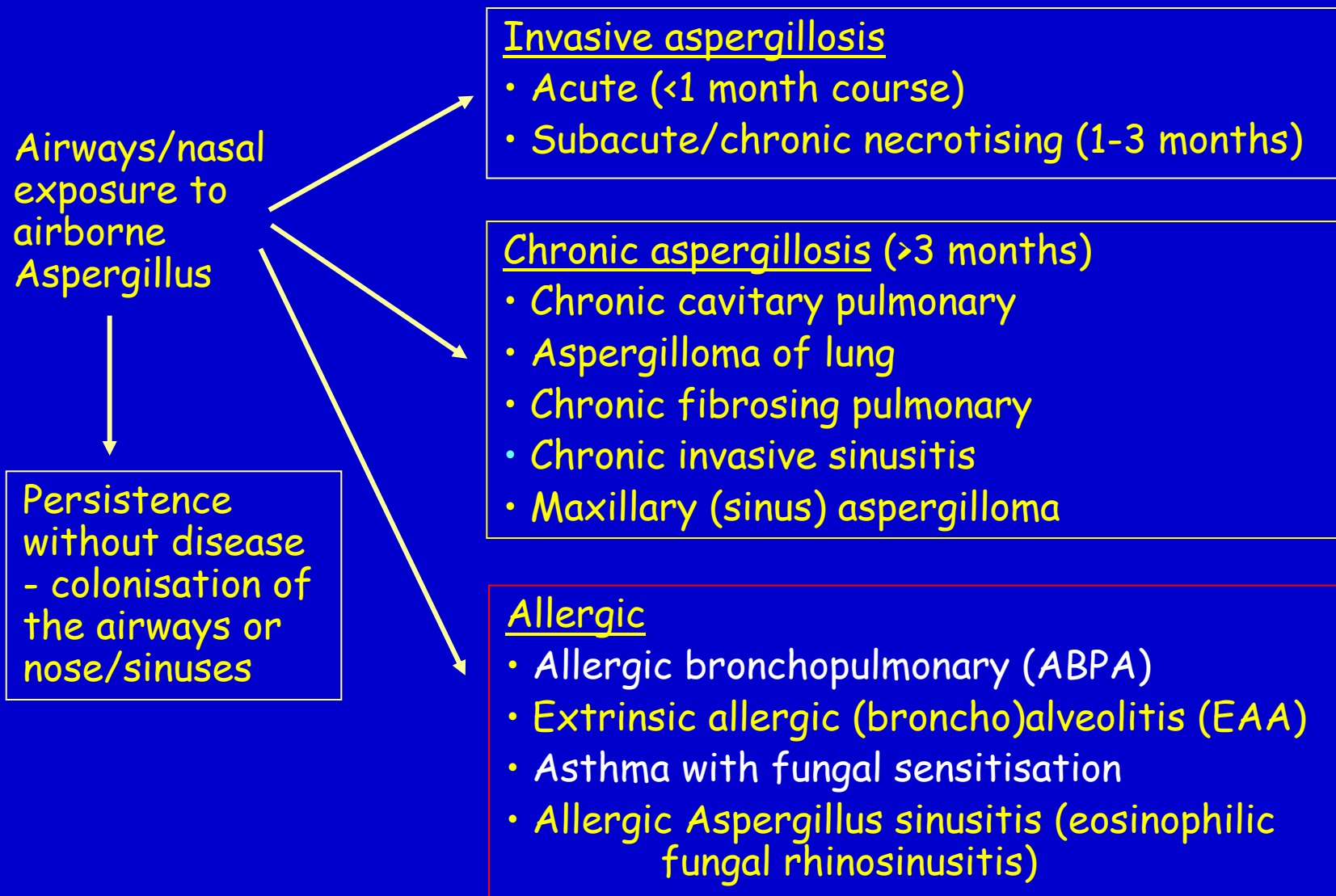
	Smith
Classical tuberculosis	17
Atypical tuberculosis	16
ABPA	14
COPD/emphysema	33
Pneumothorax	17
Lung cancer survivor	10
Pneumonia	22
Sarcoidosis (stage II/III)	7
Thoracic surgery	14
Rheumatoid arthritis	4
Asthma / SAFS	12
Ankylosing spondylitis	4
None	1

Frequency of chronic pulmonary aspergillosis after TB



25-33% of patients with TB are left with a cavity
~10% of all cases of pulmonary TB get CPA

CLASSIFICATION OF ASPERGILLOSIS



ABPA and severe asthma



Global ABPA cases per WHO region related to adult asthma (mean 2.1%)

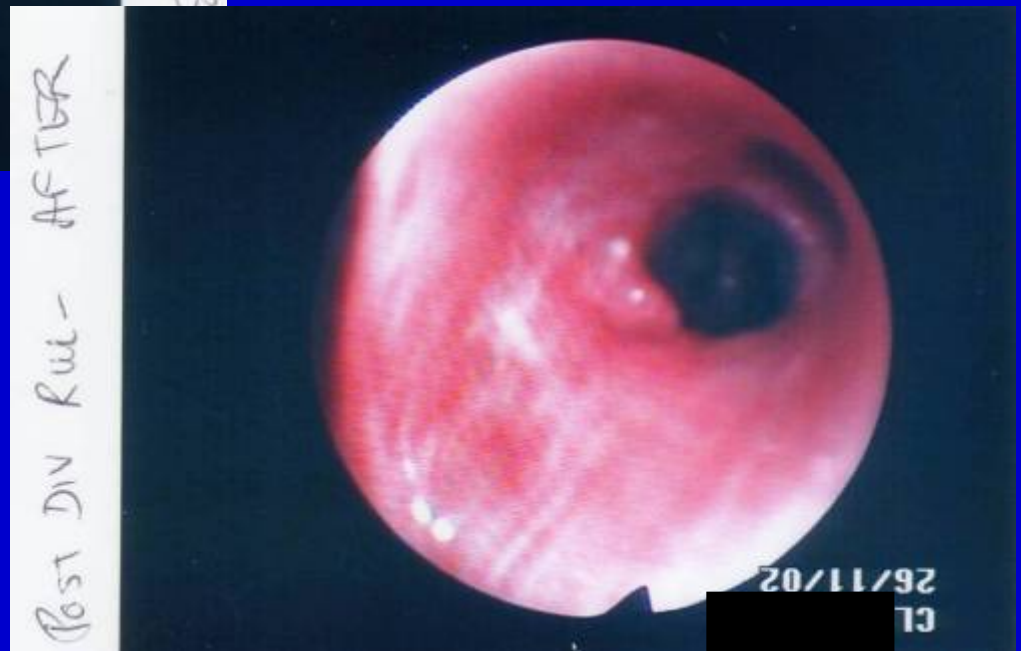
	<u>Burden</u>
Europe	466,891
Americas	704,926
Eastern Medit.	187,963
Africa	294,058
Western Pacific	881,860
SE Asia	<u>614,353</u>
TOTALS	3,150,062

ABPA - Diagnostic clues

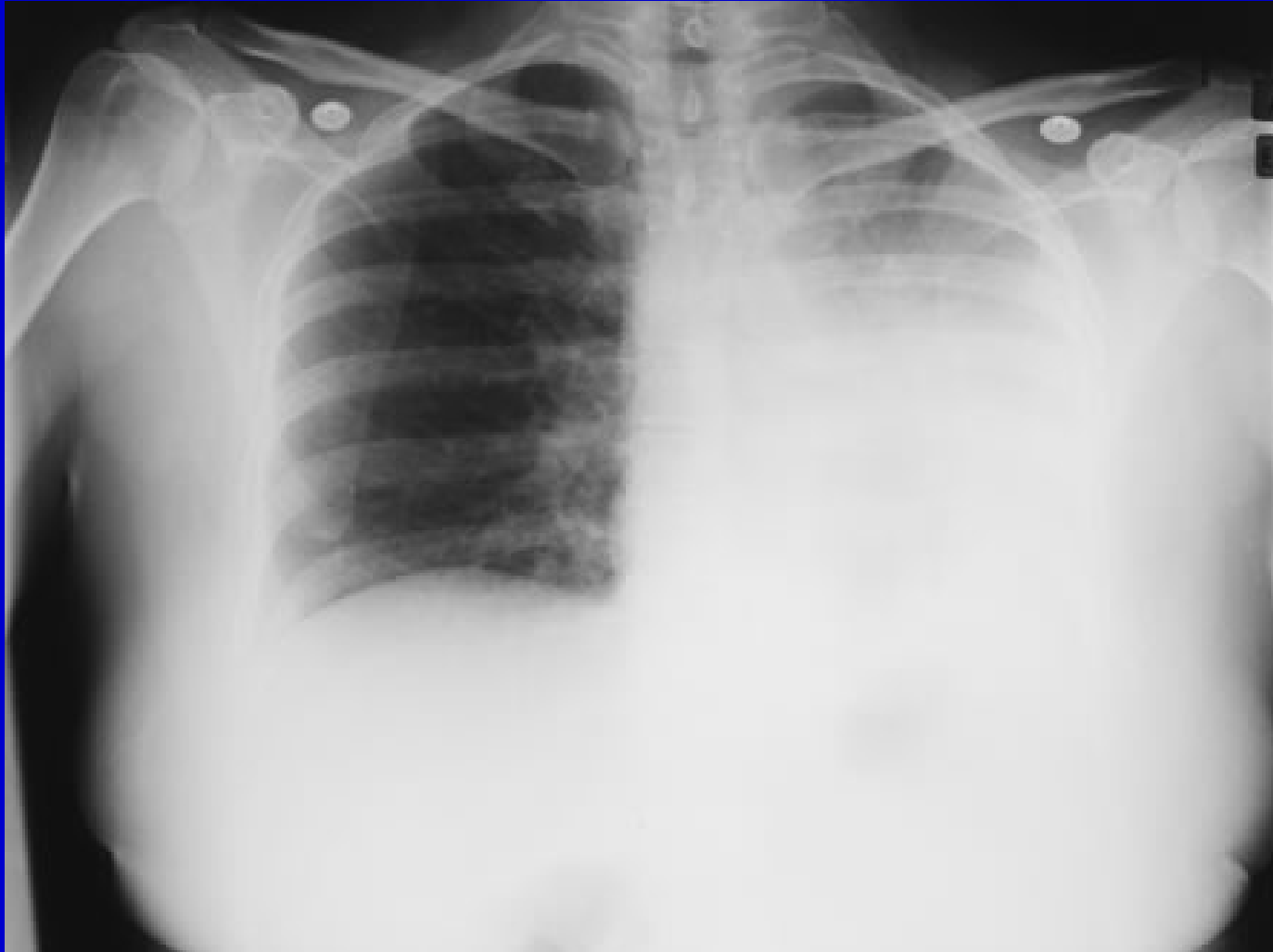
- Asthma/CF not well controlled
- History of 'pneumonia'
- History of coughing up plugs, or paroxysms of coughing that clear when chest clears
- Central bronchiectasis on CT scan, or mucoid impaction
- Eosinophilia

Rare cases in non-asthmatics, non-CF patients

ABPA - bronchoscopy views showing mucous plugging



Mucoid impaction due to ABPA



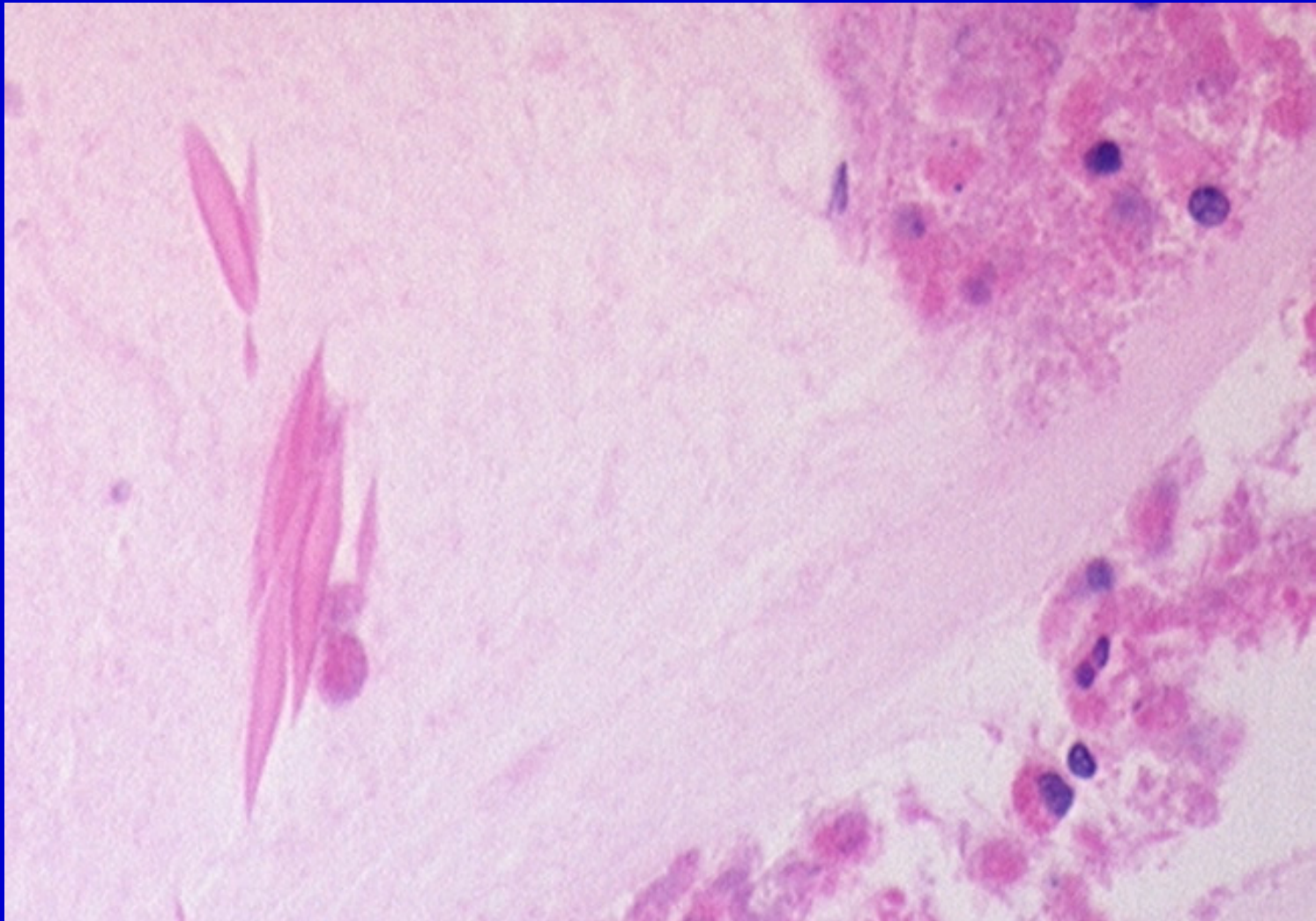
Mucoid impaction due to ABPA



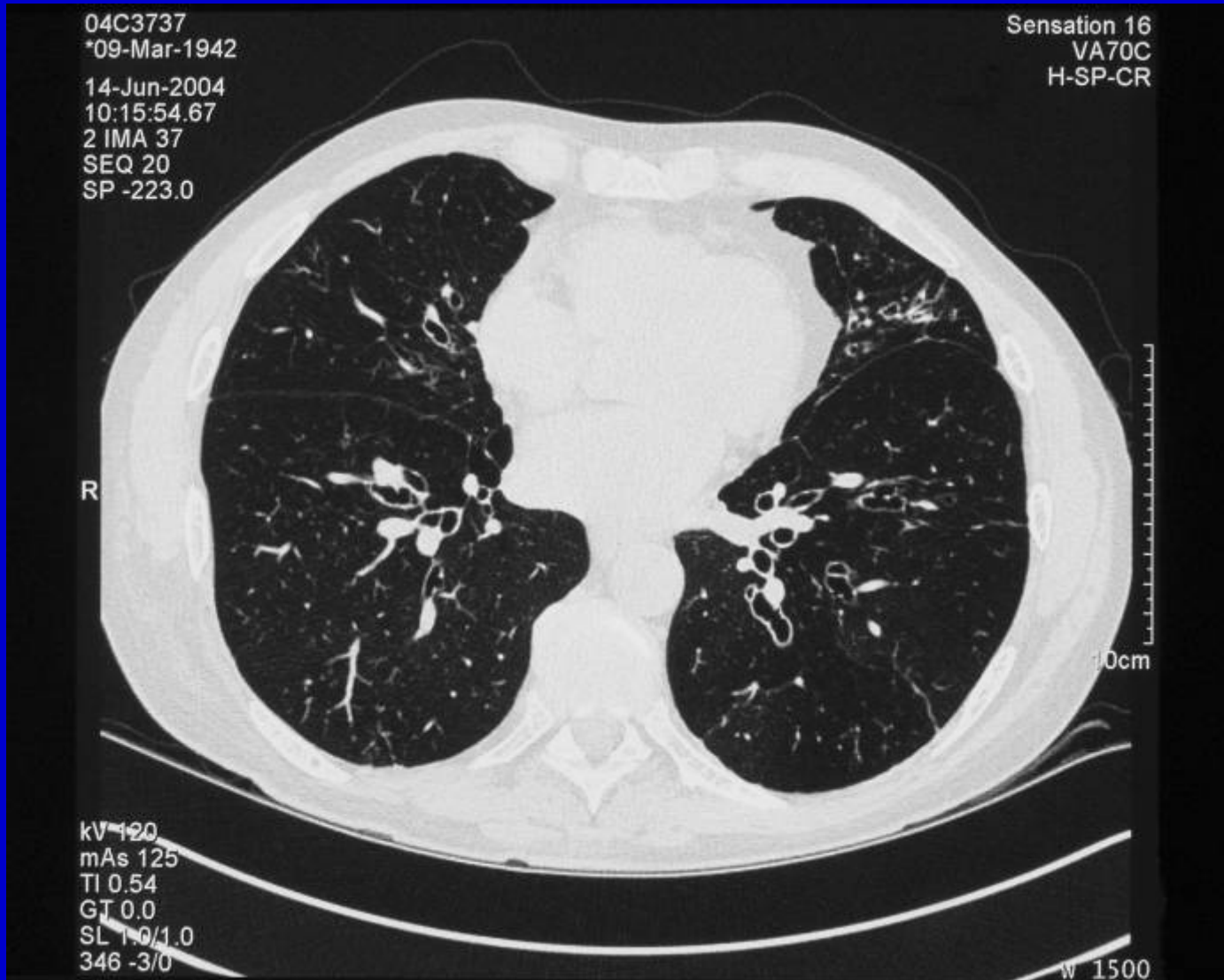
Sputum in ABPA



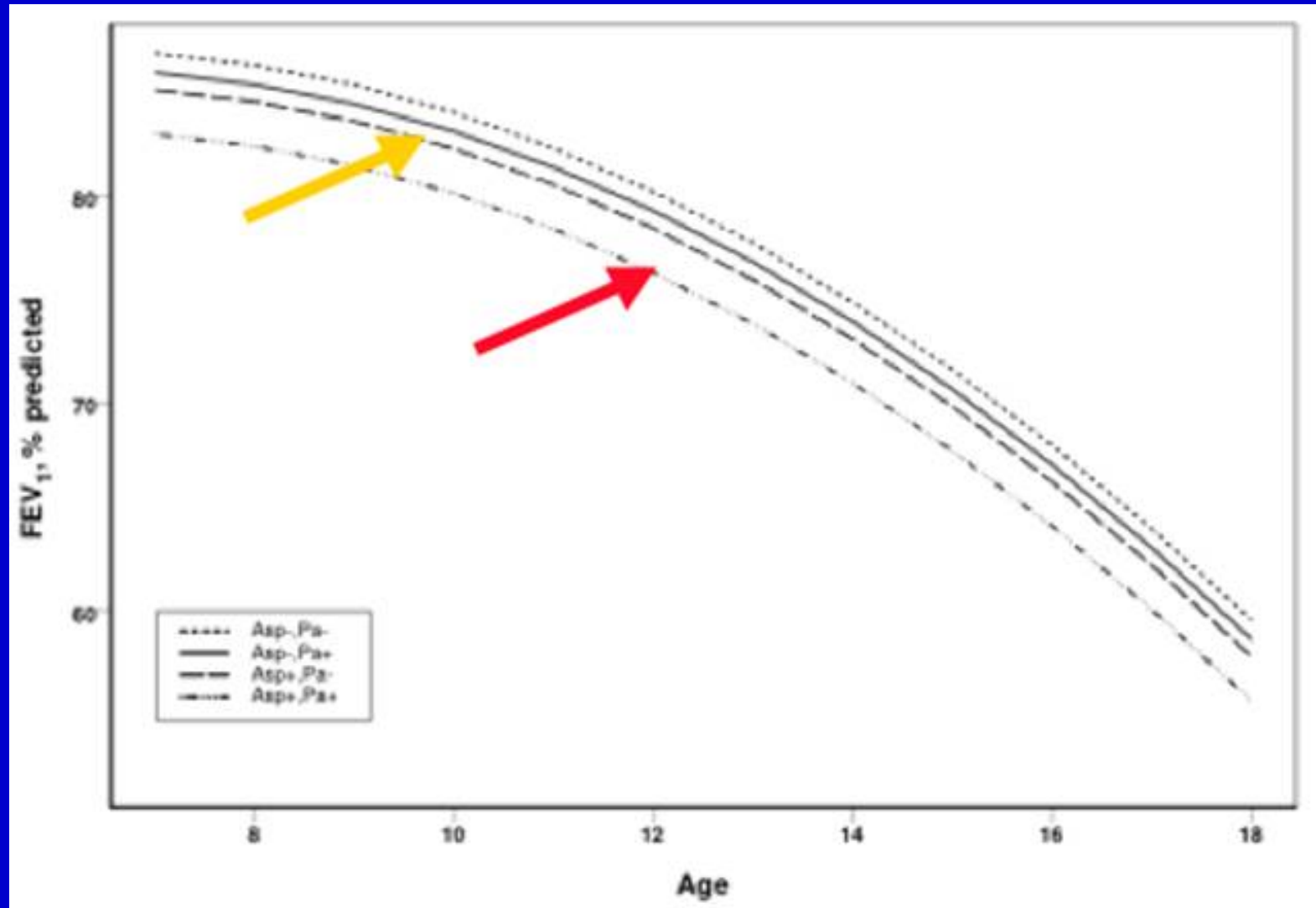
Charcot Leyden crystals



Central bronchiectasis as a complication of ABPA



CF and Aspergillus colonisation or infection



Severe asthma and fungal sensitisation (SAFS)

Criteria for diagnosis

- Severe asthma (BTS step 4 or 5)
AND
- RAST (IgE) positive for any fungus
OR
- Skin prick test positive for any fungus
AND
- Exclude ABPA (ie total IgE <1,000 iu/mL)

Comparison of ABPA and SAFS serology

ABPA results

normal range

date 1

date 2

Patient

1

Total IgE	KIU/l	(0.1-100.0)	1900.0	3000.0
aspergillus.f	KUa/l	(0-0.4)	41.6	49.2

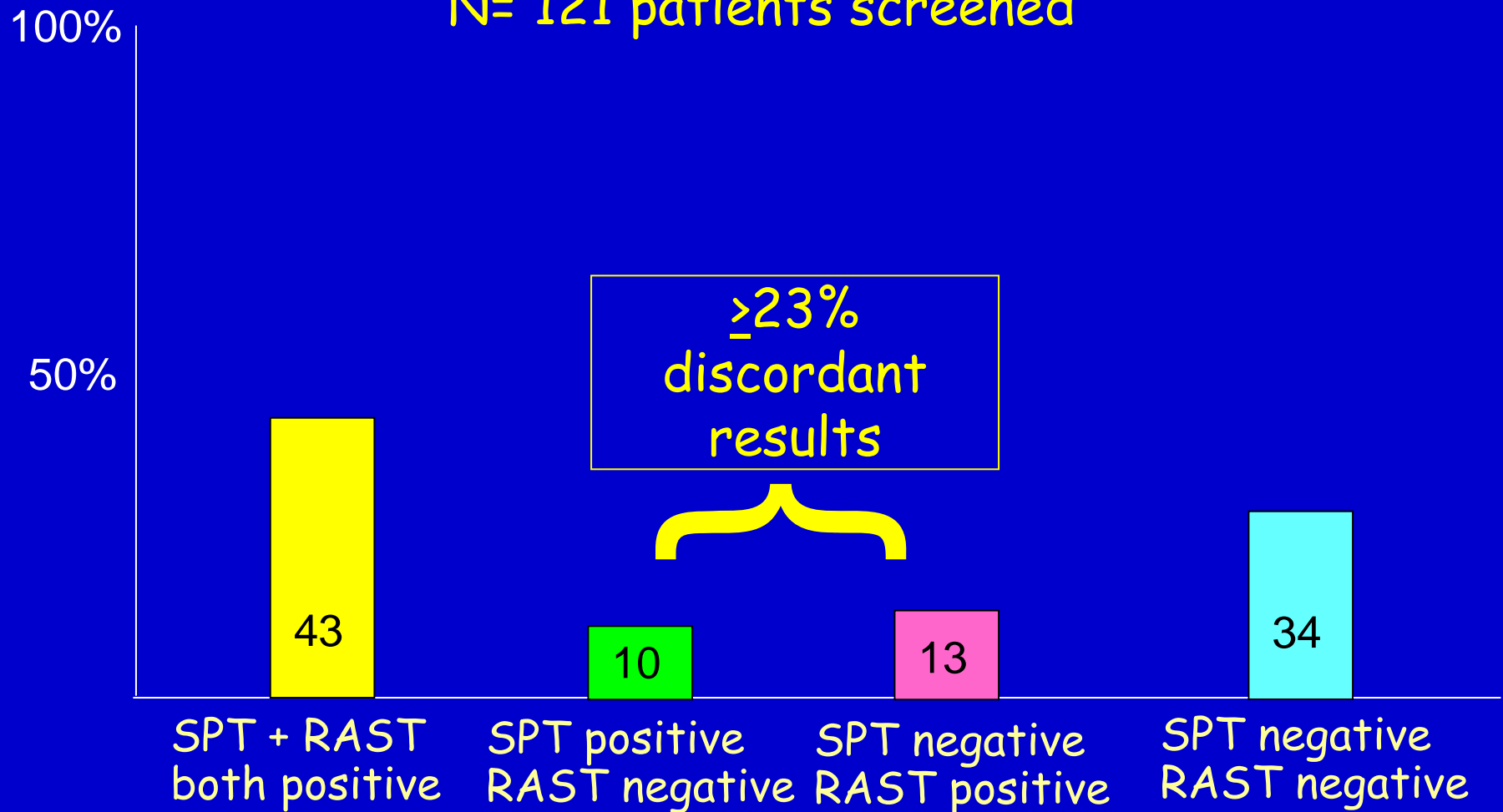
SAFS results

2

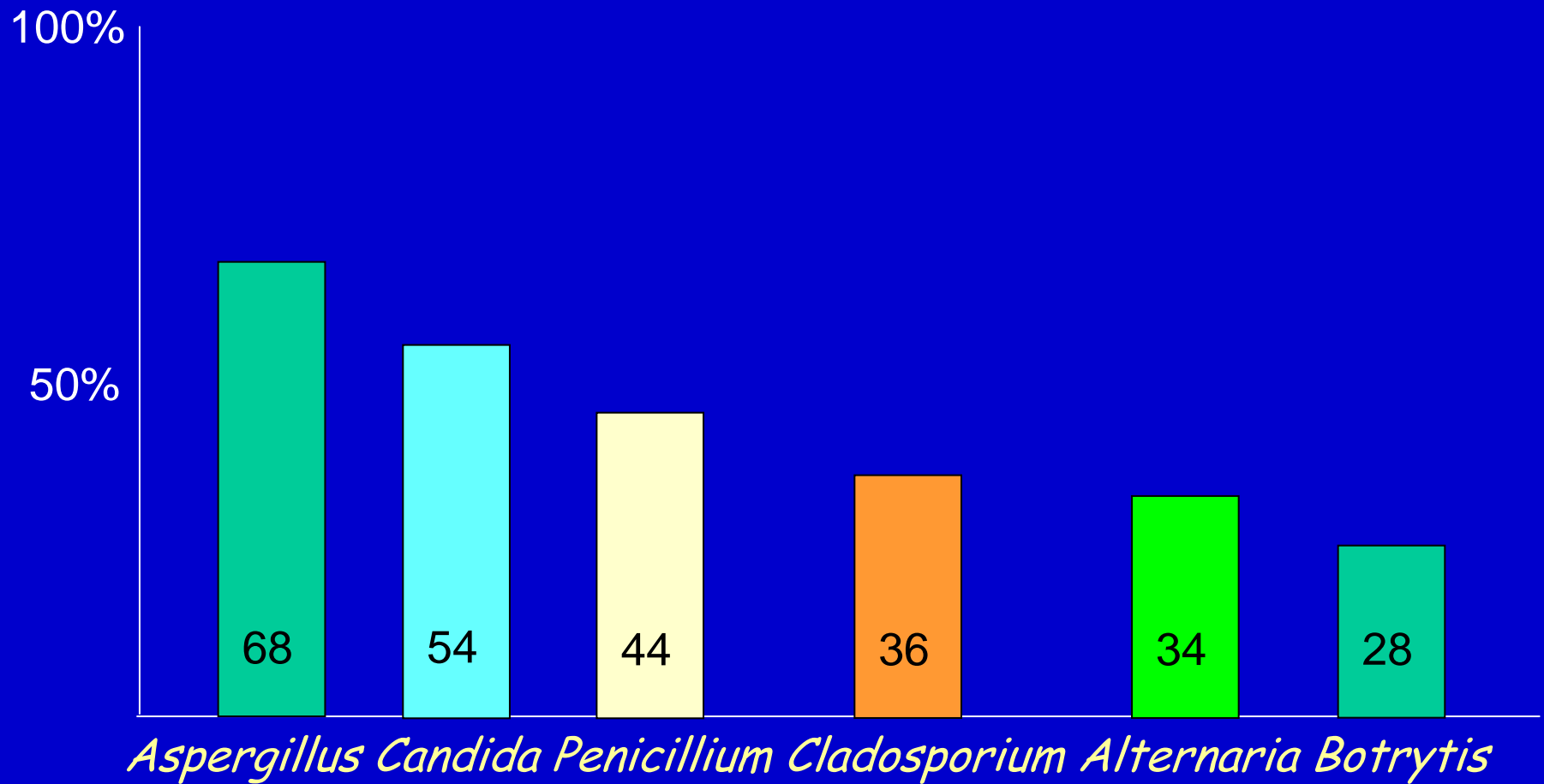
Total IgE	KIU/l	(0.1-100.0)	200.0	260.0
aspergillus.f	KUa/l	(0-0.4)	4.5	5.2

Fungal sensitisation in severe asthma - skin prick test or RAST for diagnosis?

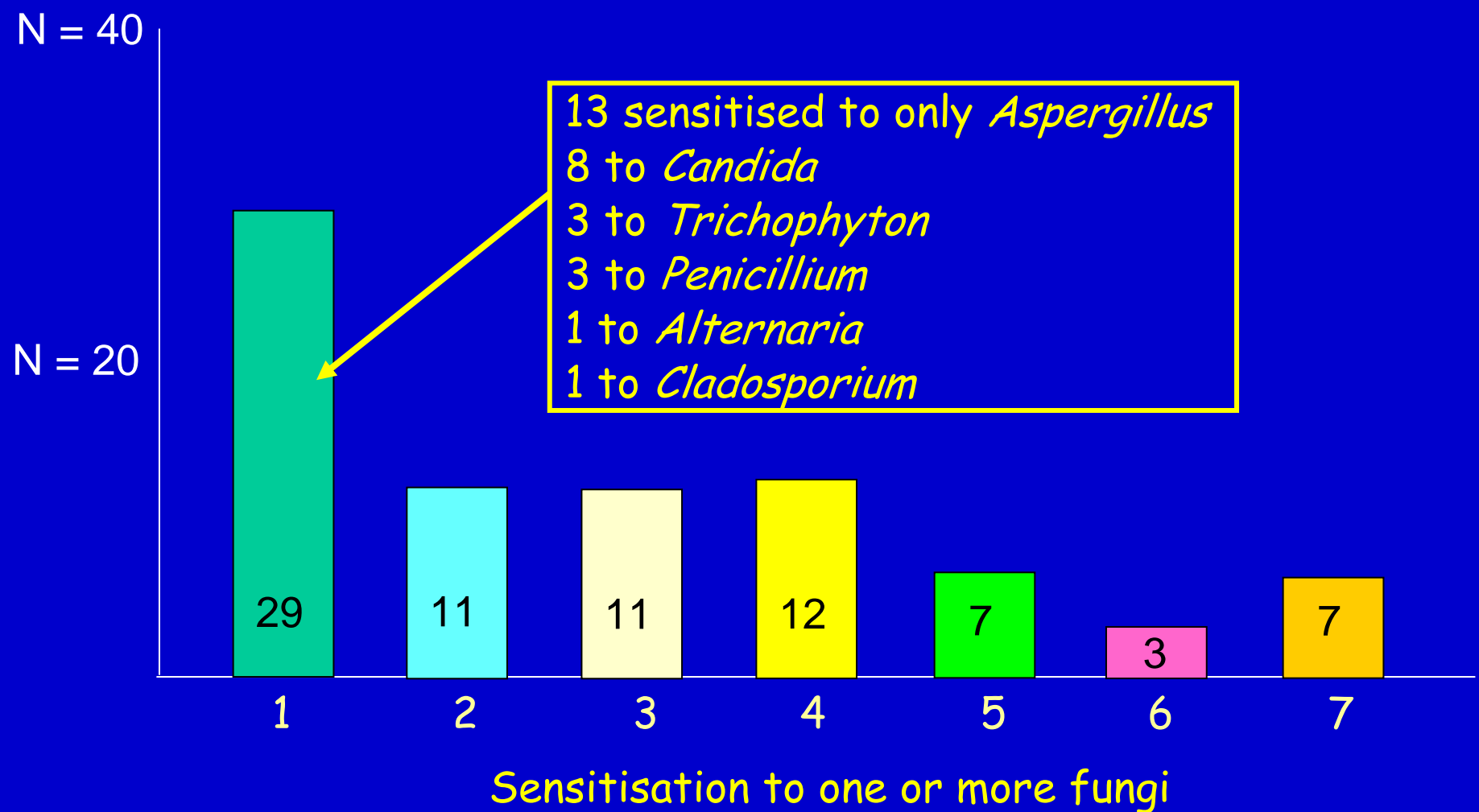
N= 121 patients screened



Fungal sensitisation in severe asthma - skin prick test or RAST



Fungal sensitisation in severe asthma - number sensitised to one or more fungi



Asthma and Aspergillus

79 adult asthmatics and 14 controls

Patients sensitised to *A. fumigatus* compared with non-sensitised asthmatics had:

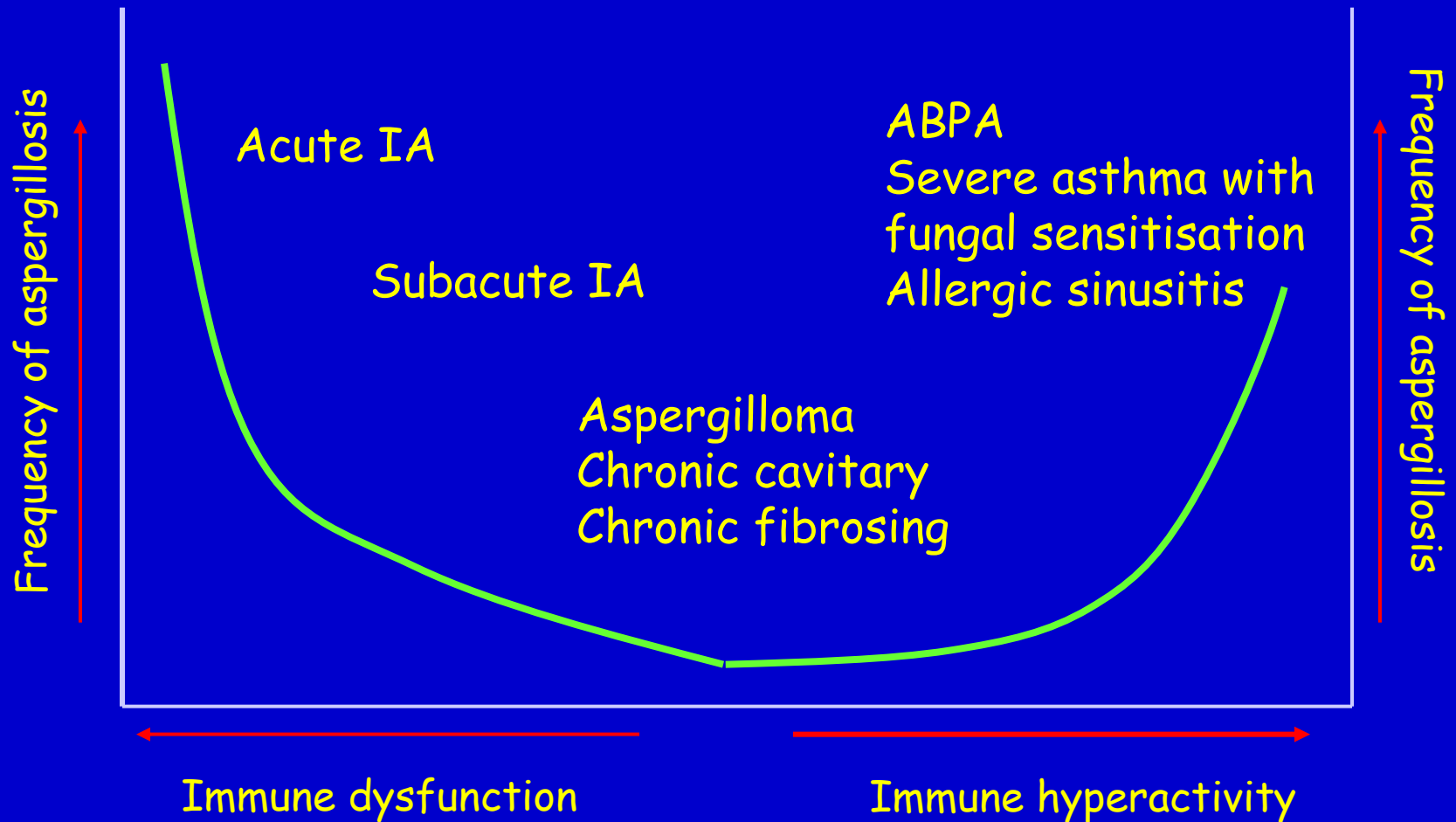
lower lung function (% pred. FEV1 68% vs 88% $p < 0.05$),
more bronchiectasis (68% versus 35% $p < 0.05$) and more
sputum neutrophils (80.9% vs 49.5% $p < 0.01$).

Randomised studies of antifungals and ABPA and/or asthma

Disease	Antifungal, duration	Benefit?	Author, year
ABPA	Natamycin inh, 52 wks	No	Currie, 1990
ABPA	Itraconazole, 32 wks	Yes	Stevens, 2000
ABPA	Itraconazole, 16 wks	Yes	Wark, 2003
"Trichophyton" asthma	Fluconazole, 20 wks	Yes	Ward, 1999
SAFS	Itraconazole, 32 wks	Yes	Denning, 2009

Interaction of *Aspergillus* with the host

A unique microbial-host interaction





The Aspergillus Website



www.aspergillus.org.uk



The Fungal Research Trust

