### FRCPath Part 2—Revision Notes on Aspergillus spp.

(Oxford Textbook of Medical Mycology, Ch 10)

#### 1. Genus at a glance

- > 200 species; > 30 human pathogens—among the most ubiquitous environmental moulds;
  conidia inhaled daily.
- Characteristic **aspergillum** (asexual conidial head); despite known teleomorphs, the 2012 "one-fungus-one-name" rule retains *Aspergillus* nomenclature.
- **Commercial uses:** A. niger → citric-acid & enzyme production; A. oryzae → sake/soy fermentation.

# 2. Key species, temperatures, toxins & clinical points

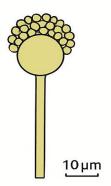
Species (complex)	Opt. Temp / Range (°C)	Colony / Microscopy	Major toxin	Salient clinical facts
A. fumigatus	37 / 12-65	Green-blue; columnar uniseriate heads	_	Commonest invasive isolate; ABPA, CPA
A. flavus	37 / 12-48	Green-yellow; radiate uni/bi-seriate	Aflatoxin	Sinusitis, keratitis, aflatoxicosis risk
A. niger	37	Black biseriate heads	_	Otomycosis, onychomycosis
A. terreus	25-40	Beige; biseriate + accessory conidia	Ochratoxin	Intrinsic AmB-R
A. nidulans	37 / 2-48	Green with red-brown cleistothecia	_	CGD infections; AmB-R
A. versicolor	22-26 (opt); ≤40	White→yellow/green; penicillium-like	Sterigmatocystin	Onychomycosis; grows best at room-temp
A. clavatus	37	Long club-shaped vesicle	_	Extrinsic allergic alveolitis ("malt-worker's lung")

# **Aspergillus species**



## A. fumigutus

- Uniseriate
- Dome-shaped vesicle
- Green conidia



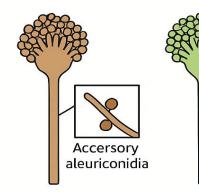
# A. flavus

- Uni--and biseriate
- Spherical vesicle
- Yellow-green conidia



### A. niger

- Biseriate
- Globose vesicle
- Black



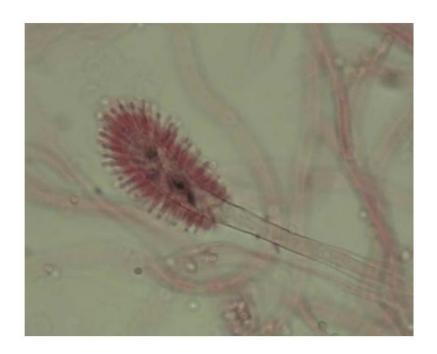
### A. terreus

- Biseriate
- Columnar head Small vesicle
- Cinnamonbrown conidia

### A. versicolor

10 µm

- Biseriate
- Light green conidia



**Fig. 1** Aspergillus clavatus clavate or "club-shaped" vesicle with a single layer of phialides

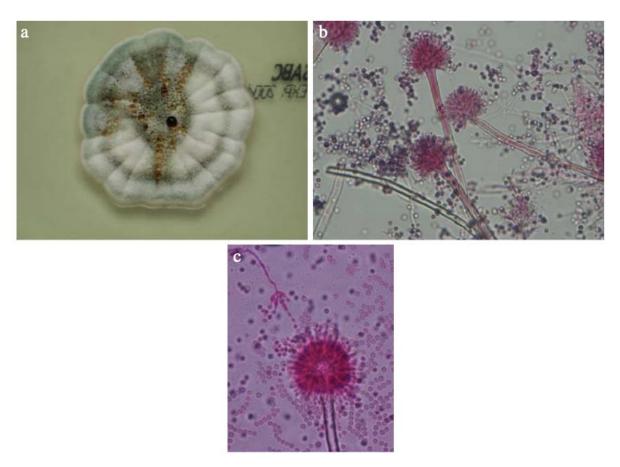


Fig. 2 Aspergillus versicolor (a) colonial form; (b) "spoon-shaped" vesicle; (c) reduced or Penicillium-type heads

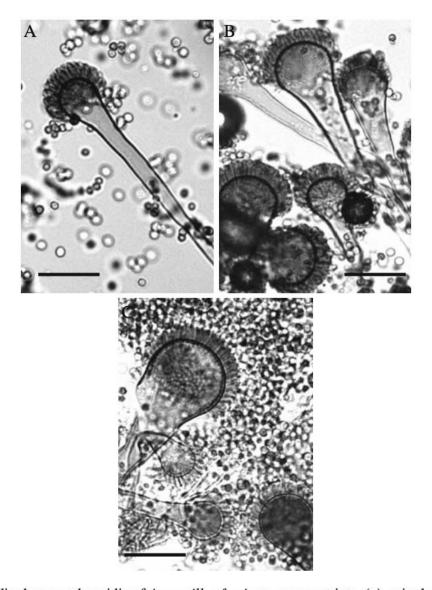


Fig. 6 Conidiophores and conidia of Aspergillus fumigatus sensu stricto. (a) a single typical conidiophore terminating in a flask-shaped vesicle bearing uniseriate phialides. Panels (b) and (c): highly variable vesicle sizes and conidiophore colorations observed with different isolates of A. fumigatus. Bar =  $25 \mu m$ 

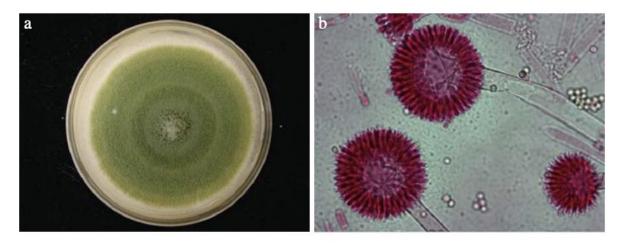
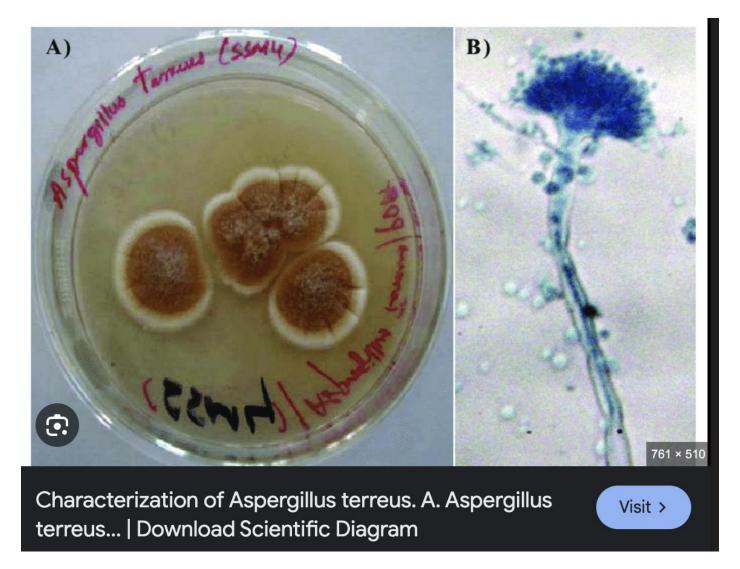


Fig. 7 Aspergillus flavus (a) colonial form; (b) conidial head showing the presence of metulae and phialides

Green-yellow radiate, compare to A. fumigatus



Cinnamon colored, columnar

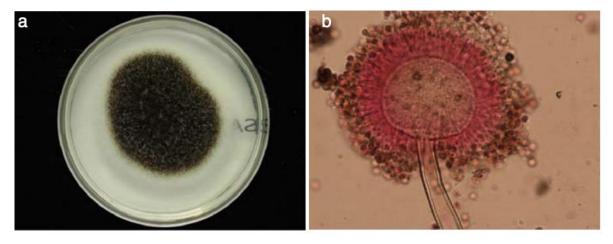


Fig. 8 Aspergillus niger (a) colonial form; (b) conidial head showing the presence of metulae and phialides over the entire surface of the vesicle and darkly pigmented, roughened spores

#### 3. Epidemiology & reservoirs

- Conidia in soil, rotting vegetation, damp building materials (wallpaper, concrete, pipelagging, carpets, HVAC); hospital construction dust → outbreaks.
- **High-risk hosts:** prolonged neutropenia, allogeneic-HSCT (~12 %), heart-lung Tx (11 %), CGD, high-dose steroids .
- CPA rising after TB, COPD, sarcoidosis.

#### 4. Pathogenesis (4-step mnemonic I-G-A-T)

- 1 Inhalation & alveolar deposition
- 2 Germination when innate immunity fails
- 3 Angio-invasion → thrombosis, infarction
- 4 Toxins & hypersensitivity drive allergic / chronic disease

#### 5. Clinical spectrum

Category	Typical entities / notes	
Non-invasive	Otomycosis (A. niger), onychomycosis (A. versicolor),	
Non-invasive	allergic fungal rhinosinusitis	
Allergic ABPA (≈16 % asthmatics); EAA by A. clavatus; SAFS		
Chronic	<b>CPA</b> continuum: simple aspergilloma → chronic cavitary →	
Cironic	fibrosing disease	
Invasive	Acute pulmonary IA ± CNS, eye, skin; sinusitis; mortality	
IIIVasive	50–85 %	

#### 6. Diagnosis workflow

- 1. **Direct / culture:** septate 45° branching hyphae; Sabouraud agar 48-90 h.
- 2. Serology & biomarkers:
  - a. Aspergillus precipitins (IgG)—best single test for CPA/ABPA support.
  - b. Galactomannan ELISA / LFD (false-pos with β-lactams).
  - c.  $(1\rightarrow3)$   $\beta$ -D-glucan (pan-fungal).
  - d. PCR on blood/BAL; combine with GM for ↑ sensitivity.
- 3. **Imaging:** HR-CT halo sign → air-crescent; MRI for CNS/sinus.
- 4. **Histology/BAL/biopsy** for EORTC "proven" disease.

#### 7. Antifungal susceptibility & resistance

Azole-R A. fumigatus increasing in Europe (environmental TR34/L98H, TR46/Y121F/T289A).

- Intrinsic AmB-R: A. terreus, A. nidulans.
- Always request MICs on invasive isolates.

#### 8. Management cheat-sheet

Condition	First-line	Key alternatives / notes	
Invasive aspergillosis	Voriconazole	Liposomal AmB; isavuconazole (non-inferior; shortens QT c)	
ABPA	Oral steroids ±		
ADFA	itraconazole/posaconazole		
CPA	Long-term oral triazole; monitor		
OFA	levels		
Onychomycosis / Otomycosis	Topical clotrimazole ± oral azole		
- C.	Resection of solitary aspergilloma;		
Surgical	debridement of sinus/CNS masses		

Supportive: remove colonised lines, taper immunosuppression, give G-CSF if neutropenic.

#### 9. Prognosis & prevention

- IA mortality: 50-60 % (SOT)  $\rightarrow$  70-85 % (other immunosuppressed). Early targeted therapy improves survival .
- **Primary prophylaxis** (e.g. posaconazole in AML/allo-HSCT) cuts incidence but monitor for resistance.
- **Environmental control:** HEPA filtration, positive-pressure rooms, meticulous dust containment during building/refurbishment.

#### 10. High-yield exam pearls

- 1. Columnar uniseriate head + growth to 65 °C = A. fumigatus.
- 2. Accessory conidia → think A. terreus (and AmB-R).
- 3. Galactomannan false-positive with piperacillin-tazobactam or Penicillium.
- 4. Sterigmatocystin  $\leftrightarrow$  A. versicolor; ochratoxin  $\leftrightarrow$  A. terreus; aflatoxin  $\leftrightarrow$  A. flavus.
- 5. Report isolates as "A. fumigatus complex" unless molecular ID performed (≥ 40 cryptic species).
- 6. Isavuconazole shortens QTc (contrast other azoles).
- 7. Memorise EORTC/MSG 2008 possible/probable/proven definitions—frequent SAQ.
- 8. **Environmental reservoirs** (damp concrete, carpets, HVAC) explain hospital outbreak questions.

9.	Room-temperature growth (~25 °C) onychomycosis isolate? Think A. versicolor.		