### **Histoplasmosis – updated FRCPath Part 2 notes (Medical Microbiology)**

#### **1. Organism & definition**

* **Histoplasma capsulatum** is a dimorphic fungus (mould ≤ 35 °C; yeast at 37 °C). Infection follows inhalation of soil/guano‑borne microconidia; no person‑to‑person spread.

#### **2. Epidemiology & transmission**

* Endemic to the Ohio, Mississippi & Missouri river valleys, parts of Latin America, Caribbean, Africa/Asia.
* Exposure via bat/bird‑contaminated soil (caves, chicken coops, demolition).

#### **3. Pathogenesis**

* Inhaled microconidia → yeast‑phase in alveoli → survive in macrophages → lymphohaematogenous spread; containment requires IFN‑γ/TNF‑α‑mediated granulomas.

#### **4. Risk factors for severe / disseminated disease**

* **CD4 < 150 cells mm⁻³ (HIV)**, infants, elderly
* TNF‑α antagonists, JAK inhibitors, prolonged steroids, calcineurin inhibitors, cytotoxic chemo‑neutropenia
* Solid‑organ / stem‑cell transplant, GVHD

#### **5. Clinical forms (memorise for viva)**

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| **Form** | **Typical host / trigger** | **Key clinical features** |
| Latent asymptomatic | Low inoculum | Incidental calcified granuloma |
| Acute pulmonary < 4 wks | Small inoculum | ‘Flu‑like’ illness |
| Acute pulmonary > 4 wks | Large inoculum | Protracted systemic/resp. Sx |
| Chronic cavitary pulmonary | COPD | Cavities, haemoptysis |
| Progressive disseminated | Immunocompromised/infants | Fever, HSM, pancytopenia |
| Mediastinal/fibrosing | Post‑acute | Obstructive syndromes |

#### **6. Presentations & associated complications (added per user request)**

Acute pulmonary histoplasmosis may trigger or be accompanied by:

* **Pulmonary complications** – pleural effusions, cavitary disease
* **Cardio‑inflammatory** – pericarditis
* **Musculoskeletal** – arthritis / arthralgia
* **Dermatological** – erythema nodosum, erythema multiforme, various skin lesions
* **Disseminated/extrapulmonary** – hepatosplenomegaly, abnormal LFTs, pancytopenia, gastrointestinal involvement, sepsis‑like syndrome
* **Central nervous system** – focal brain lesion or meningitis

(These are high‑yield short‑answer items – keep the list on standby for stem‑based questions.)

#### **7. Differential diagnosis**

CAP, **TB**, **Pneumocystis jirovecii**, **Sarcoidosis**, **Blastomycosis**, **Coccidioidomycosis**, primary lung malignancy.

#### **8. Investigations**

* **Urine/serum antigen EIA** – > 90 % sensitive in disseminated HIV, ↓30 % in acute localised disease.
* **Culture** – sputum/BAL/blood; 4–6 wks; 60–85 % yield disseminated, 15 % focal.
* **Serology** – CF ≥ 1:32 or four‑fold rise; immunodiffusion M‑band (common) ± H‑band (severe).
* **Histology** – 2–4 µm yeasts on PAS/GMS.
* **Imaging** – CXR reticulonodular ± nodes/cavities; CT “snow‑storm” pattern in heavy inoculum.

#### **9. Management (IDSA 2007 / ECMM‑ISHAM 2021)**

|  |  |  |
| --- | --- | --- |
| **Scenario** | **Induction** | **Step‑down / maintenance** |
| Severe acute or disseminated | L‑AmB 3–5 mg kg⁻¹ d⁻¹ × 1–2 wks | Itraconazole ≥ 12 mo |
| CNS disease | L‑AmB 4–6 wks | Itraconazole ≥ 12 mo |
| Mild–moderate pulmonary (> 4 wks) | — | Itraconazole 6–12 wks |
| Chronic cavitary pulmonary | — | Itraconazole ≥ 12 mo (high relapse) |
| Pregnancy | Amphotericin B throughout | Avoid azoles |

* **Adjuncts** – Isavuconazole (emerging); short early steroids for ARDS‑type hypoxaemia.

#### **10. Primary prophylaxis**

Itraconazole 200 mg d for HIV with CD4 < 150 in high‑incidence regions until CD4 ≥ 150 × 6 mo on ART.

#### **11. Follow‑up & monitoring**

Itraconazole trough ≥ 1 µg mL⁻¹; LFTs baseline → weeks 1, 2, 4 → 3‑monthly; urine/serum antigen monthly; CXR/CT q 4–6 mo.

#### **12. Complications & prognosis**

Cavitary destruction, mediastinal granuloma/fibrosis, adrenal insufficiency, chronic meningitis; untreated disseminated disease often fatal but outcomes excellent with timely therapy.

#### **13. Public‑health advice**

Avoid bat/bird‑dropping exposure; respirators for high‑risk work; counsel immunosuppressed travellers.

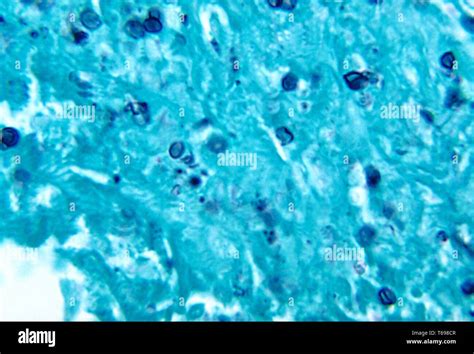
#### **14. Key guideline signposts**

IDSA 2007; ECMM/ISHAM 2021; WHO 2020 fungal guidance.

#### **15. Rapid‑recall regimen table**

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| --- | --- | --- |
| **Setting** | **Induction** | **Maintenance** |
| Severe/disseminated | L‑AmB 1–2 wks | Itraconazole ≥ 12 mo |
| CNS disease | L‑AmB 4–6 wks | Itraconazole ≥ 12 mo |
| Mild–moderate pulmonary | — | Itraconazole 6–12 wks |
| Pregnancy | Amphotericin B | — |

**Exam tip:** Keep the new complication list (Section 6) at your fingertips—you can score easy marks by naming pleural effusion, pericarditis, arthritis, erythema nodosum/multiforme, and CNS meningitis when asked for “presentations of histoplasmosis.”



### **Histopathological findings in *Histoplasma capsulatum* infection**

|  |  |  |
| --- | --- | --- |
| **Key feature** | **Exam‑ready details** | **Evidence** |
| **Specimen choice** | Always obtain tissue when possible for rapid microscopy **and** culture. |  |
| **Special stains** | • Periodic acid‑Schiff (PAS) • Grocott methenamine‑silver (GMS) |  |
| **Yeast morphology** | Small, oval, narrow‑based budding yeasts **2‑4 µm**; typically cluster **intracellularly within macrophages/giant cells** (“halo” on H&E due to shrinkage artefact). |  |
| **Tissue reaction** | Necrotising or non‑necrotising **granulomas**; may progress to fibro‑caseous nodules or fibrosing mediastinitis. |  |
| **Diagnostic yield** | Histology gives an immediate answer, but sensitivity falls with low fungal burden or heavy immunosuppression. |  |
| **Disseminated disease clues** | Bone‑marrow trephine/aspirate often packed with yeasts; especially useful in AIDS or other severe immunosuppression. |  |

**How to use this in viva/OSPE**

1. **Quote the size & location first** (“2–4 µm intracellular yeasts on GMS”); examiners expect that figure.
2. **Name at least two stains** (PAS & GMS) and why they help (highlight cell wall).
3. **Describe the host response** (granulomatous ± caseation).
4. **Link histology to clinical setting** – low organism load in acute pulmonary disease, heavy load in bone marrow of disseminated HIV cases.
5. **Remember pitfalls** – scant organisms may be missed on H&E; biopsy sensitivity varies with immunocompetence.

*(Images above illustrate classic intracellular yeasts on GMS, PAS and H&E, plus a composite bone‑marrow panel to reinforce these points.)*

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