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**Histoplasmosis: A Review of The Histopathological Features and Diagnostic Challenges**

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Author for Correspondence: omuaevelyn@gmail.com. <https://dx.doi.org/10.4314/sokjmls.v10i4.18>**Abstract**

*Histoplasma capsulatum* remains a significant global health burden because of its non-specific clinical presentation, which complicates diagnosis. This review aims to discuss the complete spectrum of the tissue changes caused by histoplasmosis. In immunocompetent hosts, granulomatous inflammation dominates, whereas in immunocompromised patients, diffuse histiocytic infiltrates may occur. Histopathology provides a rapid means of identifying infection; however, these small, narrow-based budding yeasts are not easily visualised with H&E staining. For this reason, Pathologists often use special stains, including GMS and PAS. The real challenge arises from organisms that mimic each other, such as *Leishmania spp.* and *Blastomyces dermatitidis*, as well as from technical issues involving sample errors and over-reliance on H&E stains alone. More standard techniques are required to obtain a correct diagnosis. Techniques such as immunohistochemistry and molecular studies on FFPE tissue significantly add value, although access to these tools is not available in every laboratory. This article discusses the step-by-step approach to a definitive diagnosis, which requires recognising the microscopic patterns first, ordering appropriate confirmatory tests, and finally using those results to guide therapy in the correct direction.

**Keywords:** Histoplasmosis, Histopathological Features, Diagnostic Challenges

**Introduction**

The dimorphic fungi are an emerging concern for

public health. They infect both immunocompetent and immunocompromised individuals around the world. Among them, *Histoplasma capsulatum* features prominently. This fungus is re-emerging, and its presence has been reported in areas well outside the geographic borders of its endemic regions. Travel, migration, and the increasing number of individuals with immunity deficiencies all contribute to this phenomenon (Kuate *et al.*, 2021; Schmidt *et al.*, 2025). This systemic mycosis can rapidly become fatal in case of delayed diagnosis or lack of diagnosis by the clinicians. Clinicians must be vigilant and properly diagnose the condition using the appropriate diagnostic tools for early detection.

At the centre of this issue is the fungus *H. capsulatum*, which grows in soil that contains high amounts of bird or bat droppings. This preference accounts for its usual occurrence, and it has historically been a major issue in the Ohio Valley/Mississippi River region of the U.S. (Linder and Kauffman, 2019). However, this problem is general throughout Latin America, Asia, Africa, and elsewhere in tropical, subtropical regions, and it becomes a global problem. It infects a wide variety of clinical diseases. In some patients, particularly those with previous lung disease, a severe pulmonary pattern may occur (Azar *et al.*, 2020).

In worst scenarios, however, there could be progressive disseminated histoplasmosis where the cell-mediated immunity has become impaired, like in late-stage HIV/AIDS and in patients receiving TNF-alpha inhibitors or any

other prospective immunocompromised states (Linder and Kauffman, 2019; Azar *et al.*, 2020). The symptoms do not really stand out; they can appear just like many other infections, including tuberculosis, which makes it very difficult to diagnose (Kuate *et al.*, 2021; Denning *et al.*, 2025).

Diagnosis of histoplasmosis is usually done by culture, which is widely regarded as the gold standard. The biggest concern is time, in that results can be several weeks away, delaying potential treatment (Azar *et al.*, 2020). In contrast, tissue biopsies can provide a diagnosis within hours. For critically ill patients, such rapid turnarounds are imperative (Jensen, 2021). However, there are significant limitations to histopathology. The yeast forms of *Histoplasma* are tiny, only 2 to 4 microns, and often reside inside histiocytes. Furthermore, tissue reactions may look completely different from case to case, ranging from well-developed granulomas to diffuse histiocytic, which is indeed a big diagnostic challenge (Jensen, 2021; Rech and He, 2021). In addition, *H. capsulatum* resembles many other organisms when viewed under the microscope: *Leishmania*, *Toxoplasma gondii*, as well as other yeasts like *Candida glabrata* and *Blastomyces dermatitidis*. Such resemblance means one can easily misidentify these organisms, which might have a greater effect on the treatment of the patients (Antinori *et al.*, 2018; Linder and Krauffman, 2021).

This article will, therefore, discuss the histopathological features of histoplasmosis within a wide variety of clinical and tissue contexts. Attention will be directed to the major diagnostic difficulties presented by challenging histological look-alikes and technical issues that hinder diagnosis. It starts by describing typical and atypical histopathological features. It then discusses the most important pitfalls associated with diagnosis. Finally, it focuses on how a

combination of special stains, immunohistochemistry, and molecular pathology supports pathologists in making an accurate diagnosis with speed.

### **The Histopathological Spectrum of *Histoplasma capsulatum***

Diagnosis of histoplasmosis under the microscope starts with the identification of the classic yeast form and recognition of its interaction with host tissues. The difficulty is that both the appearance of the fungus itself and the response of the tissue can vary considerably. This variability means that pathologists have to be vigilant because it is rarely clear-cut.

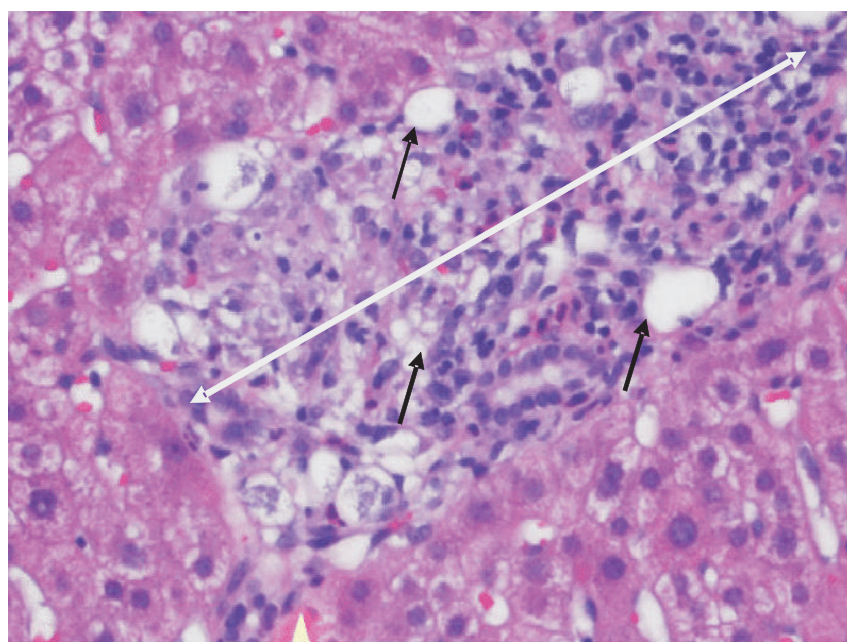
### **The Yeast Form: Classic and Diagnostic Features**

The yeast form of *H. capsulatum* can be observed directly in tissue and is the preferred method of diagnosing histoplasmosis. These minute elements, 2-4 microns in diameter, are globular or slightly oval. Their characteristic budding leads to the formation of new closely connected cells by virtue of a thin neck, resulting in the characteristic “hourglass” shape at the intersection of two cells observed under a microscope (Azar *et al.*, 2020; Jensen, 2021). Typically, these yeasts are found nestled intracellularly within the cytoplasm of macrophages and other mononuclear phagocytes, although they may also be seen extracellularly in areas of high organismal burden (see Figure 1). Where this pathogen resides within the cell has significant consequences for its ability to persist inside the host's phagocytic cells. *H. capsulatum* is quite small, and its characteristics are quite subtle, making it easy to get confused with other organisms. Because of this, the careful comparison of morphology with that of other pathogens, as shown in Table 1, should be done to avoid confusion.

**Table 1: Key Differential Diagnosis of Small Yeast Forms and Mimics in Tissue**

Organism	Size (µm)	Key Morphological Feature	Helpful Special Stains/IHC	Geographic/Clinical Note
<i>Histoplasma capsulatum</i>	2-4	Narrow-based budding; intracellular in macrophages	GMS/PAS positive; Histoplasma IHC specific	Endemic in the Ohio/Mississippi River valleys, the global tropics
<i>Blastomyces dermatitidis</i>	8-15	Broad-based budding; thick, double-contoured wall	GMS/PAS positive	Midwestern, south-central, and southeastern U.S.
<i>Candida glabrata</i>	2-4	Broad-based budding; small, uniform yeasts only (no hyphae)	GMS/PAS positive	Common commensal; opportunistic pathogen
<i>Talaromyces marneffei</i>	2-6	Elongated, sausage-shaped yeasts with septation; no budding	GMS/PAS positive	Southeast Asia, southern China
<i>Cryptococcus neoformans/gattii</i>	4-10	Wide variation in size; prominent capsule (clear halo on H&E)	Mucicarmine/Alecin blue highlights the capsule	Ubiquitous; associated with pigeon droppings
<i>Leishmania</i> spp. (amastigotes)	2-4	Internal Kinetoplast (dot-like structure); no budding	Giemsa; negative	Tropical and subtropical regions
<i>Toxoplasma gondii</i> (tachyzoites)	2-3	Crescent-shaped; no budding; typically, in clusters	IHC/PAS negative; serology crucial	Ubiquitous

Data synthesised from Taborda et al. (2018); Linder & Kauffman (2021); Jensen (2021)

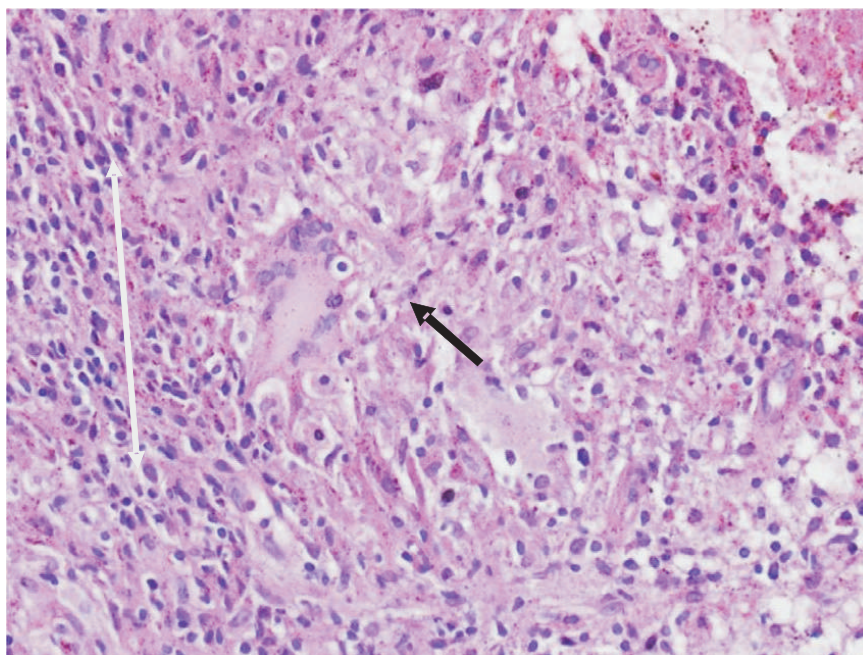


**Figure 1: Photomicrograph of a tissue section stained with Haematoxylin and Eosin (H&E) showing a diffuse infiltrate of histiocytes (double-headed arrow) filled with numerous small yeast forms (short black arrows) (Washburn et al., 2017)**

### Tissue Reaction and Granulomatous Inflammation

The reaction of the body to *H. capsulatum* is highly dependent on the status of the host's immune response, as evidenced under the microscope. In individuals with competent immune responses, there is an aggressive cell-mediated response by the body, leading to

orderly granulomas and groups of epithelioid histiocytes that may also contain classic examples of Langhans giant cells (Jensen, 2021). Only a few yeast forms are hidden in caseous necrosis, which usually shows in the middle. It is difficult to visualise in an ordinary H&E stain, hence the need for special stains (see Figure 2).



**Figure 2: Photomicrograph of an H&E-stained section showing a well-formed granuloma with epithelioid histiocytes (double-headed arrow) and multinucleated giant cells (short black arrow) (Sanae *et al.*, 2021).**

This type of granulomatous reaction serves to contain the infection, but generally looks similar to other diseases causing granulomas, particularly tuberculosis (Denning *et al.*, 2025).

In contrast, a radically different histopathological pattern is seen in the case of hosts with profoundly weakened immune systems, those, for example, with far-advanced HIV/AIDS or on potent immunosuppressive therapy. Their immune system is unable to mount well-developed granulomas. Instead, there are sheet-like proliferations of microphages packed with yeast forms, with minimal to absent granuloma formation and scarce necrosis (Azar *et al.*, 2020). This pattern may overwhelm the histiocytic infiltrate so as to mimic a storage disorder or even a histiocytic neoplasm in cases of widespread disseminated disease, sometimes referred to as 'miliary'. Consequently, Pathologists need to maintain a high index of

suspicion and apply routine fungal stains in such settings (Antinori *et al.*, 2018; Rech and He, 2021).

### Histological Variants and Uncommon Presentations

The diagnosis of histoplasmosis may sometimes pose a problem. Although some cases may appear atypical, some of their unusual variants can present even more challenges to the pathologists. Think about *H. capsulatum*, a morphologically important variant of histoplasmosis mainly encountered in Central and West Africa. The yeast cells of this organism are thick-walled and large (8-15µm) and are found within giant cells arranged in a characteristic ("string of pearl") pattern (Ekeng *et al.*, 2023). Its size and morphology can be misleading since these organisms can easily be mistaken for *Blastomyces dermatitidis* or *Coccidioides* species. It is really important to analyse the histology and the travel history of the patient.

Another example is fibrosing mediastinitis; though rare, it is a serious complication of histoplasmosis. It results from the body's fibrotic response to prior *Histoplasma* infection, leading to dense, nearly acellular collagenous tissue that may entrap mediastinal structures. Yeast forms are rarely seen in fibrotic tissues, which makes diagnosis difficult. As a result of this, clinicians often depend on patient history, blood tests, and imaging studies to make a diagnosis (Azar *et al.*, 2020). When disseminated histoplasmosis occurs, the adrenal glands are commonly involved and can result in adrenal insufficiency. Biopsies usually show granulomas or necrotising inflammation filled with yeast forms, especially if special stains are used. In areas endemic for histoplasmosis, physicians should consider it first when patients present with bilateral adrenal masses (de Oliveira *et al.*, 2023).

### Ancillary Techniques in Histopathological Diagnosis

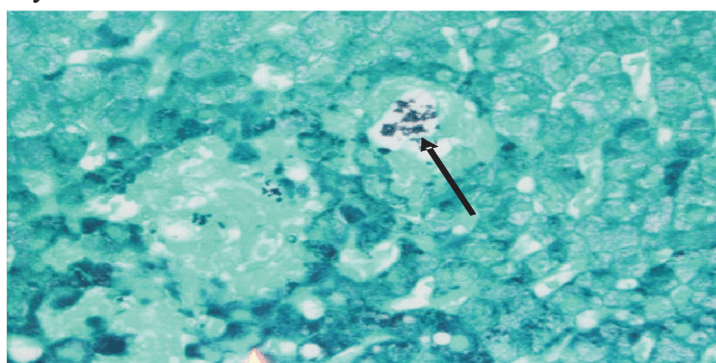
Although recognition of yeast form on a haematoxylin and eosin stain may suggest histoplasmosis, pathologists often must go further to reach a diagnosis. Ancillary techniques become important in this context. They confirm a diagnosis when fungal forms appear unusual, when there are few organisms present, or when the differential diagnoses are long. Special stains highlight features under the microscope. Immunohistochemistry adds more precision by targeting specific markers. Molecular methods applied to tissue take pathology to a higher level of accuracy. Each of these methods provides extra detail that standard techniques may not always offer.

### Special stains: Enhancing Visualisation

*H. capsulatum* is very small and often resides intracellularly, being very hard to visualise on a

routine H&E stain. In general, only a subtle blue haze within the cytoplasm of the histiocyte is noted. That is why the special stains take centre stage. Of the latter, the Gomori Methenamine Silver (GMS) is regarded as the gold standard because it stains the fungal cell wall black against a green background, where even one yeast form is readily observable (see Figure 3). It is with GMS that not only the fungus can be outlined, but the critical budding characteristics assessment can also be made, one of the key diagnostic features (Jensen, 2021; Ranjan *et al.*, 2025). Probably the next best choice, although far less dramatic than GMS, is the Periodic Acid-Schiff (PAS) stain, which outlines polysaccharides in the fungal wall in magenta. The key here is that while these stains are sensitive for the detection of fungi, they do not provide specific identification of *Histoplasma*; their role is more confirmatory in the presence of the fungus and for morphological appearance rather than definitive species identification (Linder and Kauffman, 2021).

Different cytological stains are of equal importance in certain clinical contexts. For example, in a patient with disseminated disease, bone marrow aspirates with Giesma or Wright's stains are useful for the pathologist to make a quick diagnosis. Such stains reveal small, oval yeast forms inside the cytoplasm of macrophages, usually with a clear halo surrounding the yeast, corresponding to the cell wall, and serving as a useful diagnostic feature (Azar *et al.*, 2020). This usage of these stains in bone marrow evaluation underlines the importance of choosing the right ancillary test depending on the specimen type and clinical context.



**Figure 3: Photomicrograph showing Gomori Methenamine Silver (GMS) stain vividly outlining the cell walls of *Histoplasma capsulatum* yeasts, demonstrating characteristic narrow-based budding (black arrow) (Washburn *et al.*, 2017)**

### **Immunohistochemistry: Achieving Specificity**

Traditional histochemical stains usually cannot accurately establish the cause in the tissue sample. That is why researchers have adopted Histoplasma-specific IHC. In IHC, the antibodies target *H. capsulatum* antigens, giving pathologists a much clearer diagnosis. This method is very useful in challenging cases, such as when the yeast forms are few in number, when the tissue reactions become atypical, or when differentiating Histoplasma from similar organisms like *Candida glabrata* or *Toxoplasma gondii* is needed (Jensen, 2021). This produced a decidedly strong and cytoplasmic type of staining, which permits the elimination of other pathogens more easily.

However, there is a limitation. Most laboratories, especially in areas most endemic for histoplasmosis, do not even have access to Histoplasma IHC. Ekeng *et al.* (2023) and Villareal *et al.* (2023) support this assertion as factual. Few laboratories can conduct the test. Thus, many patients miss being diagnosed. Even though IHC is effective, it is still not available for most patients.

### **Molecular Methods on Tissue: The Role of Precision Pathology**

Molecular diagnostics have revolutionised the detection of pathogens in FFPE tissues. PCR-based arrays, which amplify species-specific DNA sequences, provide a high degree of sensitivity and specificity in the diagnosis of histoplasmosis. These methods are particularly advantageous in cases where cultures are negative or when tissues do not demonstrate overt findings microscopically (Villareal *et al.*, 2023; Schimdt *et al.*, 2025). This has significantly advanced the field, making diagnoses possible in conditions where it was hitherto almost impossible, such as fibrosing mediastinitis, where organisms are difficult to find, or in central nervous system infections, where precision is critical (de Oliveira *et al.*, 2023).

The increasing utilisation of next-generation sequencing pushes these capabilities even further. Applied to FFPE tissue, NGS can detect the presence of *H. capsulatum* and other pathogens without any prerequisite assumptions about the target organism. However, access to

these advanced techniques remains limited. High costs, the need for specialised personnel, and labour-intensive processes keep them inaccessible to most laboratories. And as with any PCR-based technique, limitations include the risk of contamination and low-quality DNA from FFPE tissues, which may inhibit the process. Nevertheless, molecular pathology is beginning to change the face of diagnostic mycology. It is no longer merely a question of morphology. It enables identification at the species level and actually helps clinicians to choose the correct antifungal treatment.

### **Major Diagnostic Challenges and Histological Mimics**

Diagnosing histoplasmosis is not easy. A pathologist does more than recognise a familiar outline under the microscope; he must work his way through a maze of similarly appearing organisms and overcome technical hazards that may lead him astray. It is not enough that the laboratory work is done correctly. Mistakes at this point are real ones for the patient.

#### **“The Great Imitators”: A Differential Diagnosis**

Most of the confusion comes from the morphology of *H. capsulatum* under the microscope. The small, intracellular yeast form bears a striking resemblance to other unrelated pathogens. To distinguish them accurately, therefore, a careful, analytical approach is necessary. Of all the species, Leishmania species are probably the most difficult to distinguish from Histoplasma. The amastigotes are almost identical in size and intracellular location. The key distinguishing feature is the presence of tiny Kinetoplast, visible as a dot-like structure adjacent to the nucleus on Giesma stain, present in Leishmania but absent in Histoplasma (Linder and Kauffman, 2021). *Toxoplasma gondii* can also be confused with Histoplasma, but its tachyzoites are smaller, crescent-shaped, and do not bud; they tend to cluster together and do not multiply within the cytoplasm of macrophages as Histoplasma does.

Other fungal look-alikes further confuse the issue. *Candida glabrata* is a common source of mistaken identity. It is roughly the same size as Histoplasma, but it proliferates by way of broad-

based budding, in contrast with the narrow-based budding typical of *Histoplasma* (Jensen 2021). While *Pneumocystis jirovecii* often forms cystic structures, even though the GMS-positive wall may appear as collapsed yeast and despite staining characteristics, it does not bud. In the United States and other parts of the world where this infectious agent is endemic, *Blastomyces dermatitidis* is the most significant differential diagnosis. Mistaking it for *Histoplasma* leads to clinical consequences because their treatments differ, with an incorrect diagnosis negatively impacting patient management. *Blastomyces* is differentiated by its larger size (8 – 15 µm) and by its broad-based budding, with a wide connection between the mother and daughter cells, importantly (Linder and Kauffman 2021).

Finally, the travel history is critical. Patients originating from Southeast Asia may be infected with *Talaromyces marneffeii*. Its yeast form is sausage-shaped and is divided by septation instead of by budding, and may be identified if close observation is made. That single detail alone provides a key morphologic clue to the appropriate diagnosis.

### Technical and Interpretive Pitfalls

Even with a thorough knowledge of mimics, the diagnosis is not easy. The low yeast burden is a significant problem, especially in localised disease or in the immunocompetent patient in whom granulomas effectively contain the infection. A few scattered yeasts can be present within the large biopsy and are often missed unless multiple levels of tissue are carefully scrutinised and special stains, such as GMS, are used (Jensen, 2021).

Moreover, the pathologist must also be aware of atypically appearing yeast forms. In partially treated patients with antifungal agents, *Histoplasma* may appear larger and assume irregular shapes without any budding, hence looking very much unlike the typical forms. Such atypical forms are easily confused with other pathogens (Azar *et al.*, 2020). Then there is also the possibility of sampling error. In disorders like fibrosing mediastinitis, the fungus is only present in isolated foci within dense fibrotic tissue. A biopsy that samples only

paucicellular collagen may turn out to be falsely negative.

Perhaps the most common and preventable mistake is reliance on the H&E stain. Yeast forms are virtually invisible on H&E, appearing as faint basophilic dots, so without special stains, histoplasmosis could be missed entirely. This is more than a technicality; it is critical reasoning in diagnosis. Therefore, the application of fungal stains during granulomatous or histiocyte-rich inflammation, particularly in a patient with a poor immune system, remains the best strategy to guard against diagnostic error (Antinori *et al.*, 2018). Ultimately, success in diagnosis depends on maintaining a high index of suspicion and must be combined with a disciplined, technical multimodal approach if these pervasive challenges are to be overcome.

### Conclusion

This review summarises the crucial role of histopathology in diagnosing histoplasmosis, a pathogen whose manifestations vary greatly according to the immune competence of its hosts. The take-home message is clear: histopathology can provide quick and useful answers, but effectiveness depends on having a clear idea about the full spectrum of histological features, ranging from organised granulomas in immunocompetent patients to diffuse histiocytic infiltrates in immunocompromised patients. Accurate diagnosis requires adherence to a strict protocol, mandating special stains such as GMS for visualising characteristic yeast forms, which are not just helpful but very necessary given the fact that over-reliance on H&E staining alone is a leading cause of diagnostic failure.

And mistakes such as these have grave consequences: A misdiagnosis is much more than a minor setback; it may put the patient in jeopardy. Consider *Histoplasma capsulatum* and *Blastomyces dermatitidis* alone: Confusion between the two results in completely inappropriate therapy. Patients with severe cases of blastomycosis will not do well without azoles but, instead, will require amphotericin B as an initial treatment. Also consider the risks when the histiocytic infiltrate in disseminated histoplasmosis is mistaken for malignancy;

patients may be subjected to unnecessary chemotherapy, interventions that not only fail to help but actually increase harm. Good pathology is not an academic nicety; it is integral to selecting appropriate antifungal therapy and directly impacts patients' outcomes.

Limitations of this review need to be acknowledged. Because it is a review of published literature, publication bias is possible; unusual or complex cases may be overrepresented. Another major issue is the disparity between what advanced laboratories can achieve and what is available in less-resourced settings. Techniques such as species-specific immunochemistry or PCR on FFPE tissue are extremely valuable in difficult cases, but many areas simply do not have access to them. Clinicians, therefore, have to diagnose histoplasmosis with whatever resources are available. In many endemic areas, the ideal comprehensive approach remains more of an aspiration than a reality.

### Future Perspectives

To fill these gaps, future efforts should focus on a few key areas: first, developing diagnostic tools that are faster, cheaper, and more reliable, such as point-of-care antigen tests or low-cost IHC kits with good performance in a variety of real-world settings; second, introducing NGS as part of the FFPE tissue analysis may revolutionise the detection of subtle or mixed fungal infections; its validation and cost reduction need to be prioritised in research agendas. Lastly, the awareness of Clinicians and Pathologists in non-endemic areas will also need to be improved; they can no longer afford to ignore histoplasmosis, especially given the changes brought about by travel and climate change in the distribution of this disease. If diagnostics, research, and education are addressed together, the challenges related to histoplasmosis can be systematically overcome.

### References

Antinori, S., Corbellino, M., & Parravicini, C. (2018). Challenges in the diagnosis of invasive fungal infections in immunocompromised hosts. *Current Fungal Infection Reports*; **12(1)**: 12-22. doi:

- 10.1007/s12281-018-0306-0
- Azar, M. M., Loyd, J. L., Relich, R. F., et al. (2020). Current concepts in the epidemiology, diagnosis, and management of histoplasmosis syndromes. *Seminars in Respiratory and Critical Care Medicine*; **41(01)**: 013-030. doi: 10.1055/s-0039-1698429
- De Oliveira, V. F., Kruschewsky, W. L. L., Sekiguchi, W. K., et al. (2023). Clinical, radiological and laboratory characteristics of central nervous system histoplasmosis: a systematic review of a severe disease. *Mycoses*; **66(8)**: 659-670. <https://doi.org/10.1111/myc.13600>.
- Denning, D. W., Onikan, A., Chaves Magri, M. M., et al. (2025). Radiological features of chronic pulmonary histoplasmosis: Easily mistaken for tuberculosis. *PLOS Neglected Tropical Diseases*; **19(8)**: e0013219. <https://doi.org/10.1371/journal.pntd.0013219>.
- Ekeng, B. E., Emanghe, U. E., Davies, A. A., & Oladele, R. O. (2023). A critical review of diagnostic methods for disseminated histoplasmosis with special focus on resource-limited settings. *Current Fungal Infection Reports*; **17(1)**: 1-9. DOI:10.1007/s12281-023-00454-4.
- Jensen, H. E. (2021). Histopathology in the diagnosis of invasive fungal diseases. *Current Fungal Infection Reports*; **15(1)**: 23-31. DOI:.
- Kuate, M. P. N., Ekeng, B. E., Kwizera, R., et al. (2021). Histoplasmosis overlapping with HIV and tuberculosis in sub-Saharan Africa: challenges and research priorities. *Therapeutic Advances in Infectious Disease*; **8**: 20499361211008675. doi: 10.1177/20499361211008675.
- Linder, K. A., & Kauffman, C. A. (2019). Histoplasmosis: epidemiology, diagnosis, and clinical manifestations. *Current Fungal Infection Reports*; **13(3)**: 120-128. DOI:10.1007/s12281-019-00341-x.
- Linder, K. A., & Kauffman, C. A. (2021). Current and new perspectives in the diagnosis of blastomycosis and histoplasmosis. *Journal of Fungi*; **7(1)**: 12. DOI: 10.3390/jof7010012.
- Ranjan, R., Singh, A., & Patel, B. (2025).

- Diagnostic Accuracy of Histopathology versus Microbiological Methods in Fungal Infections: A Systematic Review of H&E, PAS, and GMS Staining Compared with Culture and PCR. *International Journal of Medical and Pharmaceutical Research*; **6**: 1482-1490. DOI : 10.5281/zenodo.17464431.
- Rech, K. L., & He, R. (2021). Challenges in the histopathologic diagnosis of histiocytic neoplasms. *Journal of the National Comprehensive Cancer Network*; **19(11)**: 1305-1311. DOI: 10.6004/jnccn.2021.7098
- Sanae, A., Hajar, E. A., Selma, K., et al. (2021). Peritoneal thickening: It's not always carcinomatosis. *Radiology Case Reports*; **16(9)**: 2620–2623. <https://doi.org/10.1016/j.radcr.2021.06.038>.
- Schmidt, T. E., Vieceli, T., Damasceno, L. S., et al. (2025). Evolving Epidemiology, Improving Diagnostic Tests and Their Importance for the Correct Diagnosis of Histoplasmosis. *Journal of Fungi*; **11(3)**: 196. DOI: 10.3390/jof11030196.
- Villareal, K., Price, A., Pasqualotto, A. C., & Bahr, N. C. (2023). The current and future states of diagnostic tests for histoplasmosis with a focus on people with HIV and disseminated histoplasmosis. *Journal of Fungi*; **9(8)**: 793. DOI: 10.3390/jof9080793.
- Washburn, L., Galván, N. T., Dhingra, S., et al. (2017). Histoplasmosis hepatitis after orthotopic liver transplantation. *Journal of Surgical Case Reports*; **2017(12)**: rjx232. <https://doi.org/10.1093/jscr/rjx232>.

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