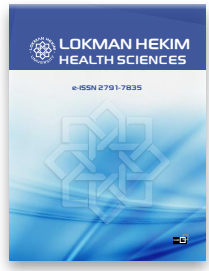
LOKMAN HEKIM HEALTH SCIENCES

DOI: 10.14744/lhhs.2025.80707
Lokman Hekim Health Sci 2026;6(1):150–158



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INVITED REVIEW

Updates on Aspergillosis in Chronic Granulomatous Disease

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Abstract

Patients with Chronic Granulomatous Disease (CGD) face the highest lifelong risk of invasive aspergillosis (IA). Effective management of IA in this population requires meticulous care and a well-coordinated, multidisciplinary approach. This includes primary antifungal prophylaxis, timely evaluation and treatment of suspected IA, and the use of diagnostic methods to make a causative diagnosis. In this review, we aim to assess recent advancements in the diagnosis and treatment of IA in patients with CGD.

Keywords: *Aspergillus*; Chronic granulomatous disease; Infections; Mycology

Chronic Granulomatous Disease (CGD) was first described in 1954 as "the fatal granulomatous disease of childhood". It is an inborn error of immunity that is inherited either through an X-linked (XL) or autosomal recessive (AR) pattern.[1,2]

CGD results from mutations in genes encoding components of the leukocyte nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complex, which plays a crucial role in the microbicidal activity of phagocytes. This complex consists of five subunits, with the primary enzymatic component, gp91phox (also known as Nox2), encoded by the *CYBB* gene on the X chromosome. Mutations in *CYBB* lead to XL CGD, while AR forms of the disease arise from mutations in one of five autosomal genes: *CYBA* (encoding p22phox), *NCF1* (encoding p47phox), *NCF2* (encoding p67phox), *NCF4* (encoding p40phox), and *CYBC1*. The *CYBC1* gene encodes cytochrome b558 chaperone-1, a recently identified protein essential for the expression of gp91phox.[3,4]

The estimated incidence of CGD is about 1 in 200,000 live births, varying by ethnicity.[2] XL-CGD is more prevalent than AR-CGD globally; however, in regions with higher consanguinity rates, AR-CGD is reported to be equally prevalent or even more common.[5,6] Males are more commonly affected than females (2:1) due to the predominant pattern of genetic inheritance.[2]

Patients with CGD typically present with recurrent infections of the lower respiratory tract, growth failure, visceral abscesses, cellulitis, lymphadenitis, and the formation of granulomatous lesions.[2,7] The disease may also be identified in a subset of children presenting with noninfectious complications, such as early-onset inflammatory bowel disease.[2]

Cite this article as: *Ergenç Z, Warris A. Updates on Aspergillosis in Chronic Granulomatous Disease. Lokman Hekim Health Sci 2026;6(1):150–158.*

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E-mail: drzeynepergenc@gmail.com **Submitted:** 15.08.2025 **Revised:** 02.09.2025 **Accepted:** 24.09.2025 **Available Online:** 16.03.2026

This review will focus on epidemiology, immunopathology, antifungal prophylaxis and management of IA, and HSCT as a curative treatment option in CGD, with a focus on children and adolescents.

Search strategy: Relevant published English-language literature was searched in the PubMed and Google Scholar databases using the keywords "aspergill*" and ("chronic granulomatous disease" OR "CGD") from 1957 to July 2025. For each relevant section, the search was further refined by adding specific terms, including "galactomannan", "BAL or bronchoalveolar lavage", "PCR OR polymerase chain reaction", "itraconazole", "voriconazole", "posaconazole", "osteomyelitis", "pulmonary", "brain OR central nervous", "liver OR spleen OR hepatic", "metagenomics", "HSCT OR hematopoietic stem cell" and "gene therapy."

Epidemiology of Invasive Aspergillosis in Chronic Granulomatous Disease

Patients with CGD exhibit the highest lifetime incidence of invasive aspergillosis (IA). A significant proportion of patients with CGD, ranging from 26% to 45%, develop IA.[8]

Among *Aspergillus* species, *A. fumigatus* is the most frequently identified pathogen in patients with CGD, followed by *A. nidulans*. Less commonly, *A. terreus* and *A. flavus* are also identified.[8,9] Remarkably, *A. nidulans* has a very unique predilection to XL-CGD, as it is exceedingly rare in other immunocompromised populations, including those with neutropenia.[8,10]

The lungs are the primary site of involvement particularly for *A. fumigatus* followed by the bones and brain.[9] The symptoms of pulmonary IA typically include a non-productive cough, fever, chest discomfort, and progressively worsening dyspnea. However, certain species demonstrate a tendency to exhibit a more indolent course. For instance, infections caused by *A. nidulans* often present with a milder clinical onset and nonspecific symptoms compared to those caused by *A. fumigatus*.[8,9] Notably, *A. nidulans* is frequently isolated in cases of osteomyelitis.[11]

A less common but highly lethal form of acute fungal pneumonia in CGD known as "mulch pneumonia", is a medical emergency. This syndrome is triggered by the inhalation of a substantial load of fungal spores (including those from *Aspergillus*) and may serve as the initial clinical presentation of CGD in affected individuals.[8,9] Affected patients typically present with sudden-onset dyspnea, hypoxia, and fever, while chest imaging shows diffuse, bilateral infiltrates after an identifiable exposure to aerosolized organic particles.[12,13]

XL-CGD is characterized by a higher incidence, earlier manifestation and worse prognosis of IA compared to AR-CGD.(8) Skin and CNS involvement are also reported more frequently in XL-CGD.[14] However, the extent of the residual NADPH oxidase activity, rather than the specific genetic defect, determines the risk of IA and severe infections in CGD.[8]

Despite a significant reduction in *Aspergillus*-specific mortality rates with the induction of azole propyhlaxis in 90's, IA remains the predominant cause of mortality and morbidity in patients with CGD.[6,8,15]

Immunopathology

IA in CGD follows a distinct pathogenesis rooted in a deficiency of NADPH oxidase, which results in impaired production of reactive oxygen species (ROS) and hyperinflammation. This deficiency compromises the direct microbicidal activity of phagocytes, rendering individuals with CGD susceptible to IA. Moreover, the absence of ROS disrupts normal inflammatory regulation, leading to excessive granuloma formation and dysregulated immune responses, hallmark features of IA in CGD.[16,17]

Despite these vulnerabilities, compensatory killing mechanisms in phagocytes provide partial protection against fungal pathogens in CGD, which might explain why almost half of the patients with CGD never develop invasive mold infections.[17]

In CGD, IA presents as a subacute, non-angio-invasive infection characterized by the overproduction of granulomas in the affected tissues. These granulomas are structured as spherical aggregates, with a core comprising tissue-resident epithelioid macrophages that fuse into multinucleated giant cells, surrounded by T lymphocytes. Additionally, mold infections in CGD may result in chronic necrotizing granulomatous inflammation, a partially invasive form of disease. This pathological state is marked by fungal hyphae embedded within necrotic areas of tissue and noticeable parenchymal invasion, yet vascular invasion is typically absent.[17]

Antifungal Prophylaxis

The high lifetime incidence of IA in patients with CGD, along with its direct association with reduced life expectancy, underscores the critical importance of preventive measures. Prevention of IA is a cornerstone of clinical management in CGD and involves minimizing environmental exposure to molds and implementing antifungal prophylaxis. Patients are advised to avoid exposure to sources with high fungal

contamination, such as mulch, hay, wood chips, rotting plant material (e.g., compost heaps), as well as visiting caves, stables, sheds, construction or renovation sites, and engaging in activities like gardening.[8]

Itraconazole or posaconazole is recommended for antifungal prophylaxis in patients with CGD. Oral itraconazole prophylaxis has been extensively utilized in this population with a well-established efficacy and safety profile. The oral suspension form is preferred over the tablet form due to its superior absorption. Posaconazole is another effective option for antifungal prophylaxis in CGD and is available in three oral formulations: an oral suspension, delayed-release tablets, and a gastro-resistant powder for oral suspension.[18] The oral suspension, licensed in 2006, was the first established formulation. However, concerns regarding the difficulty in achieving therapeutic drug levels and the risk of breakthrough infections led to the development of gastro-resistant delayed-release tablets approved by Food and Drug Administration (FDA) in 2013. While these tablets became the preferred formulation, their use in pediatric patients posed challenges, as they should not be crushed, divided, or chewed.[19] To address these limitations, a gastro-resistant powder for oral suspension has recently been introduced, demonstrating favorable pharmacokinetics and a strong safety profile in children with documented or expected neutropenia.[20]

Therapeutic drug monitoring (TDM) is critical for ensuring adequate exposure of both itraconazole and posaconazole in antifungal prophylaxis. For itraconazole prophylaxis, trough levels of 0.5 to 4 mg/L (itraconazole+hydroxy-itraconazole) should be achieved. For posaconazole prophylaxis, a trough concentration of >0.7 mg/L is recommended.[18]

Both posaconazole and itraconazole are associated with adverse effects, including hypokalemia, hepatotoxicity, cardiotoxicity (such as prolonged QTc interval, atrial fibrillation, and Torsades de Pointes), and significant drug-drug interactions.[19] To minimize the risk of hepatotoxicity, regular monitoring of liver function is essential. Additionally, electrocardiographic monitoring is recommended to mitigate the risk of cardiotoxicity. Special caution is advised when prescribing azole antifungals, especially posaconazole, in patients with known proarrhythmic conditions (e.g. cardiomyopathy).[19]

Interferon-gamma (IFN-γ), a macrophage activating cytokine produced by T cells and natural killer cells, has long been utilized to prevent fungal and bacterial infections in patients with CGD. Studies have demonstrated that IFN-γ administration reduces the incidence of fungal infections compared to control groups.[9] In a subset of patients with XL CGD, IFN-γ has been shown to enhance splicing efficiency and increase cytochrome b expression, leading to near-normal levels of superoxide production and improved bactericidal activity in neutrophils and monocytes.[21] However, IFN-γ is associated with various adverse effects, particularly with long-term use, including fever, headache, gastrointestinal symptoms, and injection site reactions. Additionally, its high cost further limits its widespread use. As a result, IFN-γ is not routinely prescribed in most centers across Europe and is generally reserved for case-specific indications. It is noteworthy that the majority of studies investigating IFN-γ in CGD were conducted prior to the establishment of modern antifungal prophylaxis as the standard of care. As a result, the potential adjunctive role of IFN-γ in the prevention of IA alongside contemporary antifungal prophylaxis remains uncertain and warrants further research.[8]

Diagnosis of Invasive Aspergillosis in Chronic Granulomatous Disease

The introduction of itraconazole prophylaxis in the 1990s significantly reduced *Aspergillus*-specific mortality.[15] However, its use has also contributed to the emergence of azole-resistant *Aspergillus* and other mould infections, which pose an increasing clinical challenge in this context.[9,19] Therefore, in patients with CGD, obtaining a sterile sample from the site of infection is essential for diagnosing IA.

Diagnosis requires either a positive culture or polymerase chain reaction (PCR) and/or histopathological evidence of hyphal growth in normally sterile tissue.[22] As a result, invasive diagnostic procedures, such as bronchoalveolar lavage (BAL) or surgical biopsy are often needed to obtain a relevant tissue, since blood cultures are typically uninformative to diagnose IA.

While imaging may raise suspicion for invasive fungal disease, particularly when abnormalities persist despite broad spectrum antibiotic therapy, they are not definitive and cannot establish a causative diagnosis.[9] The diagnostic utility of fungal biomarkers such as galactomannan and β-D-glucan, commonly recommended for neutropenic patients, remains uncertain and is inadequately studied in non-neutropenic patients. In patients with CGD, serum galactomannan often remains negative despite confirmed *Aspergillus* infection.[8,10] This may be attributed to the absence of angioinvasion, use of antifungal prophylaxis, or

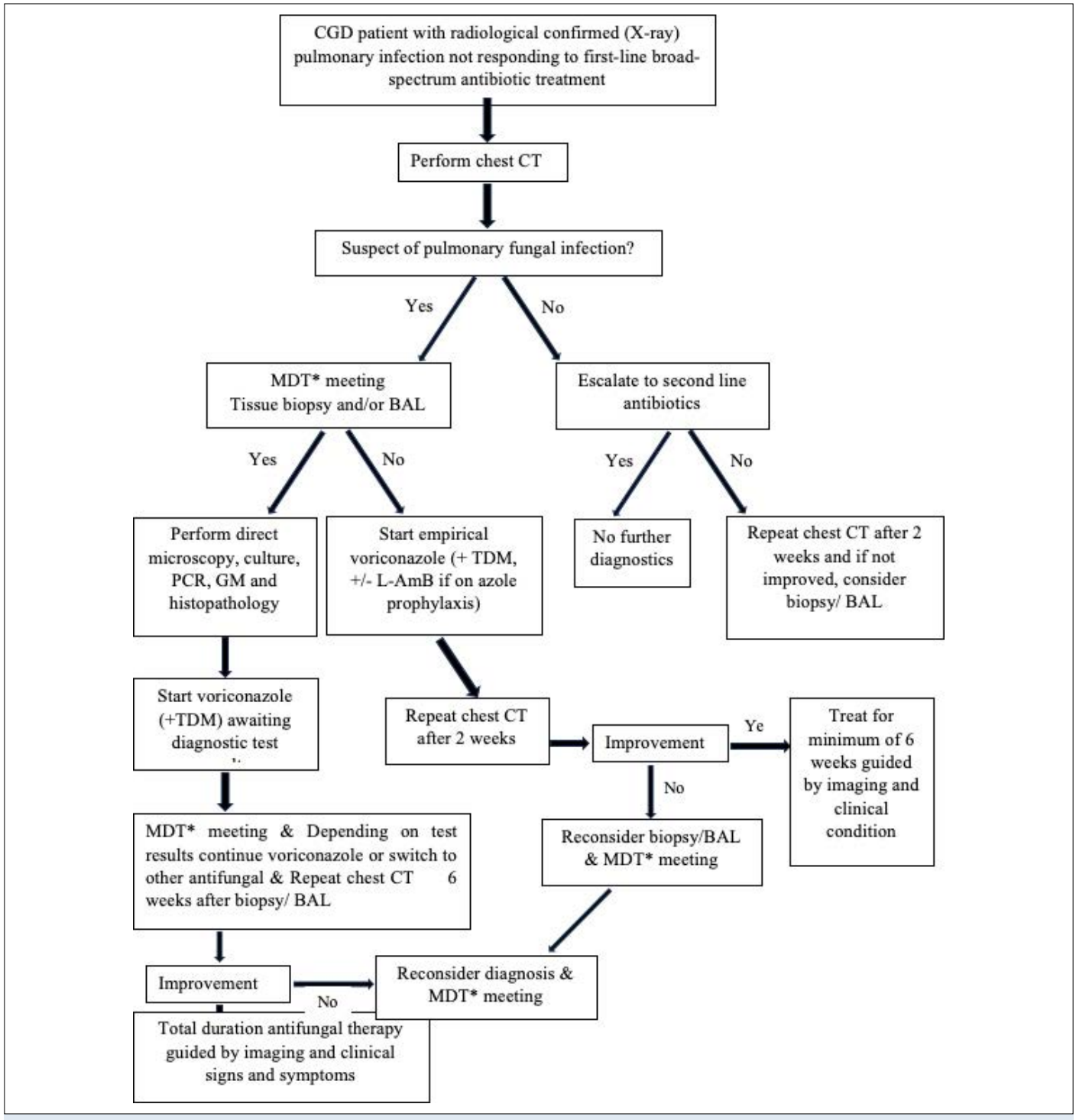

Figure 1. Diagnostic flow chart for CGD patients with suspected pulmonary aspergillosis.

CGD: Chronic granulomatous disease; CT: Computed tomography; MDT: Multidisciplinary team; BAL: Bronchoalveolar lavage; PCR: Polymerase chain reaction; GM: Galactomannan; TDM: Therapeutic drug monitorisation; L-AmB: Liposomal amphotericin B; *: Multidisciplinary team should involve a pediatric infectious diseases specialist with interest in mycology, a pediatric immunologist, a microbiologist, a pharmacist and a radiologist.

the clearance of galactomannan by neutrophils and other immune mechanisms.[8] Although specific data on BAL galactomannan testing in CGD patients is lacking, it may aid in IA diagnosis.[8]

The lungs are the most affected organ in patients with CGD and chest computed tomography (CT) remains the imaging modality of choice.[5,6,10] Diagnostic management of CGD patients with suspected pulmonary aspergillosis

summarized in Figure 1. Pulmonary nodules are the most frequent radiological finding of IA in CGD. These nodules are often multiple, bilateral, and may appear with or without a halo sign.[23,24] Approximately one-quarter of fungal infections demonstrate interstitial pneumonia patterns, including ground-glass opacities, tree-in-bud appearance, and paraseptal emphysema. Lymphadenopathy, particularly extensive conglomerate lymphadenopathy with central necrosis is a suggestive feature for aspergillosis. More distinctive and less common imaging features of IA in CGD include mass-like consolidation and chest wall involvement.[23]

The variability in radiographic presentation between patients may be attributed to age-dependent immune responses and the hyperinflammatory granulomatous process that defines CGD. Despite this heterogeneity, nodular lesions remain the most consistent and earliest CT finding in IA, as supported by Bondioni et al.,[24] who emphasized their diagnostic significance in CGD. Nevertheless, given the broad differential for nodules in immunocompromised hosts including infectious, neoplastic, and inflammatory processes, definitive diagnosis requires microbiological confirmation.

Several techniques are employed to overcome diagnostic difficulties in pulmonary IA, including bronchoalveolar lavage (BAL), fine needle aspiration (FNA), transthoracic percutaneous biopsy, and video-assisted thoracoscopic (VAT) biopsy. The diagnostic yield in CGD patients with IA ranges from 12.5% to 52%, which likely reflects variations in the localization of pulmonary abnormalities and differences in BAL techniques.[8,10] Lung biopsy has been shown to increase the pathogen detection rate from 30% to 50% in CGD patients and is generally preferred to establish a definitive etiological diagnosis.[8]

The most frequent manifestations of central nervous system (CNS) aspergillosis are single or multiple abscesses located in the brain parenchyma, cerebellum, basal ganglia and brainstem. Additional presentations can involve *Aspergillus*-induced vasculitis, meningoencephalitis, or encephalitis.[25] Histopathologically, the lesions typically show necrotizing parenchymal damage with vascular invasion and secondary hemorrhages, occasionally associated with meningoencephalitis. Hemorrhagic complications most often present as hemorrhagic infarcts, subarachnoid hemorrhages or intracerebral hemorrhages. On imaging, the abscess usually appear as one or more lesions with a hypodense center and a uniformly enhancing peripheral ring following contrast administration, consistent with fungal infection. Surrounding brain edema, visible as hypodense areas on CT or magnetic resonance imaging (MRI), may be present.[25] Diffusion weighted MRI is considered the preferred imaging modality in these cases. Evaluation of cerebrospinal fluid (CSF) is recommended, and brain biopsy should be considered.[26]

In patients with CGD, the most common form of *Aspergillus* osteomyelitis involves the small bones, particularly the vertebrae, followed by the ribs and chest wall. This typically results from the contiguous spread of a pulmonary infection.[11,27] At the time of diagnosis, the most frequent findings include osteolysis and bone destruction, often with extension of the infection into the surrounding soft tissues. MRI findings commonly reveal decreased signal intensity on T1-weighted images, increased signal intensity on T2-weighted images, and enhanced contrast on T1-weighted images following gadolinium administration.[26]

Although infrequently documented in the literature, *Aspergillus* species can cause hepatic or splenic abscesses in patients with CGD.[28] Abdominal pain, fever, and elevated liver enzymes consistent with a hepatocellular pattern of injury should warrant imaging such as abdominal ultrasound and/or CT. In a recent systematic review by Dumic et al.,[28] 21 cases of *Aspergillus* liver abscesses were analysed. The aetiology was cryptogenic in 43% of cases while 28% were linked to a pulmonary source with hematogenous spread. Gastrointestinal dissemination via the portal vein accounted for 19%, and 10% resulted from contiguous extension from adjacent structures (e.g. rib, adrenal gland).

When a consistent clinical presentation is observed, the appearance of new or rapidly progressing lesions should prompt consideration of invasive diagnostic procedures to identify the underlying pathogen. This approach is essential for ensuring targeted and effective treatment of patients with CGD.[9]

Once an appropriate sample is obtained, the initial diagnostic step should involve microscopic examination, which can provide a result within one hour. Potassium hydroxide (KOH 30%) and fluorochrome staining, such as calcofluor white, are essential to visualize the thin (3–10 µm), branching septate hyphae characteristic of *Aspergillus* spp. Culture remains the reference standard and should be performed on all samples, preferably using Sabouraud medium with chloramphenicol, to identify fungi at the genus level based on macroscopic and microscopic features and to perform antifungal susceptibility testing. Species-level identification can be confirmed using molecular biology techniques or matrix-assisted laser desorption/

ionization-time of flight (MALDI-TOF) analysis of fungal colonies. All clinical isolates of *Aspergillus* spp. from patients receiving antifungal treatment should be identified to the species complex level.[26]

Histological analysis of biopsy or surgically resected tissue requires histochemical staining, including hematoxylin and eosin (H&E), Grocott methenamine silver, or periodic acid–Schiff (PAS) staining. These methods can confirm invasive mould disease by demonstrating branching septate hyphae, with or without evidence of angioinvasion. Immunohistochemistry with anti-*Aspergillus* antibodies can also be performed; however, cross-reactivity with other moulds may limit specificity. Parallel confirmation through culture of an unfixed tissue sample or PCR analysis is recommended to verify the identification of *Aspergillus* spp.[26]

Assessing the sensitivity of FNA and percutaneous biopsy in CGD remains challenging due to the limited number of reported cases. In a review of invasive fungal infections in CGD, Henriet et al.[9] found that fine needle lung biopsies were consistently positive on microscopy or culture. However, Blumental et al.[15] reported that only 21% of pulmonary FNAs were positive, with most cases ultimately confirmed through surgical biopsy. The diagnostic yield of these techniques is likely influenced by the site of infection, accessibility for percutaneous sampling, and the use of imaging to guide sample collection.[8]

Data from a large European cohort of CGD patients, reported by van den Bergh et al.,[8] indicates that a definitive causative diagnosis is often not established in CGD patients with localized infections. The exact reason for this remains unclear, as the manuscript only states that 72% of cases involved either no culture or negative culture results. Notably, liver biopsy results were negative in 70% of CGD patients with liver abscesses who underwent biopsy.[5]

A study of 67 adults with CGD revealed that pulmonary manifestations are common (67% of patients), with 25% of respiratory events being inflammatory rather than infectious. These inflammatory manifestations were clinically indistinguishable from infections but responded to immunosuppressive therapy (e.g., corticosteroids) rather than antimicrobials. Biopsies frequently revealed granuloma without organisms, eosinophilic micro abscesses, or diffuse granulocytic infiltration. Complicating this issue, 40% of cases exhibited inflammatory pathology alongside concomitant fungal infections.[7] Similarly, a study by Galluzzo et al.[29] comparing osteomyelitis biopsies from CGD and non-CGD patients identified pathogens in all CGD cases, with *Aspergillus* species implicated in 42%. CGD-associated biopsies showed a significant overrepresentation of chronic inflammation, granulomata, multinucleated giant cells, histiocytes, and necrosis, while granulation tissue, remodeled bone, and lymphocytes were notably underrepresented. Importantly, failure to isolate an organism does not exclude infection, as low-grade pathogens can drive immunopathology in CGD, potentially improving with immune modulation.[7]

Metagenomic next-generation sequencing (mNGS) is an emerging molecular technique that has garnered increasing attention, particularly in the fields of bacteriology and virology. In a recent study involving 108 patients who underwent CT-guided lung biopsy, Yang et al.[30] conducted both mNGS and histopathological analysis on lung biopsy tissue. Their findings demonstrated that the combined use of mNGS and histopathology was significantly more effective in detecting and identifying infectious diseases compared to histopathology alone. mNGS is becoming increasingly promising in the diagnosis of IA, owing to its capability to identify rare fungal pathogens and characterize antifungal resistance mechanisms. Recent retrospective studies have indicated that integrating mNGS with conventional diagnostic methods improves sensitivity for detecting IA in both neutropenic and non-neutropenic patients.[31]

Nevertheless, several challenges associated with mNGS remain unresolved. One key issue is the potential for microbial contamination from samples, reagents, or laboratory equipment, which can complicate data analysis and interpretation, underscoring the need for rigorous quality control. Additionally, the establishment of well-defined reference standards and controls is crucial to ensure consistent quality and reliability over time. Another challenge with untargeted mNGS is the high proportion of host DNA in clinical samples, which can exceed 99% of sequence reads and reduce analytical sensitivity. While targeted sequencing can address this problem, it may introduce bias. Furthermore, the absence of user-friendly bioinformatics tools for analyzing fungal mNGS data presents an additional obstacle.[32] More research is required to evaluate the utility of mNGS in diagnosis of IA and in patients with suspected IA and CGD.

Treatment of Invasive Aspergillosis

The treatment recommendations of IA in CGD patients are derived from patients with haematologic malignancies as no studies have been performed in CGD patients.[18] The guidelines recommend intravenous voriconazole as first line treatment of IA in children above 2 years of age.[18,33] Its

activity against both *A. fumigatus* and *A. nidulans*, the most common fungal pathogens observed in CGD, and good CNS penetration are favorable in patients with CGD.[8]

Clinicians should be cautious while using voriconazole for short and long-term side-effects including general-azole related side effects such as hepatotoxicity, nausea and vomiting, and QTc interval prolongation. Voriconazole specific side effects may include neurological symptoms (e.g. hallucinations, abnormal dreams, confusion, hypoesthesia, neuropathy, and paraesthesia), visual disturbances, solar hypersensitivity and increased risk of skin malignancy.[34]

TDM of voriconazole is recommended to ensure sufficient exposures associated with clinical efficacy and to prevent high exposures associated with neurological side effects.[18,34] A plasma trough concentration of 1–5.5 mg/L is considered adequate for most patients receiving voriconazole treatment. However, a trough of >2 mg/L is recommended in patients treated for severe infections affecting sanctuary sites (e.g CNS infections) or infections caused by species with elevated MICs.[33]

Notably *A. nidulans* is commonly resistant to amphotericin B, which should be considered in the empirical treatment of IA in patients with CGD.[18]

Isavuconazole is another recommended first-line treatment agent in adults with IA.[33] While current IA guidelines do not include its use in with IA, multiple studies including a phase-2 clinical trial demonstrating isavuconazole is safe and efficacious in children consistent with adult outcomes.[35,36] Case reports have also documented successful use of isavuconazole in both adult and paediatric patients with CGD.[36]

As mentioned in the diagnosis section, every effort should be made to obtain a causative diagnosis with identification of the *Aspergillus* species and antifungal susceptibility testing to guide the clinician to choose the optimal antifungal regimen.[8,18]

Along with antifungal therapy, combination with early and extensive surgical debridement commonly is used in patients with CGD.[6,8,11,15] This combined approach not only facilitates pathogen identification through biopsy and effective source control but also significantly reduces the risk of relapse. In a review by Gamaletsou et al.,[27] patients with *Aspergillus* ostemyelitis who received both antifungal treatment and surgical management exhibited a significantly lower relapse rate compared to those treated with medical therapy alone (8% vs. 30%, p=0.006).

Another adjuntive strategy for managing IA in patients with CGD is the use of immunomodulatory therapies to either dampen the hyperinflammation or improve antifungal activity.[8,16,37] Corticosteroids, particularly in the treatment of mulch pneumonitis, have been administered alongside antifungal agents with reported benefit.[8,12,13] Another salvage strategy is granulocyte infusion, though its efficacy remains poorly documented and is particularly uncertain in patients who develop alloimmunisation. This is especially relevant for those eligible for hematopoietic stem cell transplantation, as alloimmunisation can complicate subsequent treatment by increasing the risk of graft rejection or prolonged neutropenia.[8,37] Additionally, immunomodulatory agents such as hydroxychloroquine, thalidomide, and anakinra have been reported anecdotally to provide benefit in this setting.[8]

Haematopoetic Stem Cell Transplant in Invasive Aspergillosis Setting

Allogeneic Haematopoetic Stem Cell Transplant (HSCT) is a curative treatment option for CGD, with numerous studies supporting its early implementation in patients with CGD to improve outcomes.[38] As an alternative therapeutic strategy, several gene therapy approaches are currently under investigation. Notably, in 2020, the FDA approved lentiviral gene therapy for patients with XL-CGD, marking a significant advancement in the field.[39]

Traditionally, the standard practice has been to perform HSCT in patients with CGD only when mould infections are completely resolved or well controlled. However, a recent study by Kline et al.,[40] which evaluated 26 CGD patients with proven mold infections (13 with progressive mold infections and 14 with aspergillosis), reported promising outcomes, with a 69% survival rate following HSCT. The only exception was a patient with chronic *Aspergillus felis* infection, in whom the disease progressed despite adequate neutrophil engraftment and myeloid chimerism. The improved outcomes may be explained by the ability of corrected phagocytes from HSCT to effectively clear the fungal infection with resolving of the granulomas.[17] Moreover, various studies suggest that HSCT is both feasible and effective even in CGD patients with progressive IA, challenging the previous conservative approach and expanding the potential applicability of HSCT in this population.[17,40]

Conclusion

Management of patients with CGD requires meticulous care and should be handled by an experienced team of immunologists and infectious diseases specialists amongst others in specialized centers. To improve outcomes of IA in patients with CGD, every effort should be made to obtain

an appropriate diagnostic sample to facilitate a causative diagnosis and targeted treatment. A multidisciplinary approach is essential for managing IA in CGD patients, involving expertise from infectious diseases, microbiology, radiology, and pathology.

Ethics Committee Approval: Ethical approval was not required for this study since this is a review article.

Conflict of Interest: Z.E. has nothing to declare. A.W. is supported by the Medical Research Council Centre for Medical Mycology (MR/N006364/2) and the NIHR Exeter Biomedical Research Centre (NIHR 203320). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Financial Disclosure: The authors declared that this study has received no financial support.

Use of AI for Writing Assistance: The authors declared that artificial intelligence (AI) supported technologies were not used in the study.

Authorship Contributions: Concept: ZE, AW; Design: ZE, AW; Supervision: AW; Materials: ZE; Data Collection or Processing: ZE; Analysis or Interpretation: AW; Literature Search: ZE; Writing: ZE; Critical Reviews: AW.

Peer-review: Double blind peer-reviewed.

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