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State of Medical Mycology at German Academic Medical Centres: A Survey of the German-Speaking Mycological Society (DMYKG) and the Paul-Ehrlich-Society for Chemotherapy (PEG)

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Abstract

Background: Little is known about the infrastructure to translate advances in the management of patients at risk to develop invasive opportunistic fungal diseases. To assess the current state of Medical Mycology support in Germany, we conducted a survey among all 36 academic medical centres.

Methods: The survey consisted of a 3-pages questionnaire sent out in the first half of 2019. Information included details of infrastructure, education and teaching; consultation services and interdisciplinary conferences; research activities and participation in network groups; radiology, microbiology and pharmacology support; publication activity; and European Confederation for Medical Mycology (ECMM) Excellence Center designation, if assigned.

Results: Information was returned from 24 centres (67%). Thirteen institutions (54%) reported an independent infectious disease, and two a separate Medical Mycology department (8%); a Medical Mycology working group was reported for nine institutions

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(38%). An infectious disease consultation service was existent in 16 institutions (67%) and a multidisciplinary conference in 13 (54%). Fifteen institutions reported a separate study office with activities in infectious disease studies (63%). Laboratory capability for fungal identification and susceptibility testing was confirmed by all 24 institutions; testing of galactomannan by 23 (96%), cryptococcal antigen by 21 (88%), ß-D-Glucan by 9 (38%), and panfungal and *Pneumocystis* PCR by 21 and 22 (88% and 92%), respectively. Therapeutic drug monitoring of voriconazole was reported to be available in 15 (63%) institutions with a turnaround of \leq 24 h during weekdays in 10 (42%). Two of the 24 University hospitals (8%) reported ECMM Diamond Excellence Status.

Conclusions: The results of this survey document the continuing need to improve the availability of specialised Medical Mycology support in German academic medical centres.

KEYWORDS infections, mycoses, patient care, research, teaching

1 | INTRODUCTION

Invasive opportunistic fungal diseases have emerged as important cause of morbidity and mortality in immunocompromised and severely ill patient populations¹ with an estimated annual incidence of between 18,000 and 36,000 cases in the German population.² The situation is further aggravated by the increasing occurrence of resistance in important fungal pathogens and the global spread of a new fungal pathogen, Candida auris.³ During the past two decades, considerable advances have been made in our general understanding of fungal pathogens and in the prevention, diagnosis and treatment of invasive fungal diseases.³ Apart from an increased knowledge of fungal biology, the human mycobiome and the interactions with the human host, several new antifungal agents have been developed with approved indications for treatment and for prophylaxis in high-risk patients.³⁻⁶ Refined imaging methods and antigen- and molecular-based laboratory diagnostics have become available for diagnosis and response evaluation,⁷ and definitions of fungal diseases and response criteria in clinical trials have been elaborated.^{8,9} At the same time, through the initiative of leading international societies, guidelines have been developed on the diagnosis, treatment and prevention of nearly all forms opportunistic invasive fungal diseases, 10-12 and there is an overall greater awareness of the issue of fungal infections as evidenced by the emergence of major public support groups¹³ and the recognition of fungal diseases by the World Health Organization (WHO) as a worldwide threat to human health and physical well-being.¹⁴

However, given all the progress made in recent years, little is known about the currently existing infrastructure to translate these advances to the benefit of patients. In order to explore the current state of Medical Mycology support in Germany, we conducted a standardised survey among all 36 German academic University Medical Centers.

2 | METHODS

The survey was conceived by the leadership of German-Speaking Mycological Society (DMYKG)¹⁵ and the Section of Antifungal Chemotherapy of the Paul-Ehrlich-Society for Chemotherapy (PEG)¹⁶ at a think-tank meeting conducted in Berlin upon invitation of the German Consiliary Laboratory for Cryptococcosis and Rare Systemic Mycoses located at the Robert Koch Institute (RKI).¹⁷ The aim of this meeting was to define the state of laboratory-based fungal diagnostics in Germany, and to discuss existing challenges and perspectives for the future. The survey was developed after the meeting by four participants (AHG, DB, OK and OAC) and reviewed and approved by the leadership of both societies.

German academic medical centres were identified through an Internet search by the listing of the Association of University Medical Centers in Germany.¹⁸ For contact, personally known individuals working at the 36 German University Medical Centers registered at that time in Clinical Microbiology and/or Infectious Diseases and being members of either the PEG and/or the DMYKG were selected. In cases where no contact person could be identified, the website of the respective institution was searched and individuals with responsibilities in both disciplines identified and contacted.

The survey consisted of a three-page structured questionnaire (Table S1) and was sent out by email together with an invitation letter explaining the project and the questionnaire in February 2019. In cases of missing response, contact persons were contacted by telephone as feasible and electronic reminders were sent out up to three times until June. Information from the returned questionnaires was transferred into a central database which was closed in early September 2019. The information collected was restricted to adult medicine and included details of academic infrastructure, education and teaching, consultation services and interdisciplinary conferences, research activities and participation in network groups, 3

RESULTS

Excellence Center designation. Results were extracted from the database and analysed in a descriptive manner. The survey was completed and returned for 24 of the 36 academic medical centres (67%) after a median of two invitations (range, 1-4). Thirteen of the 24 centres (54%) reported the existence of an independent Infectious Disease department, and two that of an independent Medical Mycology department separate from Medical Microbiology (8%); an Infectious Disease and a Medical Mycology working group were reported for 19 and nine institutions (79% and 38%, respectively). With consideration of all adult medicine departments, an Infectious Disease trained Department Head was present in 18 (75%), and some form of an Infectious Disease training program in 16 (67%) centres. An Infectious Disease consultation service was reported by all 24 institutions with availability 24 h on seven days 4

per week in seven (29%), and a telephone hotline and Internet presence devoted to Infectious Diseases were mentioned in 11 and 14 centres (46% and 58%), respectively. Thirteen institutions (54%) had a multidisciplinary Infectious Disease conference regularly scheduled at least once per month (Table 1).

radiology, microbiology and pharmacology support, publication ac-

tivity and European Confederation for Medical Mycology (ECMM)

Research activities in Medical Mycology were stated by 11 institutions (46%; clinical microbiology, n = 6; epidemiology, n = 7; clinical, n = 6; pharmacology, n = 2). Nineteen centres (79%) reported participation in clinical industry-sponsored Infectious Disease research; 12 (50%) had a working cooperation with a Clinical Trial Department (ZKS, Zentrum für klinische Studien) and 15 (63%) had access to support by a clinical study office within their department. Participation in study networks of professional societies was reported by most centres with variable distribution as to the specific medical societies, ranging from 38% to 67%. Local research cooperations included, in descending order, microbiology, basic research, pathology, pharmacology and radiology (58% to 33% of centres, respectively). Eighteen

centres (75%) reported scientific publications in Medical Mycology with a median of 18 publications during the five-year period between 2014 and 2018 (Table 2).

Local, in-house laboratory capability for fungal identification and fungal susceptibility testing (method not specified) offered in most instances by the Medical Microbiology departments was confirmed by all 24 institutions; testing of galactomannan was reported to be available in 23 (96%), of cryptococcal antigen in 21 (88%), of ß-D-Glucan in nine (38%) and of panfungal and Pneumocystis jirovecii PCR in 21 and 22 centres (88% and 92%), respectively. Therapeutic drug monitoring (TDM) of voriconazole was available in 15 (63%) institutions with a turnaround of \leq 24 h during weekdays in 10 (42%). In-house capacities for computed tomography (CT) and magnetic resonance imaging (MRI) were stated to be existent in all but one institution. Two of the 24 University medical centres (8%; one centre with a separate Medical Mycology department) reported ECMM Diamond Excellence status (Table 3).

DISCUSSION AND CONCLUSIONS

Considering the limitations inherent to data capture by means of a questionnaire and the coverage of only two thirds of the existing academic University Medical Centers, the results of this survey show the inconsistent establishment of Infectious Disease departments and Training Programs at German University Medical Centers, a low number of specialised Medical Mycology departments, but an encouraging number of clinical or laboratory-based Medical Mycology working groups with research activities in this field. While Infectious Disease consultation services seem to exist in all institutions, their continuous availability is limited similar to the frequency of regularly scheduled multidisciplinary Infectious Disease conferences. Along with the advent of matrix-assisted laser desorption/ionisation timeof-flight mass spectrometry (MALDI-TOF-MS), identification of fungal pathogens with subsequent susceptibility testing are available at all institutions, and modern antigen- and molecular-based laboratory diagnostic and appropriate imaging studies in the majority of them.

TABLE 1 Institutional structure, training, consultation service and conferences in the 24 centres

	Number (n) ^a	%
Infectious Disease Department	13	54
Medical Mycology Department	2	8
Infectious Disease Working Group	19	79
Medical Mycology Working Group	9	38
Infectious Disease- trained Department Head	18	75
Infectious Disease Training Program offered	16	67
Infectious Disease consultation service	24	100
24 h/7 days	7	29
Telephone hotline	11	46
Internet presence	14	58
Multidisciplinary Infectious Disease conference	13	54

^afor analysis, a response of 'no' and 'unknown' was considered as one category.

TABLE 2 Mycology research activities, clinical trial infrastructure, participation in study networks and local project cooperations in the 24 centres

	Number (n) ^a	%
Mycological research activities (clinical/ laboratory)	11	46
Industry-sponsored infectious disease research	19	79
Cooperation with Clinical Research Department ^b	12	50
Access to a departmental study office	15	63
Participation in study networks		
DMYKG	11	46
PEG	11	46
ECMM	9	38
Fungiscope [®] registry	16	67
AGIHO	11	46
Local research cooperations:		
Microbiology	14	58
Pharmacology	9	38
Pathology	10	42
Radiology	8	33
Basic research	11	46
Publications in Medical Mycology 2014-2018	18	75%
	Median 19, R 1-130	

Abbreviations: AGIHO, Working Group Infections in Hematology and Oncology by the German Society for Hematology and Oncology (DGHO); DMYKG, German-speaking Mycological Society; ECMM, European Congregation for Medical Mycology; PEG, Paul-Ehrlich Society for Chemotherapy.

^afor analysis, a response of 'no' and 'unknown' was considered as one category.

^bZentrum für Klinische Studien (ZKS).

Nevertheless, there are apparent deficits in the availability and practical usefulness of TDM that is strongly recommended during treatment with certain antifungal agents.

Although the fact that the questionnaire was not returned for all centres limits the validity of the data, a final response rate of 67% is quite acceptable for a voluntary survey¹⁹ and it remains open whether no response after three reminders reflects disinterest in the topic, lack of time, information overflow or selective networking. Further limitations of the study were the lack of inclusion of paediatric medicine and unavoidable, no consideration of structural changes potentially implemented after 2019 in the wake of the COVID-19 pandemic.

Despite all potential limitations, the results of the survey indicate the continuing need to strengthen Infectious Disease in German academic medicine and to improve the availability of multidisciplinary expert mycological support.^{20,21} Diagnosis, management and control of Infectious Diseases are not limited to laboratory diagnostics, TABLE 3Diagnostic laboratory and further diagnosticcapabilities in the 24 centres

	Number (n) ^a	%
Fungal identification and resistance testing	24	100
Galactomannan antigen	23	96
Cryptococcal antigen	21	88
Beta-D-Glucan	9	38
Panfungal PCR	21	88
Pneumocystis PCR	22	92
Pneumocystis IFT	16	67
TDM of voriconazole available	15	63
turnaround of ≤24 h during weekdays	10	42
CT/MRI capabilities in-house	23	96
Designation as ECMM Center	2	8

Abbreviations: CT, computed tomography; ECMM, European Congregation for Medical Mycology; IFT, immunofluorescence test; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; TDM, therapeutic drug monitoring.

^afor analysis, a response of 'no' and 'unknown' was considered as one category.

hospital hygiene and antimicrobial stewardship measures but requires a holistic multidisciplinary approach delivered by a physician that has direct patient contact and responsibility. As stated by others, strengthening academic Infectious Diseases in Germany requires the long-overdue formal establishment of a subspecialty of Infectious Diseases in Internal Medicine and Pediatrics by the Federal Chamber of Physicians and the creation of academic positions in University Medicine to bolster research and teaching.²² In this respect, we are pleased to communicate that, as a first and essential step, the Federal Chamber of Physician has approved a separate 72 months specialty training in internal medicine and Infectious Diseases at its 124th Annual Meeting from 4 May to 5 May 2021.²³

Apart from stronger support and recognition of the National Reference Centers at the Leibniz Institute for Natural Product Research and Infection Biology and the University of Würzburg, as well as the two consiliary laboratories at the Robert Koch Institute and the Charite University Berlin^{17,24,25} and strengthening the networking among experts, current avenues to enhance Medical Mycology support for academic centres and patients include the ongoing ECMM initiative to elaborate guidelines for diagnosis and management of fungal diseases, the creation of formally audited ECMM Excellence Centers and the ECMM Expert Consultation Service for medical centres.^{10,26,27} It is to be hoped that these initiatives will lead to improved delivery of Medical Mycology support and ultimately, improved prevention and management of invasive fungal diseases in immunocompromised and severely ill patients.

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CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

Andreas H. Groll: Conceptualization (lead); Data curation (lead); Formal analysis (lead); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Resources (lead); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (lead); Writing-review & editing (equal). Kathrin Gordon: Conceptualization (equal); Data curation (supporting); Formal analysis (supporting); Funding acquisition (equal); Investigation (equal); Methodology (equal); Project administration (lead); Resources (equal); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (supporting); Writing-review & editing (supporting). Dieter Buchheidt: Conceptualization (supporting); Data curation (supporting); Formal analysis (supporting); Investigation (supporting); Methodology (supporting); Validation (supporting); Writing-review & editing (supporting). Birgit Willinger: Conceptualization (supporting); Data curation (supporting); Formal analysis (supporting); Investigation (supporting); Methodology (supporting); Validation (supporting); Writing-review & editing (supporting). Werner J. Heinz: Conceptualization (supporting); Data curation (supporting); Formal analysis (supporting); Investigation (supporting); Methodology (supporting); Validation (supporting); Writing-review & editing (supporting). Oliver Kurzai: Conceptualization (supporting); Data curation (supporting); Formal analysis (supporting); Investigation (supporting); Methodology (supporting); Validation (supporting); Writing-review & editing (supporting). Volker Rickerts: Conceptualization (lead); Data curation (supporting); Formal analysis (supporting); Investigation (supporting); Methodology (supporting);

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DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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