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Managing Taxonomic Difficulties in Medically Significant Fungi: Suggestions for Validation and Stability

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RESEARCH ARTICLE

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Abstract: The swift alterations in names of medicinally significant fungi are posing difficulties for clinical laboratories and healthcare professionals who provide treatment to patients. We outline two different types of name change, one at the species level and the other at the genus level, with distinct motivations. To lessen the frequency of name changes, several recommendations are presented here. For taxonomic novelties, we implore taxonomists to supply diagnostic indicators. We support maintaining genera at the greatest size feasible because of the instability of phylogenetic trees caused by variable taxon sampling. It is advisable to provide the name of the main species as well as the molecular sister, which is sometimes a cryptic species, when reporting identified species in complexes or series. An open access online database is necessary since it will be impossible to avoid using different names for the same species for a long time. It is imperative to have an online database with full names of all fungi that are significant to medicine, complete with synonymy and appropriate nomenclatural designations. We further suggest that, as taxonomic discovery progresses, clinical laboratories' and physicians' adoption of new name changes be routinely reviewed by a standing committee for validation and stability over time, with reference to an open access database that transparently lists the reasons for changes.

Keywords: Synonymy, Nomenclatural stability, Taxonomic validation, Taxon sampling

Introduction

Creation of the contemporary medical mycology naming system Microbial taxonomy has been completely transformed by cutting-edge and cutting-edge diagnostic and research techniques, especially nucleic acid sequencing. Given that the names of the recently recognised entities are closely associated with changes in the Tree of Life,

 It is inevitable that things will change. This is a universal occurrence in microbial taxonomy and is the outcome of scientific advancement. Taxa within the kingdom Fungi that were formerly distinguished by their physical characteristics or physiological traits are now being recharacterized based on the sequencing information that supports their evolutionary locations. Contrary to the majority of prokaryotic bacteria, fungus feature a variety of distinctive phenotypic traits that have been used over millennia to compile clinical data. Numerous fungi have a complex life cycle, consisting of one or more asexual and sexual sporulation forms with highly varied appearances and growing requirements. Previously, it was frequently unknown that these various forms, or morphs, were members of the same species. The creation of a naming system with two distinct categories—one for the sexual

morph (teleomorph) and one or more for each asexual morph—helped to overcome this issue (anamorph). Since asexual morphs frequently predominate in vitro and in animal hosts, and sexuality is mostly exhibited in the environment, the relationship between two or more living forms has remained unclear despite the growing amount of DNA material available, pending experimental confirmation. Above the species level, taxonomic groupings were determined by the sexual the distinct system for asexual ones was widely accepted to be artificial, even though some writers even revealed the names of families and even higher ranks based entirely on asexual morphs. morph and prioritised. Giving up on the information accumulated over 270 years of mycological research under this "old" nomenclature system is more difficult than in other research domains, notwithstanding its imperfections. This is because the old nomenclature is closely related to patient management.

Molecular taxonomy's drawbacks and obstacles for therapeutically significant fungus

The system of having two names grew less and less relevant as non-microscopic techniques like as DNA sequencing were developed and could definitively establish species. Following a symposium titled "One Fungus One Name" in Amsterdam in 2011 and nearly two decades of intense debate, many members of the mycological community reached a consensus to forgo the traditional practise of naming distinct morphs of the same species separately, a move known as the "Amsterdam Declaration". This new strategy was then formally suggested during the "Rooor" debate by Redhead, contested, and ultimately accepted by the world community in the 2011 International Botanical Congress in Melbourne. The modification took effect in 2011 and applied retroactively. As opposed to phenotypic characterisation, this allowed for a more accurate portrayal of the natural system. But since the asexual-based artificial system contained many of the names used in medical and veterinary mycology, a completely different approach to systematisation was required. Through protected lists of names created by working groups under the direction of the International Commission on the Taxonomy of Fungi, formal procedures were adopted to limit the amount of revisions.Few names among the medical fungi remain unaffected by the subsequent substantial name alterations that result from the combined transition toward molecular phylogeny and priority of the oldest name regardless of sexual states. Of the names authorised in 2020, only thirty percent were still used in the same sense as in 2000 when comparing the second and fourth editions of the Atlas of Clinical Fungi.

This indicates that molecular taxonomy has had a greater influence on medical mycology than on any other field of clinical microbiology practise. Many writers have voiced their worries with the rate of nomenclature changes in mycology and have offered lists of suggested names that are mainly focused on the species level. Other authors, however, have suggested accepting and implementing changes to generic names. The goal of the current research is to counteract some of these unfavourable changes with ideas that we believe are workable and will not significantly impede scientific progress. Undoubtedly, renaming medicinally significant fungus need a significant overhaul.

Grand subdivisions based on antiquated morphological criteria are found in many historical handbooks and guidelines. Examples of these include the family name "Dematiaceae," which designates fungi with large conidia and conidiophores that carry melanin in their cell walls, and the class rank name "Coelomycetes," which designates fungi that form asexual cup- or ^ask-like spore-bearing structures at any point in their asexual life cycle. Major advancements in the logical coherence between taxonomic categories have been made possible by molecular phylogeny and have

improved our knowledge of the origins, relationships, and characteristics of fungi, including their propensity to create mycotoxin or be pathogens of concern. Such possibly common ecological strategies between species are clarified by phylogeny.

Stakeholders in the medical community readily accept name changes when there are clear advantages to the new naming scheme. One instance of an easy adoption is the separation of the purely saprobic Penicillium species from the internal pathogen Talaromyces marne^ei. Limited resistance was also reported when dermatophytes were naturally classified. Another example is the division of fungi into distinct genera, such as Geotrichum/Trichosporon and Sporothrix/Quambalaria, despite their physical similarity and extreme phylogenetically remote relationship (i.e., ascomycetous versus basidiomycetous).

A more recent instance is the genus name Phialemoniopsis/Phialemonium was replaced with Thyridium, which was really the name formerly assigned to the sexual morph. Nevertheless, a straightforward statement is insufficient to restore the proper systematic order of tens of thousands of fungalnames, and obtaining genetic data can be challenging in certain fungal species. The aforementioned, widelyrecognised examples all apply a comprehensive, biological approach to taxonomy, showing that the recently split groups differ fundamentally in terms of life cycle, habitat preference, and clinically significant parameters, with molecular phylogeny serving as a supporting element to enable definitive identifications. This illustrates the best method for achieving significant taxonomic name changes in mycology. On the other hand,Opposition to change is almost always found in situations where the group being changed is comparatively homogeneous, with no discernible character differences, and is split solely on the basis of phylogeny. One instance is the reorganisation of the 20 ecologically related genera Curvularia and Bipolaris, where the molecular barcoding did not match the multi-character phenotypic distinction. On the other hand, Chaetomium species were placed in a number of new genera. These rearrangements were made by the latter study using a data set that only included strains from indoor settings, suggesting that factors other than phylogeny were not significant; Consideration of such circumstances ought to be given to a larger range of listed species and ecologies. We support deliberate and cautious naming modifications for medically significant fungus to lessen the possibility of misunderstanding among those in charge of patient care. Only when name modifications are founded on fundamental differences that have shaped evolution and have therapeutic relevance will they be effective and widely applied. The division of a species and the reorganisation and splitting of genera are two distinct drivers of diversity. These drivers account for the two levels of diversity: that of the species and that of the genus.

Diversity of species: The fragmenting term

In biology, there are over thirty different species concepts used, and it's not always clear where one species ends and another begins . It is impossible to directly comprehend microbes using conventional biological notions. There is a range of circumstances that can cause variations in the genetic composition and viability of children, ranging from 0% to 100%. Because sexually hyperactive strains of some plant pathogenic fungi are able to couple outside of established species boundaries, they are recognised as having undergone hybridization in cases where hybrid nomenclature has been introduced. Nevertheless, progeny may not experience genetic recombination. It could produce infertile hybrids that can't mate. Crosses that seem to be sexual but may actually be uniparental serve as evidence that fungus can reproduce asexually over extended periods of time.

Many fungi have sexual strategies that do not require a partner who is opposite you.

Ideally, genetic interaction is the primary source of genetic variation within a species. Nevertheless, most fungi reproduce certain phases of their life cycle through cloning, hence increasing the number of functional genotypes. Asexual reproduction might be predominating, and sexuality is still frequently unclear. The species divides into many molecular siblings due to its nearly total lack of sexuality. Sibling recognition in fungal taxonomy is predicated on differences in barcoding locus regions, such as CAM, rDNA ITS regions, rPB1, rPB2, TEF1, or TUB2 (BenA). Genetic concordance allows for the in silico detection of sexual recombination and provides an operational benchmark for verifying the species border. On the other hand, taxonomists who work with large data sets usually employ concatenated barcoding sequences to determine molecular distances judged sufficient for defining novel species. In the case of Cladosporium and Fusarium, for example, multiple siblings were discovered based on the genes analysed. These siblings were identified as 54 in the C. cladosporioides complex and 74 in the F. fujikuroi complex, respectively. Following the horizontal gene transfer of pathogenicity islands, plant diseases can undergo clonal development, giving rise to lineages that are sometimes referred to as special forms.

Consequently, there is a greater chance that these novel genotypes may be detected by sampling, leading to the false belief that host adaptation is necessary. However, it is possible for the species to infect a different susceptible host due to redundant horizontally transferred accessory chromosomes. This is the case with Fusarium musae, the pathogen that infects banana fruits, which has been connected to human infections and has sparked worries about its possible health effects. There is a correlation between reduced sexuality and more clonal diversity.Clinical fungi known as "dermatophytes" lose their sexuality as they adapt to live in humans and show differential mating type evolution. However, several genotypes without ecological or clinical distinction may emerge within a single species.

Consequently, phylogenetic distance by itself within a particular gene region is not necessarily a sufficient criterion for the designation of new species. Clone distinction based only on molecular variations is essential for determining infection pathways and sources of contamination as well as providing answers to epidemiological questions. However, speciation is a slow process that ultimately leads to the loss of the capacity for recombination because of minute variations in the ecological preferences of future separators. Many barcoding markers lack unique traits that are important to evolution and are only proxies for significant variations found elsewhere in the genome. They are also not transcribed. The more genes added, the more stable the tree should be. A species is made up of several genetically different lineages that are getting harder and harder to recombine and produce viable progeny. In contrast to the phenotypic method, molecular data make it possible to identify each lineage. Rather than using the word "species," the term "species complex" has gained favour. Unknown gene flow connects molecular siblings in a complex under one roof. For most fungal families, the idea of sibling hybridization and recombination has not been explored.Nontranscribed marker multilocus analysis indicates almost unlimited potential variability. The distinct names assigned to the several lineages demonstrate the strong relation to the classical species of the aggregate.

Ideas for maintaining the consistency of species names in medicinal mycology

Taxonomy and epidemiology should be kept apart in light of the previously mentioned division of species into named molecular siblings and to

maintain the stability of species designations. Microbiological variety and overlap are involved in both taxonomy and epidemiology because species are distinguished from difficult-to-determine genetic differentiation within intraspecies lineages. There will be many disputed cases and rules of botanical nomenclature, such as those pertaining to typification, that need to be reviewed in retrospect. Furthermore, the field of medical mycology only makes up a very small portion of research on biodiversity worldwide. Attempts to impose medical guidelines on the considerably larger study fields of agriculture, ecology, industry, and the fungal kingdom are fruitless. Rather,

To ensure the stability of species names and account for the previously mentioned fragmentation of species into named molecular siblings, taxonomy and epidemiology must be kept apart. Since species are differentiated from intraspecies lineages by difficult-to-determine genetic separation, taxonomy and epidemiology both require microbial diversity and overlap. Many disputed situations may arise, and rules governing botanical nomenclature, such as those pertaining to typification, must be reviewed in hindsight. Attempts to impose medical criteria on the far wider study fields in agriculture, ecology, and industry, which involve the entire fungal kingdom, are fruitless, as medical mycology covers just a very small portion of global biodiversity studies. Rather,

Since species are divided into named molecular siblings as previously said, taxonomy and epidemiology should be kept apart to ensure the integrity of species names. Since it is difficult to demonstrate genetic distinction between intraspecies lineages, which distinguishes species, both taxonomy and epidemiology include microbial diversity and overlap. Plant nomenclature rules, like those pertaining to typification, must be reviewed in retrospect, and there will be many disputed situations. Furthermore, research on medicinal mycology only makes up a very small portion of the world's biodiversity studies. It is therefore fruitless to try and impose medical guidelines on the much bigger study fields of agriculture, ecology, and industry, which encompass the entire fungal kingdom. Rather,

Creating phylogenetic trees is now the almost sole method used to determine the position and size of taxa. Nonetheless, because phylogenetic trees are inherently relative and rely on the mutual comparison of their members, they suffer from inherent instability during the early stages of molecular exploration. This is because they typically use a small number of barcoding gene regions for diagnostic purposes rather than taxonomy. Despite the great level of sophistication of tree reconstruction techniques, variation arises with each selection of items in the tree due to the underlying taxon sampling effect. In well-known groups with a lengthy research history, sampling may be rather comprehensive. When determining the position and size of genera, the construction of phylogenetic trees has almost entirely replaced other methods. Nevertheless, due to their inherent instability during the early stages of molecular exploration and their fundamentally relative nature (based on the mutual comparison of its members and typically utilizing small numbers of barcoding gene regions for diagnostic rather than taxonomy), phylogenetic trees suffer from this. Even with extremely complex tree reconstruction techniques, variations arise with each choice of items within the tree due to the underlying taxon sampling effect. In well-known organizations with an extensive research background, sampling may be fairly complete.

When such clades are rearranged, new genera must be created; tiny genera with a small number of species are therefore very vulnerable to further fragmentation. For instance, the names Microascus and Scopulariopsis are now used for two groups that are molecularly distinct, with the small genus Pithoascus lying between the clades that contain the

type species of the two genera. Previously, the names were used to denote asexual or sexual behavior, respectively. The new ideas' phenotypic descriptions of Microascus and Scopulariopsis are almost the same. In this situation, it might have been more practical to synonymize Pithoascus with Microascus, the oldest genus name, which would have only required a few name changes for an uncommon fungus. Another instance is the previously discussed split between Curvularia and Bipolaris, wherein the usual traits were not supported by the phylogeny. Manamgoda et al. reshuffled species of both genera based on phylogeny, but a more frugal approach would have been to acknowledge that the bipartition appears to be nonexistent and provide preference to the single genus name Curvularia.

On the other hand, since its creation in 1809, the huge genus Aspergillus—which is distinguished by its distinctive conidiophores—has been acknowledged as a group and currently consists of numerous smaller clades. Although the genus is monophyletic, there are significantly greater distances than typical between the ultimate members of the genus clade. Furthermore, fungus lacking the distinctive aspergillus-like conidiophores may seem to share genotypes, which could result in the fusion of Aspergillus with certain species (such Phialosimplex and Polypaecilum). Smaller genera are covered by broader generic circumscriptions; as a result, genera tend to grow rather than disintegrate. As long as the taxa are monophyletic, it may generally be nomenclaturally advantageous to retain wide generic notions for taxa like Aspergillus, Chaetomium, and Fusarium in their classical sense. Although smaller genera will appear synonymous, there will often be fewer name modifications as a result.

The majority of traditional genera in yeasts are not monophyletic. The genus in the conventional sense is therefore problematic since the physiologically significant genera that have been classified in Candida on the basis of phylogenetically determined to belong to eight families. Some genera, like Debaryomycetaceae, which contains the sole genus Candida, may align with the family ranks as they exist now and maintain future instability within reasonable bounds. When the bootstrap values of the clades are consistently high, there will be a noticeable difference between them. This worked well with the dermatophytes, but statistical evidence for the backbone of trees is sometimes absent or very weak. For instance, several analyses utilizing various genes and data sets have been conducted on the family Herpotrichiellaceae (black yeasts and allies) in Chaetomyriales, but the results have been inadequate statistical support below the family level. Despite the acknowledged conflict with phylogeny, the authors chose to leave the genera defined by morphology.

Temporary nomenclatural stability is achieved, but these genera still exhibit high levels of polyphyletic relationships. Therefore, it is not advisable to handle unrelated species under the same generic did for Exophiala, in the long term. An ideal size for genera might exist. Loss of phylogenetic coherence and recognition ease is a danger associated with extensive divisions that produce unique genera for numerous medically significant species. However, creating diagnostic standards for genera that are overly inclusive can be challenging.

Recommendations to stabilize the genus concept in mycology medicine:

1. In order to ensure that the division of genera is likely to be widely understood and accepted, phenotypic characteristics should be used in addition to molecular distance. These characteristics should reflect the primary ecological and medical significance, evolutionary patterns, or other behavioral trends.

2. Based only on phylogenetic distance, the names of large genera, like Aspergillus, tend to be more

stable than tiny genera with a small number of species; if a genus is monophyletic, it is advised to keep it at its current size unless there is a strong reason to split it up.

3. If combining small, phenotypically similar genera within a clade minimizes the amount of name changes required, then so be it.

4. Writers proposing name modifications at the generic level are asked to offer or choose characteristics that allow the current genus to be identified. Only once the underlying taxonomy has been confirmed in many works by independent authors—and with the support of an evaluation committee under the aegis of ISHAM—are name modifications preferably adopted in ordinary practice.

5. Keep in mind that the Code provides mechanisms to prevent the need to use a conservation process to replace a well-known genus name with a less well-known one. Additionally, the original type species may be changed.

DISCUSSION

It is not a galactic starship working in a vacuum of science that is taxonomy. Conversely, the results of this research are used every day in hundreds of diagnostic laboratories across the globe to improve patient care in all fields of microbiology. There aren't many fundamental science fields with as many applications. Therefore, nomenclatural modifications must to be supported by solid scientific evidence and grounded in phenotypic, biological, and ecological aspects as well as clinically significant pathogenicity traits, particularly patterns of antifungal resistance.

When it comes to dividing genera in the lack of defined scientific standards, the default should be that any suggested reclassification should be advantageous to the clinical user. Over medical mycology, there is a current debate regarding the bipartition of Fusarium between Fusarium s.str. and Neocosmospora. The latter serves as an intriguing example of how generic fragmentation has negative effects. The evolutionary gap between Fusarium and Neocosmospora may support their split, but it requires the preservation of 21 other fusarium-like genera that are phylogenetically closer to Fusarium s. str. than to Neocosmospora.

The medical community does not have to adopt the separation of Neocosmospora right now; this can wait until taxonomists have stabilised the classification through years of research and agreement. Redhead made a similar argument when he suggested reclassifying species that resembled coprinus, saying that we don't have to use these names right once and that we should start off being cautious. The pathogens identified from asexual cultures, Hormographiella aspergillata and H. verticillata, were later synonymized with the mushroom species Coprinopsis cinereus and Coprinellus domesticus, respectively, after molecular testing by various laboratories.

Massive differences below the level of genetic exchange can be seen at the species level, and this is still the gold standard for conspecificity (organisms belonging to the same species). It is rare to assign species classification to interbreeding creatures, despite the fact that this boundary is ill-defined, prone to numerous exceptions, and frequently challenging to establish in research domains beyond microbiology. More items can be separated in a number of groupings than is taxonomically significant. Tang et al. recommended that only siblings who are pertinent to clinical practise be properly named in dermatophytes. For instance, Sklenář et al. synonymized several of the identified taxa in the A. versicolores clade, while Bian et al. did the same for the Aspergillus niger clade.

When the siblings are only distinguishable by experimental, non-microscopic techniques like multi-locus sequencing and have no wider importance, the need to separate a large number of

molecular siblings without clinical relevance would negatively affect clinical practise and patient care.

How should the name of a species be reported? It has been stated that species complex identification is typically sufficient for routine clinical practise, albeit this may vary depending on the particular fungal group or clinical issues. Without knowing that the sibling name belongs to a certain species complex, sequencing or MALDI-ToF MS (Matrix Assisted Laser Desorption/Ionization linked to time-of-flight mass spectrometry) may be able to identify it directly. Since the spectrum database used for comparison may have an impact on MALDI-ToF MS results, it is advised to identify and include the database in the lab report for retrospective study, along with its version number.

In clinical laboratory reports, both the species complex and the sibling should be identified, with the siblings reported either by name or lineage number as relevant, as almost all significant pathogenic species comprise subspecific entities. Thus, reporting would look like this: Trichophyton interdigitale, a member of the T. mentagrophytes species complex, or Trichophyton mentagrophytes species complex in the event that a lineage is unnamed (molecular sibling ITS XIV). The single suggested name is adequate for the many species that do not belong to a complex.

The case of Fusarium/Neocosmospora highlights how, in practise, multiple names may continue in use concurrently for some fungi until phylogenetic disagreements can be addressed, given the lack of clear limits surrounding genus size. This might get really perplexing at times. For instance, Apophysomyces elegans is a totally distinct species from Mucor elegans, which is synonymous with Actinomucor elegans and Rhizopus elegans.

Creating a comprehensive and user-friendly platform where current and historical names can be located and mapped to the species complex they belong to is one way to lessen naming confusion. Open access to a list of currently suggested names for medical fungus can be found nomenclature, which also offers synonyms and species complex affiliation. The database includes a handy search feature and a printable version of the suggested names list. By using the database, clinical reports can avoid using both new and old names.

Under the auspices of the International Society for Human and Animal Mycology (ISHAM), Working Groups on Nomenclature and Fungal Diagnostics, a committee comprising clinical microbiologists, physicians, and medical mycologists has been established. The committee will review, discuss, and decide on names based on their medical relevance, validity, and stability, consulting with experts in the field. Transparency will be ensured by making recommendations public. It is highly recommended that representative strains be deposited in the established collections of fungal cultures for further study.

Conclusion

The essay emphasises the difficulties caused by the quickly changing names of medically significant fungi, which is a result of advancements in research and diagnostic techniques, especially nucleic-acid sequencing. Clinical laboratories and physicians who provide patient care must consider the dynamic nature of taxonomy, particularly when it comes to species and genus classifications. The authors put up doable recommendations to lessen the effects of these modifications and improve the consistency of fungal nomenclature.

The essay highlights the fragmentation of epithets at the species level as a result of the imprecise boundary between species and the occurrence of molecular siblings within species complexes. The authors propose using official nomenclatural categories for closely related things and numbering individual clones and genotypes below the species level in an effort to distinguish taxonomy from

epidemiology. Additionally, they support the inclusion of living cultures in reference collections and the development of standards for characterising closely related species that go beyond phylogenetic distance.

The paper addresses the difficulties in reclassifying fungus at the genus level, where no functional molecular criteria exist, with regard to genus diversity. The authors suggest that, in order to reflect ecological and medicinal value, genera should be classified based on phenotypic traits as well as molecular distance. They advise keeping big genera at their current size, merging smaller, phenotypically related genera, and offering standards for differentiating genera when reclassifying.

The paper highlights the necessity of taxonomic modifications being supported by strong scientific data, taking into account phenotypic, biological, ecological, and therapeutically significant aspects. It proposes the creation of a committee made up of taxonomists, doctors, clinical microbiologists, and medical mycologists to assess proposed name modifications for stability, validity, and medical relevance. Additionally, the authors emphasise how crucial it is for taxonomists and clinical users to stay in constant communication in order to provide a seamless transition throughout nomenclatural modifications.

Practically speaking, the paper suggests that in clinical laboratory results, species names should be included at both the species complex and molecular sibling levels. It recommends making use of an extensive online database, updated and reviewed on a regular basis by a committee, that contains suggested names for medically significant fungus. Although the paper accepts that name changes are inevitable, it recommends using a measured and careful approach to guarantee the stability of fungal nomenclature in the context of clinical uses.

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