Empirical Antimicrobial Data for Bacteria and Yeast

The purpose of this Doctor's Data Inc. (DDI) White Paper is to inform healthcare providers around the world about the antibiogram data compiled during 2022. The White Paper is the result of DDI's antimicrobial stewardship efforts, a series of meetings, feedback from clinical providers, and data collected from our expert microbiology department. DDI is fully committed to supporting and upholding the concepts of Antimicrobial Stewardship. This White Paper reviews antibiotic stewardship and antibiogram data collected during 2022, and provides opportunities for healthcare providers to utilize antibiogram data to aid in clinical decision-making, evaluate antimicrobial resistance trends, understand the process, and highlight DDI's ongoing stewardship efforts.

Antimicrobial Stewardship & Antibiograms

Antimicrobial Stewardship is critical to human health worldwide as resistance to conventional antimicrobial drugs continues to grow and spread. Antimicrobial resistance is evolving more and more rapidly, especially amongst Gram-negative bacteria. Furthermore, the unnecessary use of broad-spectrum agents is contributing to this rise in organisms for which there are fewer and fewer effective treatments. There is an urgent need to improve the use of antimicrobial agents to aid in the appropriate use of these agents to minimize antimicrobial resistance, antimicrobial toxicity, adverse drug reactions, and unintended diseases such as *Clostridioides difficile* toxin disease (1). The establishment of empiric antibiotic recommendations serves to minimize antimicrobial resistance, antimicrobial toxicity, and adverse drug reactions.

Antimicrobial Stewardship is using antimicrobials responsibly—the correct agent, at the right dose, for the right length of time (2). Antimicrobial Stewardship is the effort to measure and improve how antimicrobials are prescribed by clinicians and used by patients. A key part of this process is to understand the resistance patterns in an individual patient and a population. To measure and improve the effectiveness of antimicrobials, DDI has formulated antibiogram data for dysbiotic bacteria and yeast. This antibiogram allows for accurate, reliable, and valid data regarding antimicrobial therapy. Developing an antibiogram as an evidence-based approach realizes antimicrobial stewardship tenants.

Antibiograms are a compilation of antimicrobial susceptibility test results derived directly from patients' bacteria and yeast. The data garnered from the antibiogram is intended to inform treatment decisions regarding directed antimicrobial therapy. Antibiograms are useful as the data allows for identifying and monitoring microbial resistance patterns and they will be updated routinely. Accurate antimicrobial treatment is associated with improved clinical outcomes and is useful for monitoring resistance patterns. An individualized approach to antimicrobials is warranted as there is no "one size fits all" approach.

DDI's Bacteria and Yeast Antibiograms 2022

Methodology

Susceptibility testing. DDI uses the conventional antimicrobial susceptibility testing method known as the Kirby-Bauer method, which has been a standard for decades. In brief, pure cultures of organisms are placed onto solid microbiological media, followed by the application of paper disks containing the antimicrobial agent to be tested. The agent diffuses into the agar plate and inhibits the growth of the test organism. Following incubation of the organism and antimicrobial agent for 18-24 hours, the zone of inhibition around the disk is measured, with smaller zones indicating less susceptibility of the organisms and a larger zone around the disk a more susceptible organism. There are national and international guidelines for interpreting the sizes of the zones to determine susceptibility or resistance to prescriptive agents. In the case of natural agents, we use

the Kirby Bauer method and adapt it to work similarly. This validated method is reported as a range of more to less activity of the natural agent tested. Of note, yeast exists within the human colon in small amounts within normal limits. Sensitivities are provided for yeast that exceeds normal limits as evidenced by a culture of 2+ or greater.

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Antibiogram development. The data comprising these antibiograms were collected from 10,000 samples collected in 2022. Antibiograms usually require culture results for one year to provide statistically valid data for analysis (3). For yeast, breakpoints for prescription agents have been established by global EUCAST (The European Committee on Antimicrobial Susceptibility Testing) guidelines for the prescriptive agents and nystatin. For bacteria and prescriptive agents, breakpoints have been established via CLSI (Clinical Laboratory Standards Institute) guidelines for prescriptive agents. These data are presented as the percentage of all organisms tested that were "susceptible" to that agent. For natural agents, the antibiogram captures the percent of organisms tested that were "highly sensitive".

Results

Figure 1: Bacteria Antibiogram 2022

| | | D | octor's | Data I | BACTER | RIA Ant | tibiogra | am 202 | 22 | | | | | |
|-------------------------------|---|---------------------------------|-------------|-----------|---------------|------------|------------------------------------|--|----------------------------|-----------|--------------|---------------|---------|----------|
| | Prescriptive Agents Percent Susceptible | | | | | | | Natural Agents Percent Highly Sensitive | | | | | | |
| Organism | Ampicillin | Amoxicillin- Clavulanic Acid | Ceftazidime | Cefazolin | Ciprofloxacin | Gentamicin | Sulfamethoxazole / Trimethoprim | Silver | Grapefruit Seed Extract | Berberine | Black Walnut | Caprylic Acid | Oregano | Uva Ursi |
| Aeromonas spp | 0 | 0 | 100 | 0 | 99 | - | 92 | 99 | 100 | 0 | 70 | 80 | 24 | 100 |
| Citrobacter farmeri | 0 | 61 | 99 | 3 | 99 | - | 98 | 94 | 94 | 1 | 8 | 17 | 7 | 100 |
| Citrobacter freundii complex | 0 | 0 | 99 | 0 | 99 | - | 98 | 94 | 95 | 1 | 6 | 25 | 5 | 100 |
| Citrobacter koseri | 0 | 98 | 100 | 97 | 100 | - | 97 | 90 | 92 | 0 | 9 | 23 | 9 | 100 |
| Enterobacter cloacae complex | 0 | 0 | 100 | 0 | 100 | - | 99 | 1 | 94 | 1 | 7 | 32 | 6 | 100 |
| Klebsiella oxytoca | 0 | 98 | 100 | 64 | 100 | - | 99 | 93 | 94 | 2 | 6 | 48 | 6 | 100 |
| Klebsiella pneumoniae | 0 | 98 | 100 | 97 | 99 | - | 97 | 90 | 93 | 4 | 7 | 54 | 8 | 100 |
| Morganella morganii | 0 | 0 | 99 | 0 | 93 | - | 91 | 83 | 94 | 0 | 11 | 16 | 18 | 99 |
| Proteus mirabilis | 91 | 98 | 99 | 86 | 98 | - | 91 | 48 | 93 | 1 | 15 | 28 | 10 | 95 |
| Proteus vulgaris group | 0 | 72 | 99 | 0 | 100 | - | 97 | 56 | 92 | 5 | 17 | 26 | 13 | 98 |
| Providencia alcalifaciens | 0 | 0 | 100 | 0 | 97 | - | 95 | 94 | 94 | 6 | 6 | 14 | 6 | 100 |
| Providencia rettgeri | 0 | 0 | 100 | 0 | 99 | - | 97 | 92 | 95 | 4 | 5 | 43 | 7 | 99 |
| Pseudomonas aeruginosa | - | - | 100 | - | 98 | 97 | 0 | 90 | 94 | 1 | 10 | 10 | 7 | 100 |
| Yersinia enterocolitica group | 0 | 0 | 99 | 0 | 99 | - | 100 | 100 | 100 | 0 | 12 | 50 | 4 | 99 |

Percent Susceptible, CLSI guidelines for prescriptive agents. Percent Highly Sensitive DDI Data for Natural Agents.



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| | | Do | ctor's Da | ta YEAST | Antibio | ogram 20 | 22 | | | | | |
|--|-------------|--------------|------------------------|----------|--|---------------|----------|------------------|---------|----------------------|----------------------------|--|
| | | | tive Agen Susceptib | | Natural Agents Percent Highly Sensitive | | | | | | | |
| Organism | Fluconazole | Itraconazole | Ketoconazole | Nystatin | Berberine | Caprylic Acid | Uva Ursi | Allicin (garlic) | Oregano | Undecyclenic Acid | Grapefruit Seed Extract | |
| Candida albicans | 100 | 90 | 100 | 98 | 38 | 98 | 27 | 2 | 1 | 4 | 100 | |
| Candida colliculosa | 96 | 37 | 95 | 100 | 72 | 99 | 99 | 67 | 60 | 27 | 41 | |
| Candida dubliniensis | 100 | 97 | 100 | 98 | 22 | 100 | 27 | 2 | 2 | 9 | 100 | |
| Candida glabrata | 0 | 59 | 91 | 99 | 87 | 97 | 99 | 3 | 6 | 37 | 98 | |
| Candida guilliermondii | 51 | 7 | 55 | 99 | 13 | 100 | 96 | 7 | 4 | 13 | 99 | |
| Candida holmii | 14 | 14 | 17 | 86 | 24 | 95 | 95 | 69 | 60 | 7 | 21 | |
| Candida inconspicua | 0 | 56 | 78 | 100 | 68 | 100 | 83 | 24 | 17 | 29 | 88 | |
| Candida intermedia | 98 | 81 | 95 | 99 | 25 | 91 | 96 | 22 | 17 | 7 | 84 | |
| Candida krusei | 0 | 21 | 29 | 98 | 98 | 81 | 98 | 3 | 3 | 3 | 99 | |
| Candida lambica | 0 | 16 | 79 | 98 | 66 | 100 | 98 | 90 | 88 | 8 | 9 | |
| Candida lusitaniae | 99 | 88 | 99 | 100 | 2 | 89 | 99 | 0 | 0 | 1 | 99 | |
| Candida metapsilosis | 94 | 85 | 100 | 99 | 76 | 98 | 60 | 3 | 0 | 5 | 99 | |
| Candida orthopsilosis | 95 | 38 | 95 | 98 | 76 | 86 | 64 | 13 | 1 | 1 | 100 | |
| Candida parapsilosis | 99 | 76 | 99 | 98 | 5 | 97 | 48 | 3 | 3 | 1 | 96 | |
| Candida pararugosa | 76 | 79 | 97 | 98 | 6 | 95 | 13 | 3 | 0 | 58 | 97 | |
| Candida pelliculosa | 96 | 35 | 96 | 98 | 16 | 96 | 96 | 12 | 8 | 47 | 92 | |
| Candida tropicalis | 98 | 41 | 99 | 98 | 94 | 68 | 9 | 6 | 0 | 1 | 100 | |
| Candida utilis | 94 | 47 | 97 | 97 | 78 | 91 | 69 | 25 | 13 | 6 | 91 | |
| Candida valida | 15 | 42 | 70 | 98 | 82 | 100 | 94 | 92 | 89 | 8 | 8 | |
| Candida zeylanoides | 97 | 65 | 97 | 100 | 96 | 91 | 96 | 100 | 97 | 4 | 0 | |
| Cryptococcus diffluens | 37 | 27 | 90 | 100 | 12 | 98 | 99 | 12 | 2 | 89 | 98 | |
| Cryptococcus liquefaciens | 10 | 15 | 46 | 97 | 40 | 100 | 97 | 19 | 5 | 90 | 100 | |
| Cryptococcus saitoi | 42 | 32 | 89 | 100 | 30 | 97 | 92 | 14 | 0 | 95 | 100 | |
| Exophiala dermatitidis | 59 | 92 | 86 | 99 | 27 | 99 | 64 | 7 | 4 | 95 | 98 | |
| Geotrichum spp | 49 | 12 | 23 | 98 | 31 | 96 | 94 | 13 | 10 | 21 | 100 | |
| Lodderomyces elongisporus | 95 | 79 | 95 | 100 | 95 | 95 | 44 | 5 | 3 | 3 | 97 | |
| Pichia manshurica | 12 | 75 | 64 | 99 | 95 | 98 | 64 | 20 | 36 | 67 | 85 | |
| Rhodotorula mucilaginosa | 0 | 0 | 93 | 99 | 27 | 100 | 98 | 7 | 2 | 93 | 100 | |
| Saccharomyces cerevisiae/ boulardii | 98 | 20 | 96 | 99 | 65 | 99 | 65 | 56 | 9 | 34 | 50 | |
| Trichosporon spp | 94 | 44 | 51 | 100 | 9 | 88 | 56 | 8 | 7 | 93 | 96 | |

Percent Susceptible, EUCAST guidelines for prescriptive agents and nystatin. Percent Highly Sensitive DDI Data for natural agents.



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The results of these antibiograms may be utilized for individualized medicine in a clinical setting. Equally, the results may be employed to monitor antibiotic resistance patterns.

Conclusion

Alexander Flemming said, "The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organism" (5). If the current trend in the worldwide development of antimicrobial resistance continues, it is predicted that in 2050 deaths due to antibiotic-resistant bacteria will supersede deaths due to cancer (5). There exists an antimicrobial stewardship action to explore direct individualized antimicrobial susceptibility testing. Laboratory tests that offer individualized antimicrobial susceptibility testing for bacteria and fungus is an astute clinical decision that will benefit individuals alongside public health today and in the future.

Microbiology laboratories are needed to contribute reliable antimicrobial data to a scientific consensus regarding the global health threat of antibiotic resistance (4). As a laboratory, DDI is uniquely qualified to contribute data to the scientific community regarding antimicrobial agents as applied to bacteria and yeast. The use of antibiogram data regarding appropriate antimicrobial agents is relevant to both individual and public health as antibiotic resistance threatens human health globally. Antibiograms provide clear and reliable information assisting in guiding clinician selection for empiric antimicrobial therapy leading to improved clinical outcomes. DDI's antibiogram provides a valuable tool addressing antibiotic resistance, antimicrobial stewardship, and guiding antimicrobial therapeutics in clinical settings.

References

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