Pathogen Prevalence Comparison between Cystic Fibrosis Patients with and without Cystic Fibrosis-Related Diabetes

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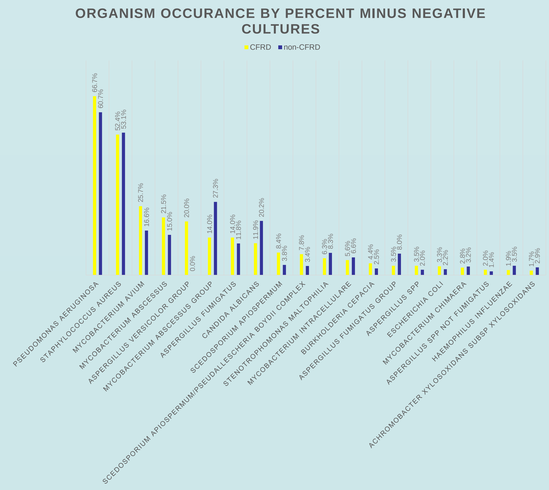
Microbiology Laboratory, National Jewish Health, Denver, CO

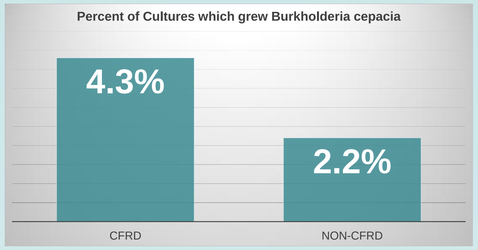
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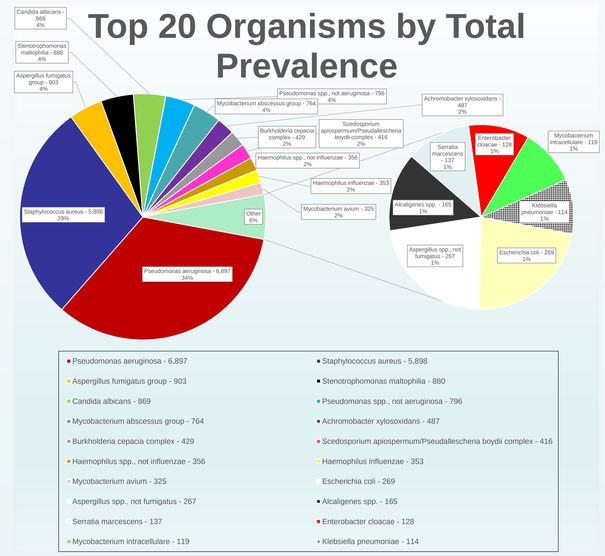
Advanced Diagnostic Laboratories

ABSTRACT

- Chronic respiratory tract infection leading to respiratory failure is the major cause of morbidity and mortality for patients with cystic fibrosis (CF). Pathogens causing infective exacerbations must be treated appropriately to minimize lung function attrition.
- Two distinct patient populations were compared to identify trends in recognized pathogens isolated from lung secretions: CF patients with a diagnosis of CF-related diabetes (CFRD) and CF patients without CFRD.
- Electronic medical records from 2008-2017 were scrutinized, and 4,157 bacterial isolates from 5,324 cultures performed on 88 patients with CFRD were compared to 17,766 isolates from 23,831 cultures from 722 patients without CFRD. Identification of microorganisms was performed using standard clinical microbiology techniques in accordance with guidelines published by the Cystic Fibrosis Foundation in a medical laboratory accredited by the College of American Pathologists.
- Patients with CFRD had a 7% higher probability of having an organism recognized as a respiratory pathogen isolated than patients without CFRD, but CFRD patients had nearly twice the chance of being infected with *Burkholderia cepacia,* the organism often attributed to end-stage CF disease (growth in 4.3% of cultures from CFRD patients vs. growth in 2.2% of cultures from non-CFRD patients).
- The findings from this study raise the question of whether or not the CFRD disease state impacts the probability of a patient becoming infected with *B. cepacia* specifically, and what, if any, are the mechanisms of that process. One possible explanation for these results is the correlation between increasing age and higher prevalence of diabetes and the established evidence that age is usually higher when CF patients become infected with *B. cepacia*. Due to the impact a diagnosis of *B. cepacia* infection has on the CF patient, any factors which impede or promote the growth of that organism will have clinical significance.





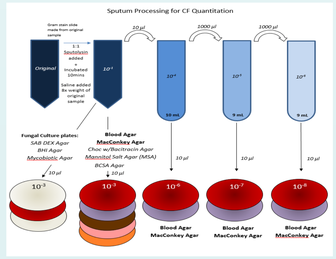


	Diabetic	Non-diabetic	Total
Total Organisms	4157	17766	21923
Total CF Respiratory Cultures	2273	9886	12159
Total Fungal Cultures	1553	6908	8461
Total AFB Cultures	1498	7037	8535

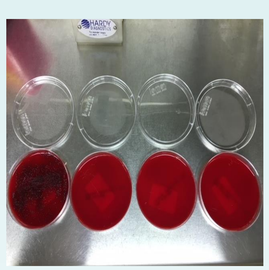
				Percent of Total		
	Diabetic	Non-diabetic	Total	Diabetic	Non-diabetic	Total
Negative CF Respiratory Cultures	60	953	1013	2.6%	9.6%	8.3%
Negative Fungal Cultures	645	3147	3792	41.5%	45.6%	44.8%
Negative AFB Cultures	1284	5410	6694	85.7%	76.9%	78.4%
Positive CF Respiratory Cultures	2213	8933	11146	97.4%	90.4%	91.7%
Positive Fungal Cultures	908	3761	4669	58.5%	54.4%	55.2%
Positive AFB Cultures	214	1627	1841	14.3%	23.1%	21.6%
Patients	88	722	810	10.9%	89.1%	

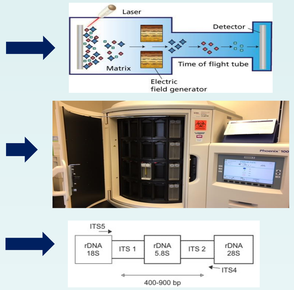
Method:





Specimens were processed using a dilution procedure which allows quantitation of growth using selective and differential agar. Growth was then analyzed by microbiologists using a variety of methods including traditional biochemical, MALDI-TOF, PCR, sequencing, and phenotypic techniques. The methods performed during this study changed with advances in technology and updates to available equipment.



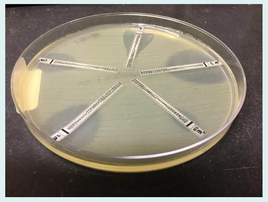


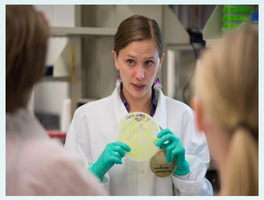
Incidence and Percentages by Organism

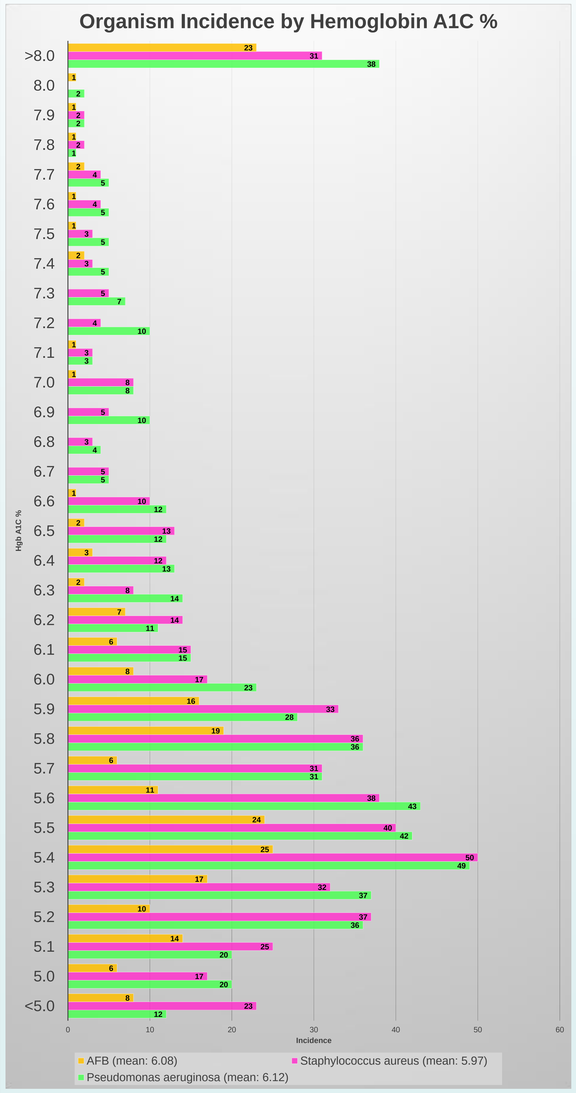
				~Percent of prevalence including negative cultures			~Percent of prevalence excluding negative cultures		
	Diabetic	Non-diabetic	Total	Diabetic	Non-diabetic	Total	Diabetic	Non-diabetic	Total
Bacteria	**3468**	**14344**	**17812**						
Achromobacter xylosoxidans subsp xylosoxidans	38	261	299	1.7%	2.6%	2.5%	1.7%	2.9%	2.7%
Acinetobacter baumannii/hemolyticus	24	62	86	1.1%	0.6%	0.7%	1.1%	0.7%	0.8%
Acinetobacter lwofii	5	20	25	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
Alcaligenes spp	24	141	165	1.1%	1.4%	1.4%	1.1%	1.6%	1.5%
Burkholderia cepacia	97	219	316	4.3%	2.2%	2.6%	4.4%	2.5%	2.8%
Chryseobacterium indologenes	5	29	34	0.2%	0.3%	0.3%	0.2%	0.3%	0.3%
Citrobacter freundii complex	1	46	47	<0.1%	0.5%	0.4%	0.1%	0.5%	0.4%
Enterobacter cloacae	20	108	128	0.9%	1.1%	1.1%	0.9%	1.2%	1.2%
Escherichia coli	74	195	269	3.3%	2.0%	2.2%	3.3%	2.2%	2.4%
Haemophilus influenzae	42	311	353	1.9%	3.2%	2.9%	1.9%	3.5%	3.2%
Haemophilus spp not influenzae	33	180	213	1.5%	1.8%	1.8%	1.5%	2.0%	1.9%
Hafnia alvei	3	18	21	0.1%	0.2%	0.2%	0.1%	0.2%	0.2%
Klebsiella oxytoca	8	75	83	0.4%	0.8%	0.7%	0.4%	0.8%	0.8%
Klebsiella pneumoniae	15	99	114	0.7%	1.0%	0.9%	0.7%	1.1%	1.0%
Nocardia cyriacigeorgica	2	6	8	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Nocardia farcinica	2	9	11	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Nocardia nova	0	6	6	0.0%	0.1%	0.1%	0.0%	0.1%	0.1%
Pseudomonas aeruginosa	1476	5421	6897	64.9%	54.8%	56.7%	66.7%	60.7%	61.9%
Pseudomonas fluorenscens/putida	11	114	125	0.5%	1.2%	1.0%	0.5%	1.3%	1.1%
Pseudomonas mendocina	5	18	23	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
Pseudomonas stutzeri	3	15	18	0.1%	0.2%	0.1%	0.1%	0.2%	0.2%
Ralstonia pickettii	2	13	15	0.1%	0.1%	0.1%	0.1%	0.2%	0.1%
Serratia marcescens	16	121	137	0.7%	1.2%	1.1%	0.7%	1.4%	1.2%
Staphylococcus aureus	1159	4739	5898	51.0%	47.9%	48.5%	52.4%	53.1%	52.9%
Stenotrophomonas maltophilia	139	741	880	6.1%	7.5%	7.2%	6.3%	8.3%	7.9%
Streptococcus agalactiae	1	16	17	<0.1%	0.2%	0.1%	0.1%	0.2%	0.2%
Streptococcus pneumoniae	0	10	10	0.0%	0.1%	0.1%	0.0%	0.1%	0.1%
Streptococcus pyogenes	2	32	34	0.1%	0.3%	0.3%	0.1%	0.4%	0.3%
Mycobacteria	**156**	**1235**	**1391**						
Mycobacterium abscessus group	30	444	474	2.0%	6.3%	5.6%	14.0%	27.3%	25.8%
Mycobacterium avium	55	270	325	3.7%	3.8%	3.8%	25.7%	16.6%	17.7%
Mycobacterium chimaera	6	52	58	0.4%	0.7%	0.7%	2.8%	3.2%	3.2%
Mycobacterium intracellulare	12	107	119	0.8%	1.5%	1.4%	5.6%	6.6%	6.5%
Fungi	**533**	**2187**	**2720**						
Aspergillus flavus group	11	22	33	0.7%	0.3%	0.4%	1.2%	0.6%	0.7%
Aspergillus fumigatus	127	444	571	8.2%	6.4%	6.8%	14.0%	11.8%	12.2%
Aspergillus niger	8	14	22	0.5%	0.2%	0.3%	0.9%	0.4%	0.5%
Aspergillus terreus group	5	51	56	0.3%	0.7%	0.7%	0.6%	1.4%	1.2%
Candida albicans	108	761	869	7.0%	11.0%	10.3%	11.9%	20.2%	18.6%
Exophiala dermatitidis	1	20	21	0.1%	0.3%	0.3%	0.1%	0.5%	0.5%
Penicillium spp	12	76	88	0.8%	1.1%	0.1%	1.3%	2.0%	1.6%
Rasamsonia argillacea	11	8	19	0.7%	0.1%	0.2%	1.2%	0.2%	0.4%
Scedosporium apiospermum/Pseudallescheria boydii complex	71	126	197	4.6%	1.8%	2.3%	7.8%	3.4%	4.2%

Several studies have shown that conventional biochemical and/or automated, commercial microtiter assays can misidentify newly emerging pathogens such as *Stenotrophomonas maltophilia* and *Achromobacter xylosoxidans*. Thus, laboratories processing cystic fibrosis specimens need access to molecular identification strategies.

Standardized methodologies for antimicrobial susceptibility testing are highly desirable to facilitate clinical management and to track trends in antimicrobial resistance in the cystic fibrosis population. *Pseudomonas aeruginosa* strains from cystic fibrosis patients often have unique characteristics, including multidrug resistance, a mucoid phenotype which is associated with chronic infection and clinical deterioration, and slower growth rates; these bacterial characteristics can adversely impact the performance and interpretation of antimicrobial susceptibility testing with automated, commercial microtiter assays. While agar-based diffusion assays are recommended to minimize very major (false-susceptibility) and major (false-resistance) errors, only 52% of protocols surveyed by the Cystic Fibrosis Foundation specified their use.







Hemoglobin A1C was used as a metric to compare pathogen prevalence associated with degree of diabetes management.

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