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Futility of bacterial bone marrow cultures: the NIH experience over a 19 year period

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Introduction

Bone marrow biopsies are often performed on patients with unclear diagnoses. As part of this work up, cultures may be ordered for both routine bacterial, mycobacterial and fungal pathogens. They are performed in semi-sterile conditions and involve penetration through the skin. As such, there poses an increased risk of skin and other flora contaminating the cultures and limiting their utility. Processing of these specimens and work up of the cultures requires a substantial amount of laboratory personnel time. This work aims to assess the utility of bone marrow cultures at the NIH

Methods and Results

Bone marrow cultures collected from 2001-2020 were surveyed in the laboratory information system. We assessed which types of bone marrow cultures were ordered (fungal, bacterial, mycobacterial), and the presence of possible pathogens and contaminants. An organism was deemed a contaminant if it was consistent with skin flora, *Corynebacteria, Paenibacillus*, or listed as a contaminant in the culture report given to the physician. Organisms for which the role in bone marrow disease is unclear were included as possible pathogens. Additionally, for questionable non-contaminant organisms, clinical significance was determined based on whether a patient was treated for the organism. For all bone marrow cultures, growth of the same organisms in other culture types within 1 month of the bone marrow specimen was surveyed to determine whether the organism would have been found by alternative methods.

Figure 1. Distribution of 158 bone marrow culture isolates from 110 positive bone marrow cultures from 2001-2019

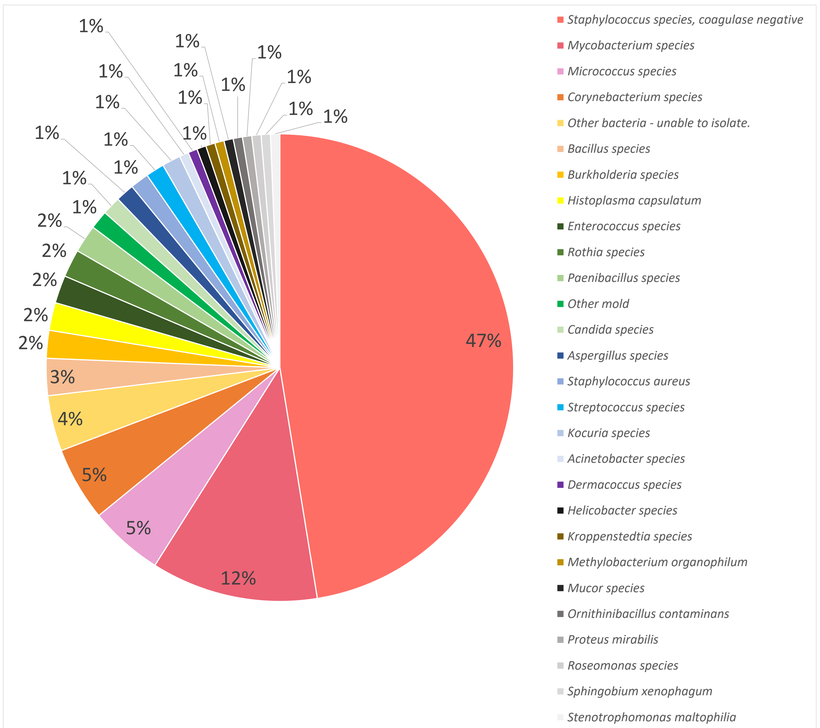

Table 1: List of possible non-pathogens by organism name/culture type.

Organism	Culture
Bacterial	
Acinetobacter johnsonii	AFB
Bacillus cereus	AFB
Burkholderia cepacia complex	Bacterial
Burkholderia gladioli	AFB
Enterococcus faecalis	AFB
Enterococcus faecium	Bacterial
Escherichia coli	AFB
Helicobacter species	Bacterial
Moraxella- like gram-negative rod	AFB
Proteus mirabilis	AFB
Roseomonas species	Fungal
Mycobacterial	
Mycobacterium abscessus subsp. Bolletii	AFB
Mycobacterium avium complex	AFB
Mycobacterium kansasii	AFB
Fungal	
Alternaria species	Fungal
Aspergillus ustus	Fungal
Candida parapsilosis	AFB
Histoplasma capsulatum	Fungal
Mucor species	Fungal

Figure 2. Breakdown of culture type that grew a potential non-pathogen from above (total = 37 cultures)

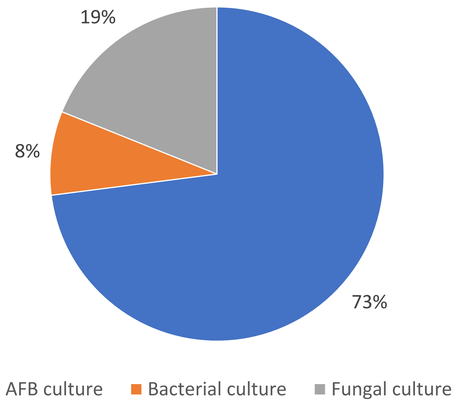

Table 2. Rate of Positive Blood Cultures Corresponding to Bone Marrow Culture by Organism Type

Pathogen Type	Number of Isolates	Corresponding Blood Culture Ordered	Corresponding Blood Culture Positive
Bacterial	13	8	4 (50%)
Fungal	7	3	2 (67%)
Mycobacterial	18	16	15 (94%)

*Total number of positive cultures is 38 because one bone marrow specimen was positive for both *Histoplasma capsulatum* and *Mycobacterium avium complex*

Table 3. Positive Predictive Value of Various Bone Marrow Culture Types

	Bacterial	Fungal	AFB	Combined
True Positives (All Possible Pathogens)	3	10	28	41
False Positives (Contaminants)	19	13	54	86
Total Positives	22	23	72	117
PPV	**0.14**	**0.43**	**0.39**	**0.35**
True Positives (All appropriate Pathogen)	3	6	17	26
False Positives (Contaminant/Not Appropriate)	19	17	65	101
Total Positives	22	23	72	117
PPV (Appropriate Pathogen)	**0.14**	**0.26**	**0.23**	**0.22**

*Total number of positives is 117 because isolates may have grown in different culture types from the same specimen. Appropriate pathogen is a pathogen determined by the culture type (AFB = mycobaceteria, Fungal = mold, yeast, nocardia, Bacterial = bacteria)

Discussion and Conclusions

Between the period of 2001 and 2020, we performed 483 bone marrow cultures (many of which included additional fungal and mycobacterial cultures). There were 110 (23%) positives, of which 73 (66%) were deemed contaminants. Nineteen (26%) of the 73 contaminants grew in the routine bacterial culture. However, 54 (74%) of the contaminants grew in the AFB culture, of which 8 also grew in the bacterial culture. For the 37 cultures which grew non-contaminant organisms, 25 were determined to be clinically significant. One culture grew both a fungus and a mycobacterium. Interestingly, 21 of the 25 significant cultures had a matching alternative culture (usually blood) growing the organism within 1 month. The large majority of the non-contaminant organisms were mycobacteria (18 of the 37). Fungal organisms were found in 7 of the cultures and 12 were bacterial. Of the 13 possible non-contaminant bacterial organisms, 1 was a Helicobacter species for which the culture was designed for such, and 4 had a matching positive blood culture. The remaining genuses were *Bacillus (cereus), Roseomonas, Stenotrophomonas, Acinetobacter, Enterococcus, Escherichia* and a *Moraxella*-like gram negative rod. Only 3 (1% of 483) total bacterial non-contaminants grew in the routine bacterial culture. Given that we do not know the number of true negatives, we can only conclude a positive predictive value (PPV) of 0.14 for routine bacterial culture at the NIH. Including AFB and fungal cultures, the PPV increased to 0.35

Our findings indicate that bone marrow routine bacterial culture is unlikely to yield a result not already found by other means and is likely a poor use of lab resources and staff.