SH35: Does virulence of organism cultured influence the likelihood of PJI? Should it still be included in the minor criteria?

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Response: While traditionally high virulent organisms are more likely to demonstrate obvious clinical signs of infection, organism virulence is ill-defined and should not be included in the PJI criteria.

Strength of Recommendation: Limited

Delegate Vote: 54 (100%) agree; 0 disagree; 0 abstain

Rationale: The virulence of a bacteria is defined by the organism's ability to cause disease[1]. While there are certain bacteria (eg, *Staphylococcus aureus*) that are more commonly associated with clinically-apparent signs and symptoms of shoulder PJI such as sinus tract or intra-articular pus, characterization of a bacteria as "virulent" or "low-virulence" is not based on bacterial species but rather on the associated clinical signs and symptoms. The term "virulence" must be taken in context of the patient's presentation.

Specifically in the shoulder, *Cutibacterium acnes* (*C. acnes*) is the most common bacteria identified at revision shoulder arthroplasty and is commonly labelled as a "low virulence" bacteria that often may be a contaminant or commensal rather that a pathogenic organism[2,3]. This concept is supported by multiple studies that suggest that the finding of "unexpected positive cultures" does not lead to inferior clinical outcomes after revision arthroplasty compared to revision with no bacterial growth[4,5]. However, these studies exclude shoulder PJIs caused by *C. acnes* that presented with more obvious infectious signs and symptoms. In the American Shoulder and Elbow Surgeons (ASES) Revision Arthroplasty / Prosthetic Joint Infection Multicenter database, the most common bacteria to cause ***definite*** signs of infection (intra-articular pus or sinus tract) was *C. acnes*, more so than the commonly-regarded "virulent" organisms including methicillin-sensitive *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) (Table 1). *C. acnes* was the most common bacteria to be defined as "Definite PJI" by the 2018 ICM definition, even though other bacteria such as *Staphylococcus* could meet criteria for "Definite PJI" without presence of a sinus tract or pus.

Subtyping or phylotyping of *C. acnes* has been performed in multiple studies in attempts to associated certain subtypes with strains of *C. acnes* that are clinically more virulent[6-10]. However, subtyping or phylotyping is not a direct correlation with virulence factors that assist the bacteria in colonizing the host and evading the host immune system. As an example, virulence of *Staphylococcus aureus* can be characterized by testing for the presence of the mecA gene which is strongly associated with antibiotic-resistant strains[11]. To date, however, there has not been a measurable virulence factor or a virulence gene identifiable by genetic testing of *C. canes* that can be used to characterize virulence.

It is unclear if the number of positive cultures is an indication of virulence. There are no studies demonstrating that any particular threshold of positive cultures indicates more clinically severe disease. While surgeons often use a treatment threshold of 2 or more positive or 3 or more

positive cultures, there has been no evidence to date demonstrating that more positive cultures are associated with increased clinical signs or symptoms or any adverse effects on treatment outcome[4].

Table 1:

	Microbiology	Frequency of two or more positive cultures [n (%)]	Signs of Obvious Infection within Definite Infection Cohort [n (%)]	Gross Intra-articular Pus within Definite Infection Cohort [n (%)]	Draining Sinus Tract within Definite Infection Cohort [n (%)]
Definite Infection (n=71)	No Positive Cultures	20 (28.2%)	20 (100.0%)	14 (70.0%)	6 (30.0%)
	1 Positive Culture	7 (9.9%)	7 (100.0%)	3 (42.9%)	4 (57.1%)
	2 or more Positive Cultures (Identical Organisms)	48 (67.6%)	33 (68.8%)	29 (60.4%)	14 (29.2%)
	Cutibacterium acnes	14 (19.7%)	13 (92.9%)	10 (71.4%)	5 (35.7%)
	Coagulase-negative *Staphylococcus*	3 (4.2%)	3 (100.0%)	2 (66.7%)	1 (33.3%)
	Methicillin-sensitive *Staphylococcus aureus*	11 (15.5%)	7 (63.6%)	7 (63.6%)	3 (27.3%)
	Methicillin-resistant *Staphylococcus aureus*	4 (5.4%)	2 (50.0%)	2 (50.0%)	1 (25.0%)
	Serratia sp.	4 (5.4%)	2 (50.0%)	2 (50.0%)	1 (25.0%)
	Streptococcus sp.	3 (4.2%)	2 (66.7%)	2 (66.7%)	0 (0.0%)
	Pseudomonas aeruginosa	2 (2.8%)	2 (100.0%)	2 (100.0%)	2 (100.0%)
	Klebsiella sp.	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Enterococcus sp.	1 (1.4%)	1 (100.0%)	1 (100.0%)	0 (0.0%)
	Kocuria sp.	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mycobacterium sp.	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Enterobacter sp.	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Proteus sp.	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Escherichia coli	1 (1.4%)	1 (100.0%)	1 (100.0%)	1 (100.0%)

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