

Central Venous Catheters and Candidemia: Remove them All!

Peter G. Pappas, MD, FACP
Division of Infectious Diseases
University of Alabama at Birmingham

Interactive Slide

What this discussion is and isn't about:

- Removal of central venous catheters, including percutaneous, tunneled, and other surgically placed venous access devices
- It is not about peripheral catheters
- It is not about arterial catheters
- It is not about vascular shunts for hemodialysis
- It is not about other intravascular devices

The Status Quo:

- In clinical trials, the vast majority (approx 70-80%) of cases of candidemia occur among patients with indwelling central venous catheters.
- While not always the *cause* of candidemia, retention of these catheters is associated with a greater length of candidemia in several large randomized trials
- Higher mortality is reported among patients with retained catheters in selected comparative trials
- Anecdotal reports recognize patients in whom candidemia was not cleared until the CVC was removed
- Despite these less than perfect data, all clinical trials since Rex 1994 have mandated early CVC removal as part of patient management

Problems Associated with CVC Removal

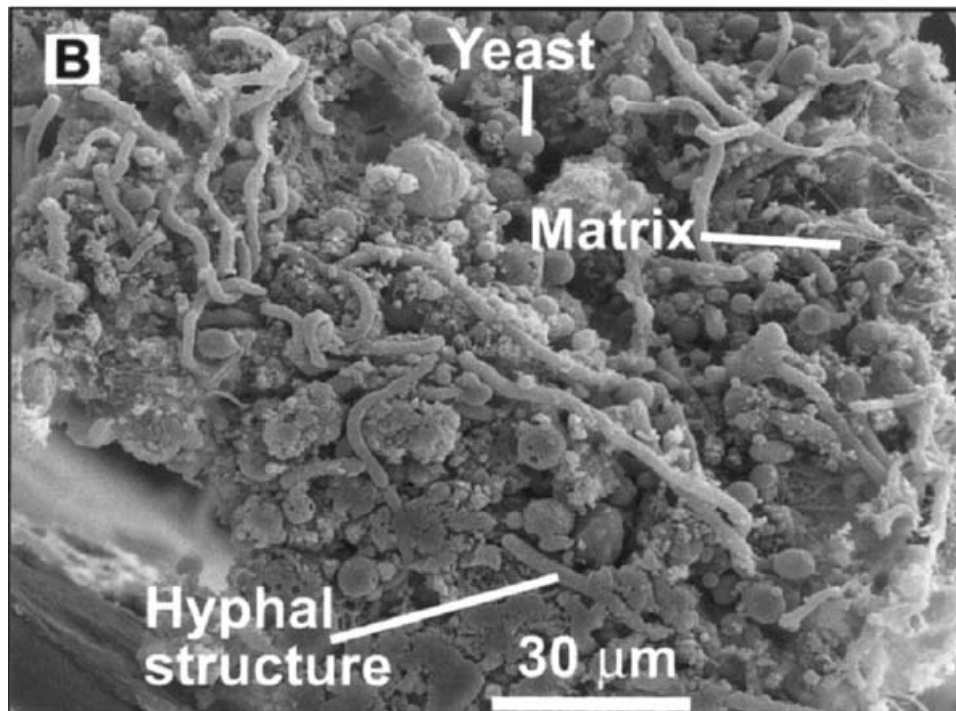
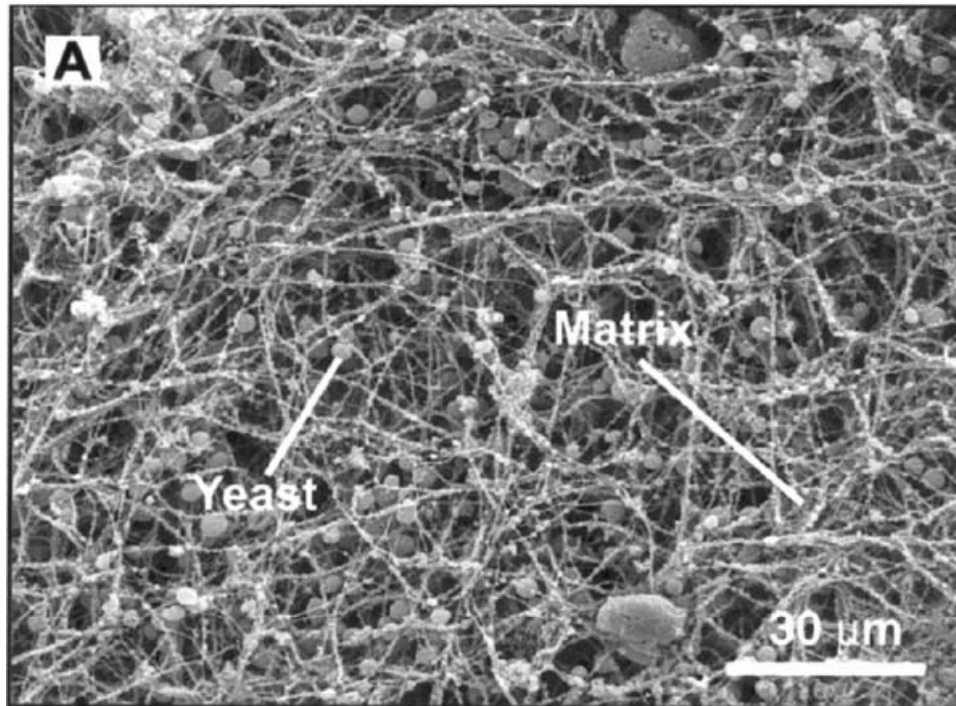
- There are a few....bleeding, requirement for anesthesia (local or general) for imbedded catheters, local pain
- No other *major* risks associated with CVC removal

Problems Associated with CVC Replacement

- It is usually time-consuming
- Limited alternative access sites
- Risk of bleeding (esp among pts with thrombocytopenia)
- Risk of infection
- Other risks associated with procedure
- Not everyone is a suitable candidate

What Are Biofilms?

- Structured microbial communities characterized by irreversible attachment to an artificial surface; organisms become embedded in a matrix of extracellular polymeric substances produced by these cells
- Organisms demonstrate phenotypic traits distinct from planktonic strains, ***notably resistance to antimicrobial therapy***

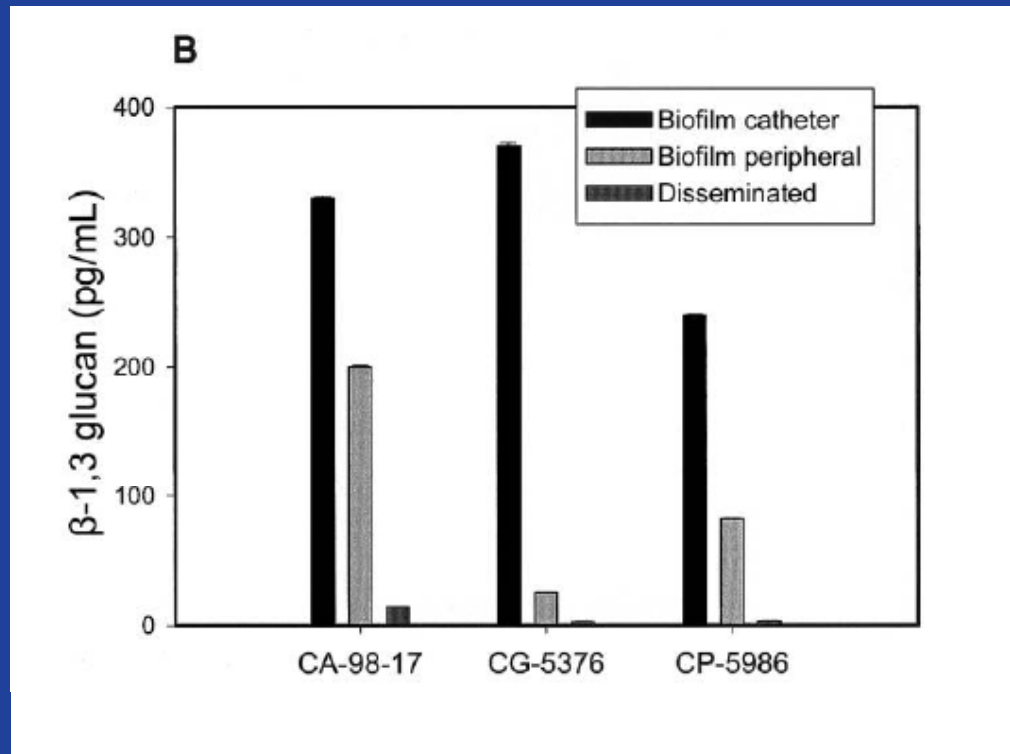


Andes et al, Infect
Immun 2004

The Role of Biofilms in Candidemia

- Biofilms probably play a pivotal role in the persistence of candidemia among pts with retained CVCs
- Among *Candida* spp, resistance genes are upregulated in the biofilm matrix (eg fluconazole efflux pumps, CDR1 and CDR2)
- Most biofilm-associated *Candida* spp retain susceptibility to echinocandins and lipid formulations of AmB

1,3 β -D Glucan Levels



**Now, let's look at some data from
several clinical trials evaluating
therapy for candidemia.....**

Candidemia I^{1,2}

- 206 evaluable nonneutropenic pts with candidemia (78% of pts with CVCs)
- Investigators strongly encouraged to remove CVCs as early as possible
- Removal/replacement over a wire was discouraged
- **Duration of candidemia was 2.6d vs 5.6d (p<.001) for complete exchange vs none**
- Pts without exchange has higher APACHE II scores, more catheters
- Individual cases of failure to clear bloodstream asso with retained catheters of all types (central, peripheral, arterial)

¹Rex et al, NEJM 1994;331:1325

²Rex et al CID 1995;21:994

High vs Low-dose AmB, AmB vs Flu

- Not a formal randomized, double blind study- more of an observational study
- Two studies in one: high vs low dose AmB; and AmB vs Flu
- 427 consecutive pts enrolled
- Mortality was 21% vs 41% ($p < .001$) among pts with catheter removal vs none

Candidemia in Neonates

- 50 neonates with candidemia given AmB, randomized to early CVC removal (within 3d) vs late CVC removal (>3d)
- Mortality difference in ER vs LR for neonates with *C. albicans* fungemia:
0/21 (0%; CI 0-14%) vs 9/23 (39%, CI 19-59%)

Candidemia II

- **Similar criteria for enrollment, outcome as Candidemia I**
- **219 pts met ITT criteria**
- **>90% with recent CVCs**
- **Complete catheter exchange resulted in clearance of bloodstream 1 day sooner compared to pts with no complete exchange (p=.08)**
- **No difference in APACHE II scores**

Anidulafungin vs. Fluconazole

- Randomized, double blind study of pts with candidemia (97% non-neutropenic)
- 78% with CVC at baseline
- Most CVCs removed at or near study entry (93%)
- 3 of 4 (75%) anidulafungin vs 3 of 11 (27%) fluconazole recipients without catheter removal were successfully treated
- No firm conclusions, but suggestive of poor effect of fluconazole on catheter associated candidemia

Micafungin vs Caspofungin

- Largest candidemia study to date
- Three arm, randomized, double-blind trial comparing mica 100, mica 150, and caspo 50 for invasive candidiasis
- 595 evaluable pts, 40 were neutropenic
- CVC removal strongly advised at study entry and within 3 days of randomization
- Similar eligibility criteria, outcome measures as previous studies

CVC removal vs non-removal

Pappas PG, et al CID 2007
45:883-93

Table 5. Characteristics of patients for whom treatment was successful.

Characteristic	Micafungin arms		Caspofungin arm (n = 188)	P
	100 mg arm (n = 191)	150 mg arm (n = 199)		
Candidemic	124/163 (76.1)	125/163 (74.4)	118/161 (73.3)	.85
Noncandidemic ^a				
Overall	22/28 (78.6)	16/30 (53.3)	17/26 (65.4)	.14
Acute disseminated	6/7 (85.7)	3/11 (27.3)	5/8 (62.5)	.06
Peritonitis	4/6 (66.7)	4/7 (57.1)	2/5 (40.0)	
Abscess	5/5 (100.0)	5/6 (83.3)	6/9 (66.7)	.42
Chorioretinitis	4/6 (66.7)	2/4 (50.0)	1/1 (100.0)	
Other	3/4 (75.0)	2/2 (100.0)	3/3 (100.0)	
Candida species recovered at baseline ^b				
<i>C. albicans</i>	71/92 (77.2)	71/102 (69.6)	61/83 (73.5)	.5
Non- <i>C. albicans</i>	78/104 (75.0)	73/102 (71.6)	81/114 (71.1)	.78
<i>C. glabrata</i>	24/28 (85.7)	30/34 (88.2)	22/33 (66.7)	.07
<i>C. tropicalis</i>	21/31 (67.7)	20/33 (60.6)	24/32 (75.0)	.5
<i>C. parapsilosis</i>	22/29 (75.9)	15/21 (71.4)	27/42 (64.3)	>.99
<i>C. krusei</i>	6/8 (75.0)	5/8 (62.5)	3/4 (75.0)	.59
Other ^c	10/14 (71.4)	6/12 (50.0)	10/12 (83.3)	
WBC count at baseline, cells/mm ³				
<500	18/22 (81.8)	9/17 (52.9)	7/11 (63.6)	.14
≥500	128/169 (75.7)	133/182 (73.1)	129/177 (72.9)	.8
APACHE II score at baseline				
≤20	125/156 (80.1)	120/159 (75.5)	115/152 (75.7)	.54
>20	21/35 (60.0)	22/40 (55.0)	21/36 (58.3)	.91
Intravascular catheter present at baseline				
Removed, time after baseline ^d				
Overall	100/120 (83.3)	102/139 (73.4)	97/125 (77.6)	.16
≤24 h	36/46 (78.3)	37/51 (72.5)	38/49 (77.6)	
25–48 h	19/23 (82.6)	15/21 (71.4)	14/18 (77.8)	
>48 h	45/51 (88.2)	50/67 (74.6)	45/58 (77.6)	
Not removed	29/47 (61.7)	32/47 (68.1)	30/50 (60.0)	.75

Current Recommendations Regarding CVC Management in Candidemia

- For non-neutropenic patients:
‘...intravenous catheter removal is strongly recommend in nonneutropenic pts with candidemia.’ (All)
- For neutropenic patients:
‘...intravenous catheter removal should be considered.’ (BIII)

So, what's the answer?

- It is dangerous to be too dogmatic about this issue....every pt should be managed individually.
- For most non-neutropenic pts with candidemia and a CVC, the catheter can and should be removed
- Neutropenic pts are more challenging....the CVC should be removed if it can be done without significant risk, *and* another source of candidemia has been reasonably excluded.
- For pts with implanted catheters and tunnel infection due to *Candida*, removal is always necessary.
- For pts with candidemia due to *C. parapsilosis*, CVC removal is almost always necessary, independent of neutrophil count.

Interactive Slide
