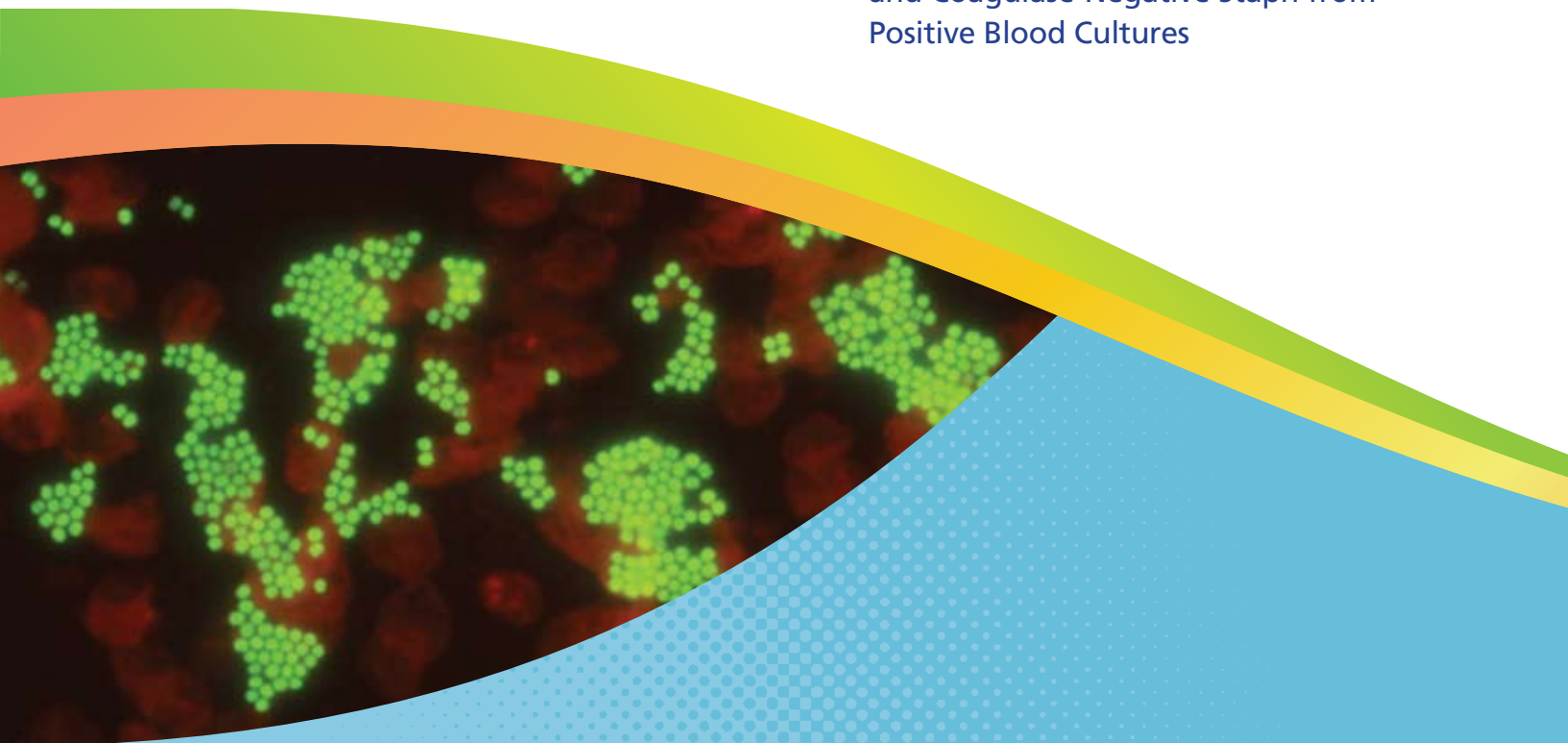


PNA FISH[®] ***Staphylococcus* sp.**

90 Min. Identification of *S. aureus*
and Coagulase-Negative Staph from
Positive Blood Cultures



Infection vs. **Contamination**

AdvanDx

“In this study we demonstrate that combining a rapid diagnostic test (PNA FISH) with prompt and direct communication of microbiological results is associated with improved outcomes.”

Ly et al. Therapeutics and Clinical Risk Management. 2008 June; 4(3):637-40.

Accuracy You Can Trust

PNA FISH Reliability: Sensitive and Specific

PNA FISH tests have been validated on all major blood culture systems and compared to identification results obtained via conventional, phenotypic identification methods. Refer to the package insert for complete performance data.

S. aureus PNA FISH® (KT001)

		Conventional Identification			Total
		<i>S. aureus</i>	Other Species*		
PNA FISH®	<i>S. aureus</i>	60	0	60	Sensitivity: 100% Specificity: 100% PPV: 100% NPV: 100%
	Negative	0	148	148	
	Total	60	148	208	

* Coagulase Negative Staphylococci (142), Other Species (6)

S. aureus/CNS PNA FISH® (KT005)

		Conventional Identification			Total	
		<i>S. aureus</i>	CNS	Other Species*		
PNA FISH®	<i>S. aureus</i>	113	0	0	113	Sensitivity <i>S. aureus</i> : 100% Sensitivity CNS: 100% Specificity: 81.8% PPV <i>S. aureus</i> : 100% PPV CNS: 99% NPV: 100%
	CNS	0	278	2	280	
	Negative	0	0	9	9	
	Total	113	278	11	402	

* Micrococcus spp. (4), Other Species (7)

The Challenge

Appropriate Therapy for Patients with Staphylococcal Bloodstream Infections

Staphylococci are the most frequent causes of bloodstream infections. Staphylococci are also the most frequent causes of blood culture contamination. True infections with *Staphylococcus aureus* present considerable clinical challenges and increase mortality rates, prolong hospital stays and add significant extra costs. Blood culture contamination with Coagulase-Negative Staph (CNS) on the other hand leads to unnecessary coverage with broad-spectrum antibiotic therapy, extra length of stay and unnecessary extra costs.

The challenge for clinicians is how to ensure early, appropriate therapy for patients with true *S. aureus* infections while avoiding unnecessary therapy for patients with contaminated blood cultures.

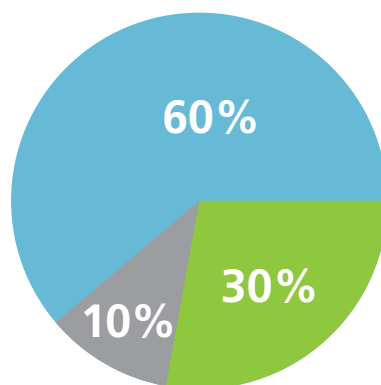
GPCC-Positive Blood Cultures: Species Distribution¹

CNS Contamination (60%)

- 60% of GPCC-Positive Blood Cultures
- Leads to unnecessary therapy with broad-spectrum antibiotics such as vancomycin
- Results in extra hospital length of stay (LOS) and more than \$4,000 in extra bed, pharmacy and laboratory costs²
- CDC Recommendations: Vancomycin should be discouraged for patients with single positive blood culture and other blood cultures that are negative³

CNS Bacteremia (10%)

- 10% of GPCC-Positive Blood Culture
- Associated with indwelling devices and catheters⁴



S. aureus Bacteremia (30%)

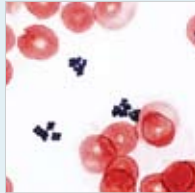
- 30% of GPCC-Positive Blood Cultures
- Associated with high mortality rates and requires early and aggressive therapy
- Up to 30% of patients with septic shock due to *S. aureus* receive inappropriate therapy⁵
- 50% of patients with MRSA bloodstream infection receive inappropriate empirical antimicrobial therapy⁶
- Emergence of vancomycin-intermediate *S. aureus* (VISA)⁷
- IDSA recommends higher vancomycin loading dose and higher serum concentrations to improve clinical efficacy due to VISA prevalence⁷

The Dilemma

Staphylococci in Positive Blood Cultures: Infection or Contamination?

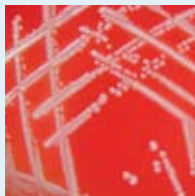


Gram stain: *S. aureus* or Coagulase-Negative Staph (CNS)?



- Cannot distinguish *S. aureus* from CNS in Gram stain.
- **Dilemma:** Does the staphylococci in the positive blood culture represent **true infection or contamination?**
- When to **escalate therapy for *S. aureus* infection?**
- When to **discontinue therapy for CNS contamination?**

Culture: Identification in 1-3 days.

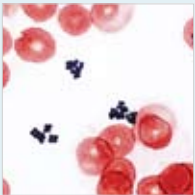


- **Conventional culture** and phenotypic identification can take an additional **1-3 days**.
- **Dilemma: Clinicians can't wait** an additional 1-3 days to prescribe antimicrobials to cover for true infections.

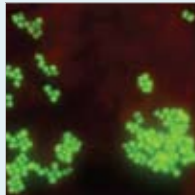
The Solution

90 Minutes Identification and Differentiation of *S. aureus* and CNS

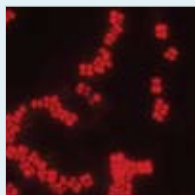
Gram Stain



PNA FISH®: Identification directly from Positive Blood Cultures



S. aureus



CNS

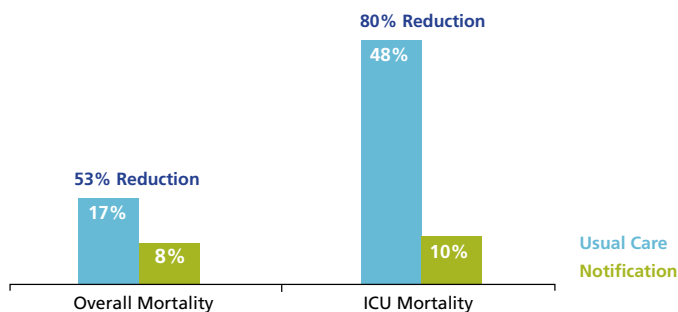
- **90 minutes, molecular identification** and differentiation of *S. aureus* (green) and Coagulase-Negative Staph (red) directly from positive blood cultures.
- Results **1-3 days earlier** than conventional methods.
- Identify patients with **true *S. aureus* and CNS infections** earlier.
- Ensure early, aggressive and **appropriate therapy** for patients with true infections.
- Identify patients with **CNS contaminated blood cultures** earlier.
- **Avoid broad-spectrum antimicrobials** (e.g. vancomycin) for patients with contaminated blood cultures.
- **Reduce** antimicrobial use.
- **Reduce** extra hospital length of stay (LOS).
- **Reduce** unnecessary bed, pharmacy and laboratory costs.

Proven Clinical Benefits

Use of PNA FISH to rapidly identify staphylococcal species from positive blood cultures has been shown in clinical studies at major medical centers to significantly improve patient outcomes and reduce costs.

Reduce Mortality

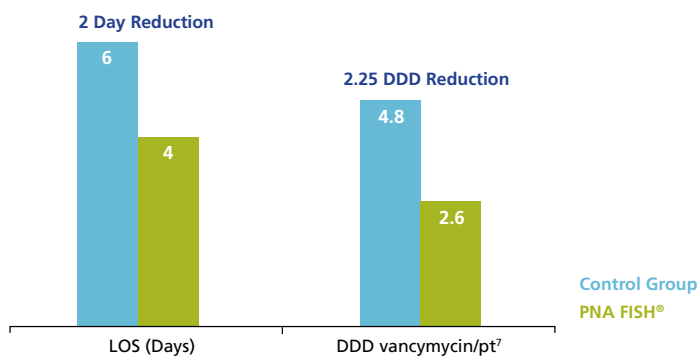
Prospective, randomized, controlled study of 202 patients (101 usual care, 101 notification) with GPCC-positive blood cultures performed at Washington Hospital Center (Washington, D.C.)⁸



- Early identification and notification of *S. aureus* and CNS result by PNA FISH
- Reduced overall mortality rate by 53%
- Reduced ICU mortality rate by 80%
- Reduced ICU mortality rate due to *S. aureus* BSI by 82%
- Reduced median antibiotic days for CNS by 2.5 days

Reduce Length of Stay (LOS) and Antimicrobial Use for CNS Contamination

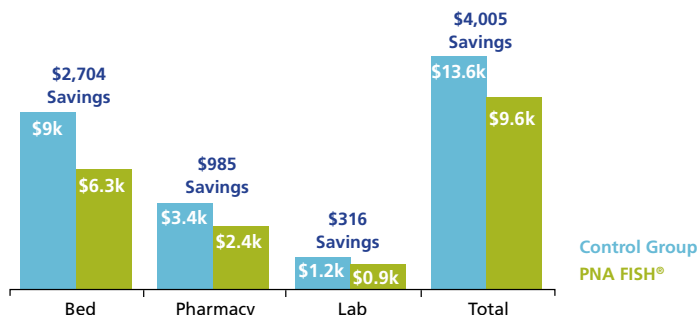
Retrospective study of 87 patients (34 control, 54 PNA FISH) with Coagulase-Negative Staph positive blood culture performed at the University of Maryland Medical Center (Baltimore, MD)⁹



- Early identification of CNS contamination
- 2 days reduction in length of stay (LOS)
- Discontinued unnecessary vancomycin use
- 2.25 defined daily dose (DDD): (4.5 doses) reduction in vancomycin use
- Sustained reduction in vancomycin use over 4 years

Lower Hospital Costs per Patient

University of Maryland Medical Center Study⁹



- Early identification of CNS contamination
- \$2,704 reduction in hospital bed costs due to reduction in length of stay
- \$985 reduction in pharmacy costs
- \$316 reduction in lab costs
- Total cost-savings of \$4,005 per patient
- Sustained cost-savings over 4 years

Bloodstream Infections and Positive Blood Cultures:

PNA FISH® tests provide rapid identification results for 95-99% of positive blood cultures.

Improving Care and Outcomes

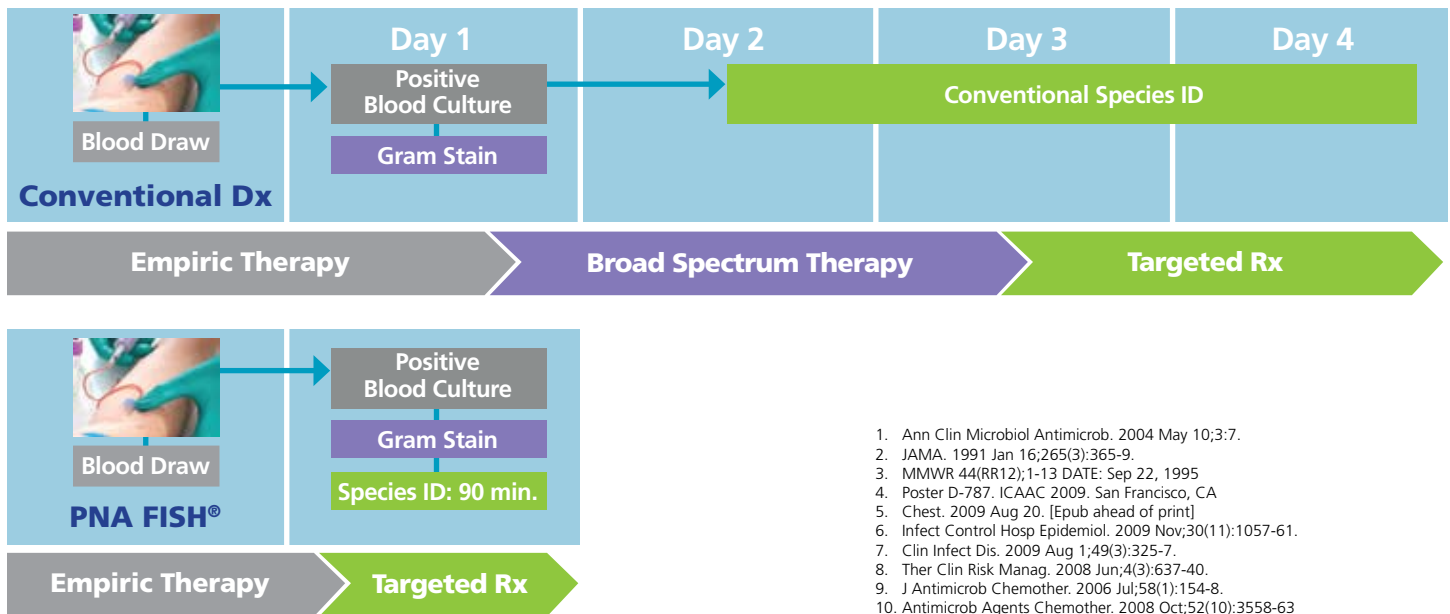
Rapid identification of bloodstream pathogens with PNA FISH can help physicians improve antimicrobial selection and has been shown to:

- **Reduce mortality rates** for *S. aureus* bacteremia⁸
- **Reduce unnecessary vancomycin** use, LOS and costs due to blood culture contamination⁹
- **Improve time to appropriate therapy** for *E. faecium* bacteremia by 1.8 days¹⁰
- **Reduce mortality rates** for *E. faecium* bacteremia¹⁰
- **Improve antifungal selection** for candidemia¹¹

Species Distribution in Positive Blood Cultures

Gram Stain - Dilemma	Species	% of Group
GPCC (55%) Infection vs. Contamination	<i>S. aureus</i>	25%
	Coagulase-Negative Staph	75%
GPCPC (15%) Ampicillin and Vancomycin Resistance	<i>E. faecalis</i>	40%
	<i>E. faecium</i>	25%
	<i>Streptococcus</i> sp.	35%
GNR (20%) <i>P. aeruginosa</i> vs. non- <i>P. aeruginosa</i>	<i>E. coli</i>	35%
	<i>K. pneumoniae</i>	20%
	<i>P. aeruginosa</i>	15%
	Other GNRs	30%
Yeast (5%) Echinocandin vs. Fluconazole	<i>C. albicans</i>	50%
	<i>C. glabrata</i>	20%
	<i>C. parapsilosis</i>	15%
	Other <i>Candida</i> sp.	15%
Other (5%)		

PNA FISH® vs. Conventional Dx (90 Min. vs. 1-3 Days)



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4. Poster D-787. ICAAC 2009. San Francisco, CA
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US HEADQUARTER

400 TRADE CENTER
WOBURN, MA 01801
+1 866 376 0009 (toll free)
+1 781 376 0111 (fax)

EU HEADQUARTER

BYGSTUBBEN 11
2950 VEDBAEK DENMARK
+45 45 16 07 99
www.advandx.com

AdvanDx