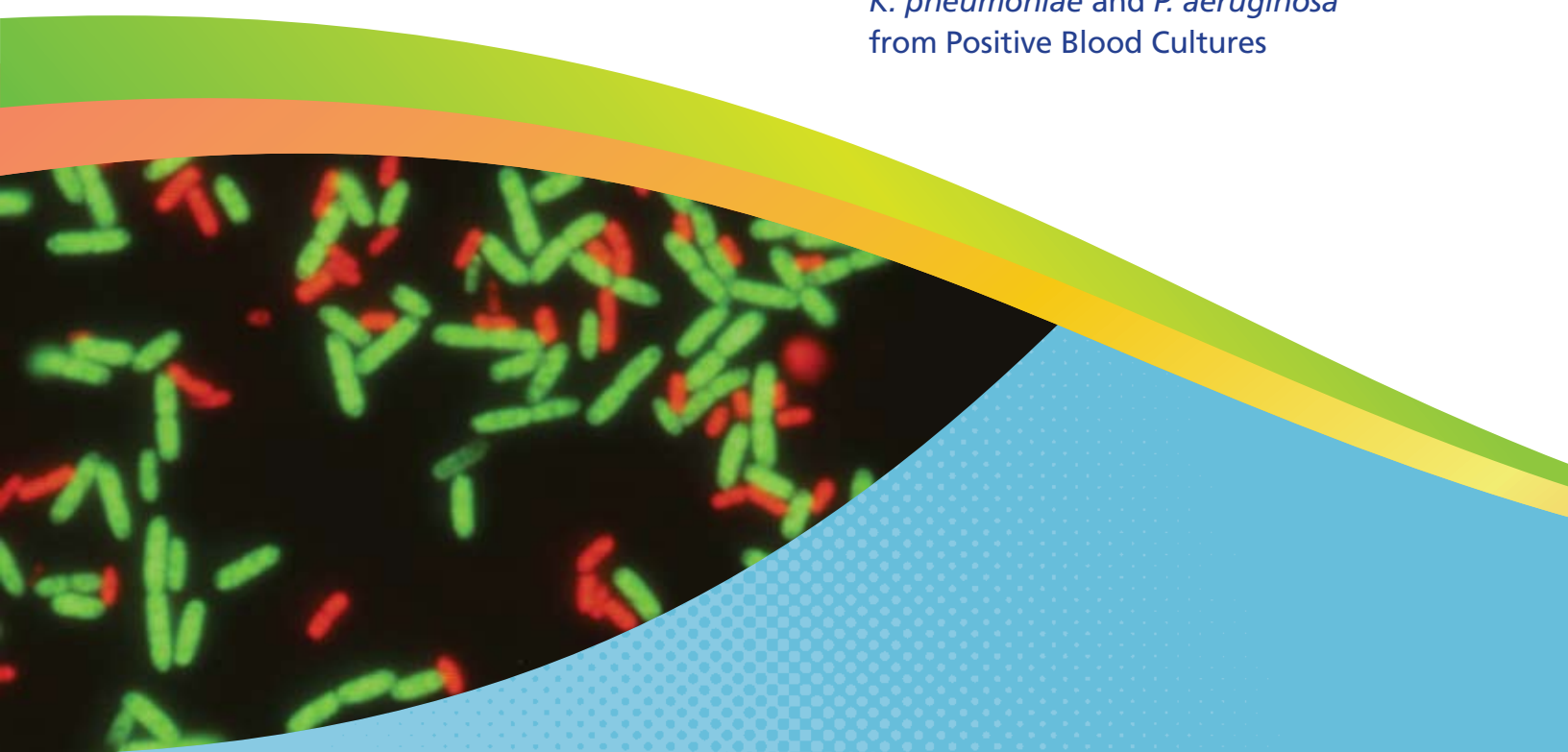


PNA FISH[®] Gram-Negatives

90 Min. Identification of *E. coli*,
K. pneumoniae and *P. aeruginosa*
from Positive Blood Cultures



Pseudomonal vs. Non-Pseudomonal Rx

AdvanDx

“Delay in starting effective antimicrobial therapy for *P. aeruginosa* bacteremia tended to be associated with higher mortality.”

Kang et al. Clin Infect Dis. 2003; 37: 745-51

Accuracy You Can Trust

PNA FISH Reliability: Sensitive and Specific

PNA FISH tests have been tested 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.

E. coli/*P. aeruginosa* PNA FISH® (KT007)

		Conventional Identification			Total
		<i>E. coli</i>	<i>P. aeruginosa</i>	Other Species	
PNA FISH®	<i>E. coli</i>	158	0	0	158
	<i>P. aeruginosa</i>	0	39	0	39
	Negative	0	1*	187	188
	Total	158	40	187	385

Sensitivity *E. coli*: 100%
 Sensitivity *P. aeruginosa*: 97.5%
 Specificity: 100%
 PPV *E. coli*: 100%
 PPV *P. aeruginosa*: 100%
 NPV: 99.5%

* Mixed Culture

E. coli/*P. aeruginosa* PNA FISH® (KT008)

		Conventional Identification			Total
		<i>E. coli</i> and/or <i>K. pneumoniae</i>	<i>P. aeruginosa</i>	Other Species	
PNA FISH®	<i>E. coli</i> and/or <i>K. pneumoniae</i>	215	0	0	215
	<i>P. aeruginosa</i>	0	35	0	35
	Negative	0	1*	119	120
	Total	215	36	119	370

Sensitivity *E. coli* and/or
K. pneumoniae: 100%
 Sensitivity *P. aeruginosa*: 97.2%
 Specificity: 100%
 PPV *E. coli* and/or
K. pneumoniae: 100%
 PPV *P. aeruginosa*: 100%
 NPV: 99.1%

* Mixed Culture

The Challenge

Appropriate Therapy: Pseudomonal vs. Non-pseudomonal Therapy

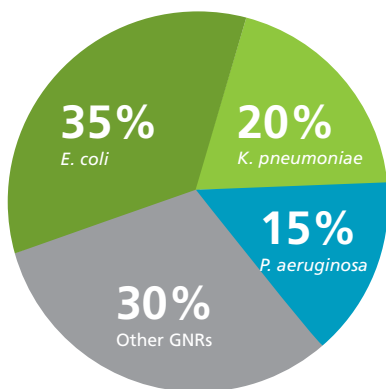
Gram-negative bloodstream infections (BSI) are associated with high mortality rates and can be difficult to treat due to increasing resistance to antimicrobial agents, especially for *Pseudomonas aeruginosa*. Treatment challenges are further compounded by current laboratory testing methods that can take 24 to 48 hours or longer to identify the specific pathogen, forcing clinicians to treat patients empirically. This makes choosing the right, empiric antibiotic coverage for patients with Gram-negative BSI challenging, especially as the decision to add an anti-pseudomonal drug is based primarily on knowledge of the infecting species.

As a result, patients with Gram-negative bloodstream infections are either subjected to broader-than-necessary antimicrobial therapy that can lead to subsequent infections with multi-drug resistant pathogens and the risk of toxicity complications, or are undertreated, increasing the risk for adverse patient outcomes.¹

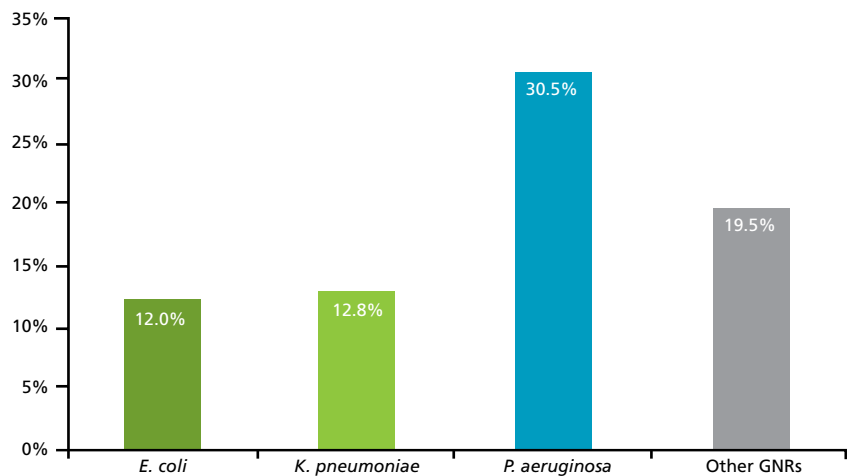
The challenge for clinicians is to decide when to initiate or discontinue anti-pseudomonal therapy for patients with Gram-negative rod (GNR) positive blood cultures.

GNR-Positive Blood Cultures:

Species Distribution²



Rate of Inappropriate Therapy for GNR Associated Septic Shock³

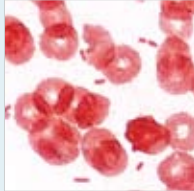


The Dilemma

Gram Negatives in Positive Blood Cultures: *P. aeruginosa* or non-*P. aeruginosa*?

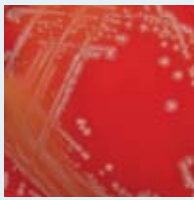


Gram Stain: Is it *P. aeruginosa*?



- Cannot distinguish between different Gram-negative rod species from a Gram stain.
- **Dilemma:** Does the GNR species in the positive blood culture represent *P. aeruginosa* or another GNR species such as *E. coli* or *K. pneumoniae*?
- When to initiate anti-pseudomonal therapy for *P. aeruginosa*?

Culture: Identification in 1-2 days.

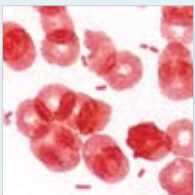


- **Conventional culture** and phenotypic identification can take an additional **1-2 days**.
- **Dilemma: Clinicians can't wait** to initiate aggressive antibiotic therapy to cover for resistant Gram-negative species.

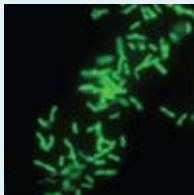
The Solution

90 Minutes Identification and Differentiation of *E. coli*, *K. pneumoniae* and *P. aeruginosa*

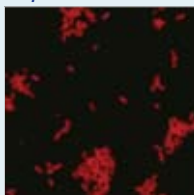
Gram Stain



PNA FISH®: Identification Directly from Positive Blood Cultures



E. coli and/or
K. pneumoniae



P. aeruginosa

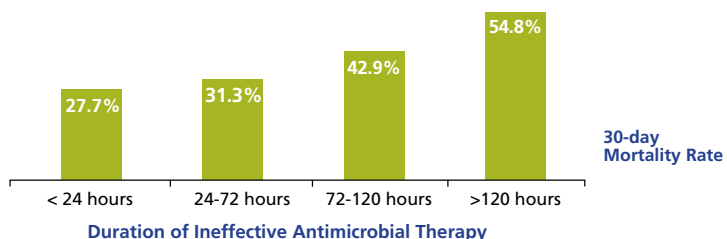
- **90 minutes, molecular identification** and differentiation of *E. coli*, *K. pneumoniae* and *P. aeruginosa* directly from positive blood cultures.
- Results **1-2 days earlier** than conventional methods.
- Ensure early, **appropriate antimicrobial therapy**.
- Help clinicians improve decision of when to initiate or discontinue anti-pseudomonal therapy to improve clinical outcomes.

Early, Effective Therapy Enables Optimal Patient Care and Outcomes

Rapid, accurate species identification from positive blood cultures may help clinicians select appropriate therapy for Gram-negative pathogens. Early initiation of effective antimicrobial therapy for patients with bloodstream infections due to *P. aeruginosa* and other Gram-negative pathogens has been shown to improve mortality rates.

Greater Mortality Associated with Treatment Delay for *P. aeruginosa* BSI

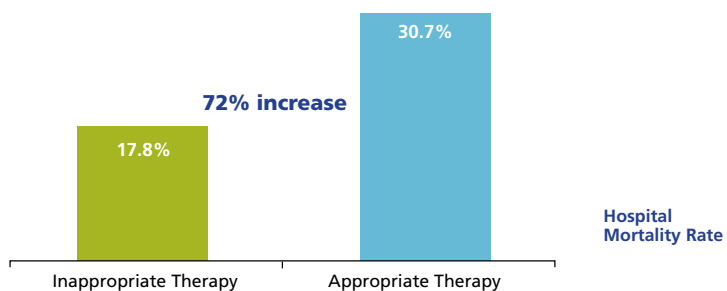
Retrospective cohort study of 136 patients with *P. aeruginosa* bloodstream infections looking at the influence of delay in effective antimicrobial therapy on patient outcomes. Performed at the Seoul National University Hospital (Seoul, Korea)⁴



- Demonstrated a trend toward higher mortality with longer delay of appropriate antimicrobial therapy
- Appropriate antimicrobial therapy reduced 30-day mortality by 36%

Inappropriate Antimicrobial Therapy Increases Mortality

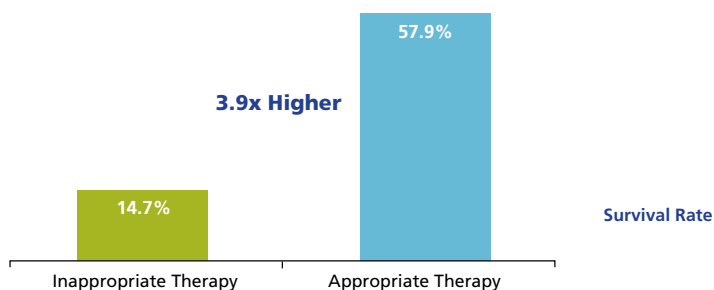
Retrospective cohort study measuring the effect of appropriate initial antimicrobial therapy on hospital mortality for 305 patients with *P. aeruginosa* bloodstream infections at Barnes-Jewish Hospital (St. Louis, MO)⁵



- Higher mortality rate (30.7%) for patients receiving inappropriate initial antimicrobial treatment
- Inappropriate initial antimicrobial therapy increased mortality rate by 72%

Appropriate Initial Therapy Improves Patient Survival

Retrospective review of appropriateness of initial antimicrobial therapy, clinical infection site and relevant pathogens in 5,715 septic shock cases from 22 medical institutions in the US, Canada and Saudi Arabia.³



- Survival rates for patients with septic shock associated with a Gram-negative infection were 3.9 times higher for those receiving appropriate initial therapy

Bloodstream Infections and Positive Blood Cultures:

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

Improving Care and Outcomes

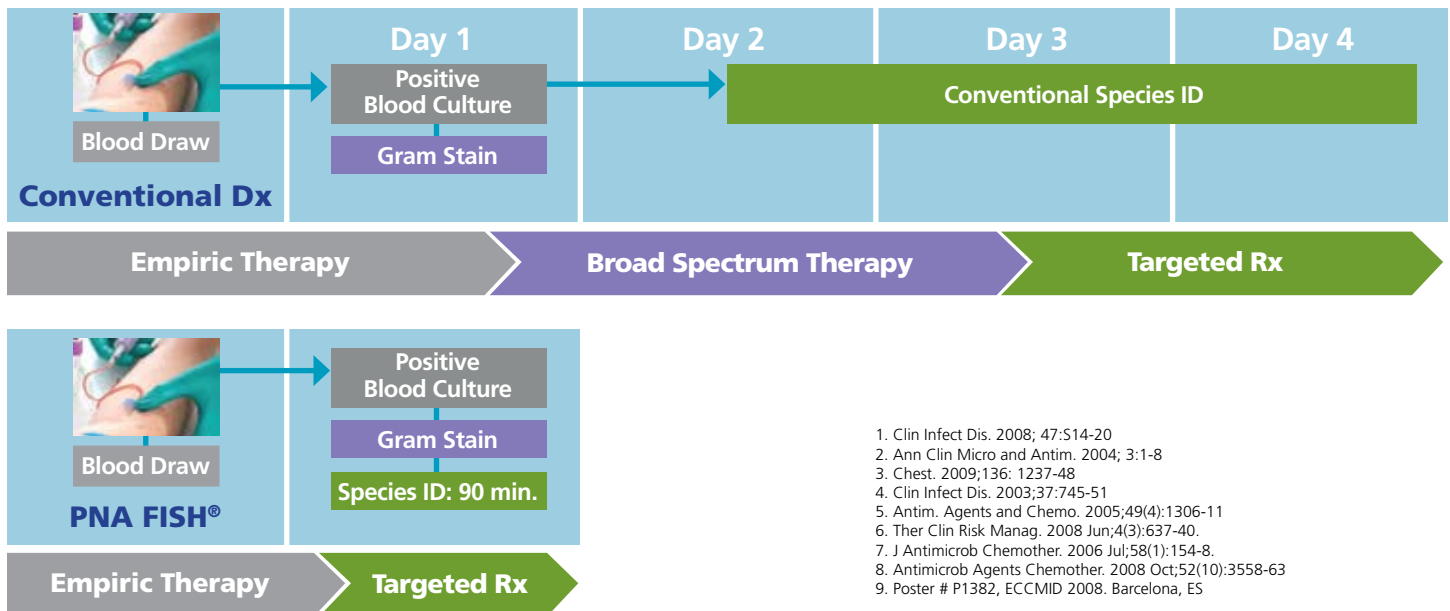
Rapid identification of bloodstream pathogens with PNA FISH can help physicians improve antimicrobial selection and has been shown to:

- **Reduce mortality rates** for *S. aureus* bacteremia⁶
- **Reduce unnecessary vancomycin** use, LOS and costs due to blood culture contamination⁷
- **Improve time to appropriate therapy** for *E. faecium* bacteremia by 1.8 days⁸
- **Reduce mortality rates** for *E. faecium* bacteremia⁸
- **Improve antifungal selection** for candidemia⁹

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)



1. Clin Infect Dis. 2008; 47:514-20
2. Ann Clin Micro and Antim. 2004; 3:1-8
3. Chest. 2009;136: 1237-48
4. Clin Infect Dis. 2003;37:745-51
5. Antim. Agents and Chemo. 2005;49(4):1306-11
6. Ther Clin Risk Manag. 2008 Jun;4(3):637-40.
7. J Antimicrob Chemother. 2006 Jul;58(1):154-8.
8. Antimicrob Agents Chemother. 2008 Oct;52(10):3558-63
9. Poster # P1382, ECCMID 2008. Barcelona, ES

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