



# Impact of Repeating Blood Cultures on Detecting Unpredicted Causative Microorganisms

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## ABSTRACT

**Background:** Blood cultures (BCs) are important for diagnosis and management of patients with infection. However, the impact of repeating BCs have not elucidated yet. The objective of this study was to assess the difference between initial and repeated BCs results over the past decade.

**Methods:** We retrospectively analyzed all consecutive BCs performed episodes at the Mie University Hospital, Japan from January 2006 till December 2015. All patients with repeating BCs were recruited to this study. Any episode occurred 31 or more days after previous BC was considered as a separate condition. The timings of repeating BCs after initial episode (Day 0) were categorized as follows: Day 1-2, Day 3-5, and Day 6 or later. The following microorganisms were considered as probable contaminants: CNS, *Bacillus* species, *Corynebacterium* species, *Propionibacterium* species, and *Micrococcus* species. The frequencies of BCs' positivity and distribution of detected microorganisms in the initial and repeated BCs were analyzed.

**Results:** Among a total of 12,593 cases with initial BCs, repeating BCs were performed in 4,136 cases. True positive rate (excluding probable contaminants) at Day 0, Day 1-2, Day 3-5, and Day 6 or later were 8.8%, 7.8%, 4.7%, and 7.2%, respectively. The pseudo-positive rates among each group were between 2.7-4.0%. The frequently detected microorganisms at initial BCs were as follows: CNS (25.0%), *E. coli* (13.0%), MSSA (9.4%), *Streptococcus* sp. (7.8%), *Klebsiella* sp. (7.1%), MRSA (6.6%), and *E. faecalis* (5.4%). However, at Day 3-5, increasing frequencies of MSSA, MRSA, and *E. faecalis* detection and decreasing of *E. coli*, *Streptococcus* sp., *Klebsiella* sp. were observed. At day 6 or later, *Candida* sp. (6.0%) and *E. faecium* (5.7%) came up to the top 5 organisms following CNS (26.2%), MRSA (11.9%) and *E. coli* (7.9%). The results of repeated BCs among initial positive cases were same pathogen (21.5%) and new pathogen (11.1%). The positive rates of repeating BCs among initial pseudo-positive and negative cases were 10.2% and 9.8%, respectively.

**Conclusion:** A certain number of repeating BCs cases showed different microorganisms from initial one. There were several changes in the distribution of detected microorganisms from initial BCs to repeating ones with chronologically increased frequencies of drug resistant organisms. These results suggest repeating BCs are needed in cases of unfavorable clinical course.

## BACKGROUND

Blood cultures (BCs) are important for diagnosis and management of patients with BSIs. Most patients taken BCs with suspected BSI are prescribed antibiotics, and some of them are performed follow-up BCs in order to confirm negative BC results or due to unfavorable clinical course. Follow-up BCs might give us useful information such as identification of unpredicted antimicrobial-resistant microorganisms, however, there is little evidence of the timing and value of repeating BCs.

Accordingly, the objective of this study was to assess the difference between initial and repeated BCs results over the past decade.

## METHODS

This study was conducted at the Mie University Hospital, a 685-bed educational hospital, in Japan. We performed a retrospective evaluation of the results of all BCs from the both inpatient and outpatient department in hospital between January 2006 and December 2015.

A blood culture incubation was conducted using an automated computer-monitoring system, and was continued for 7 days if there was no growth.

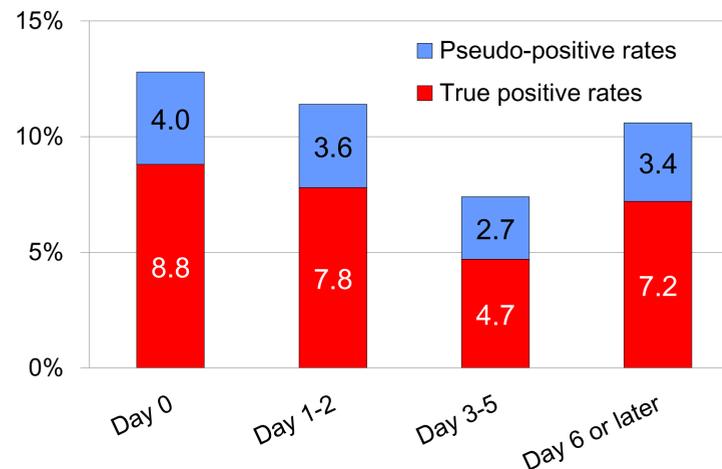
- Bact/ALERT® 3D system (January 2006 to December 2012)
- BACTEC™ FX system (January 2013 to December 2015)

A second episode occurring 31 or more days after previous BC was considered as a separate case. The timing of follow-up BCs after initial episode (**Day 0**) were categorized as follows: **Day 1-2**, **Day 3-5**, and **Day 6 or later**.

Commensal organisms such as Coagulase-negative *staphylococci*, *Bacillus* spp., *Corynebacterium* spp., *Propionibacterium* spp., and *Micrococcus* spp. were considered as potential contaminants.

Isolation of one of these organisms was considered as contamination (**pseudo-positive BC**) regardless of clinical situation in this study, whereas isolation of pathogenic organisms, except potential contaminants listed above, was considered as bacteremia (**true-positive BC**). Isolation of both pathogenic organisms and potential contaminants was considered as mixed bacteremia.

In total, 23,297 BCs in 12,593 cases (11,584 inpatients and 1,009 outpatients) and 10,704 follow-up BC in 4,136 patients were performed during this study period.



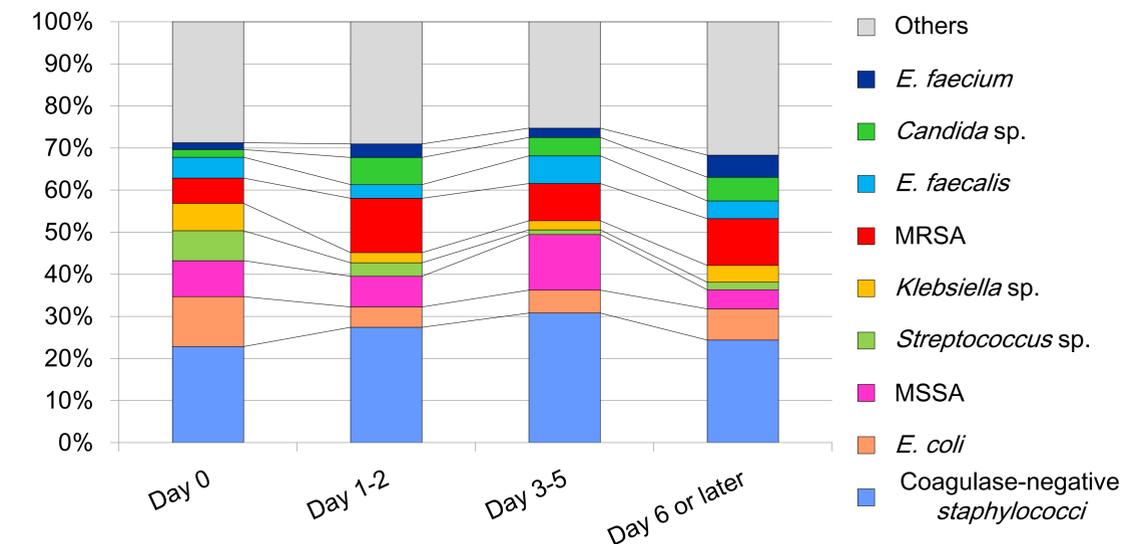
**Figure 1 : True positive and pseudo-positive rates.**

True positive rate (excluding probable contaminants) at Day 0, Day 1-2, Day 3-5, and Day 6 or later were 8.8%, 7.8%, 4.7%, and 7.2%, respectively. The pseudo-positive rates among each group were between 2.7-4.0%.

**Table 1 : The results of repeated BCs among initial positive cases.**

Initial BCs results		Follow-up BCs results		(%)
True-positive	549	Same pathogen	118	21.5
		New pathogen	61	11.1
		Negative	392	71.4
Pseudo-positive	246	True-positive	25	10.2
		Pseudo-positive	48	19.5
		Negative	176	71.5
Negative	3315	True-positive	324	9.8
		Pseudo-positive	191	5.8
		Negative	2812	84.8

## RESULTS



**Figure 2 : The frequently detected microorganisms initial and repeated BCs.**

The frequently detected microorganisms at initial BCs were as follows: CNS (25.0%), *E. coli* (13.0%), MSSA (9.4%), *Streptococcus* sp. (7.8%), *Klebsiella* sp. (7.1%), MRSA (6.6%), and *E. faecalis* (5.4%). However, at Day 3-5, increasing frequencies of MSSA, MRSA, and *E. faecalis* detection and decreasing of *E. coli*, *Streptococcus* sp., *Klebsiella* sp. were observed. At day 6 or later, *Candida* sp. (6.0%) and *E. faecium* (5.7%) came up to the top 5 organisms following CNS (26.2%), MRSA (11.9%) and *E. coli* (7.9%).

## CONCLUSIONS

A certain number of repeating BCs cases showed different microorganisms from initial one. There were several changes in the distribution of detected microorganisms from initial BCs to repeating ones with chronologically increased frequencies of drug resistant organisms. These results suggest repeating BCs are needed in cases of unfavorable clinical course.

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The results of repeated BCs among initial positive cases were same pathogen (21.5%) and new pathogen (11.1%). The positive rates of repeating BCs among initial pseudo-positive and negative cases were 10.2% and 9.8%, respectively.