JOURNAL OF CLINICAL MICROBIOLOGY, May 1988, p. 1045–1046
0095-1137/88/051045-02$02.00/0

Vol. 26, No. 5

Differential Quantitation with a Commercial Blood Culture Tube for Diagnosis of Catheter-Related Infection

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Received 16 October 1987/Accepted 3 February 1988

Central-venous-catheter-related infection is readily diagnosed by comparing simultaneous quantitative cultures of blood samples obtained via the catheter and a peripheral vein. The DuPont Isolator 1.5 (Du Pont Co., Wilmington, Del.) microbial culture tube was evaluated as an aid in diagnosing catheter-related bacteremia and fungemia in children and was found to be a reliable and convenient laboratory device for determining whether a long-term central venous catheter is a focus of infection.

Simultaneous quantitative blood cultures obtained via an indwelling central venous catheter and a peripheral vein are considered by many investigators to be the method of choice for diagnosing catheter-related bacteremia (1, 4, 5). Unfortunately, techniques used in previous studies require special processing of the specimen either by house staff or by laboratory personnel. Wing et al. (5) used a pour plate technique to diagnose a multiorganism episode of catheter-related bacteremia. Raucher et al. (4) applied 0.5 ml of blood to an agar plate at the bedside, and Flynn et al. (1) performed cultures of serial dilutions of blood obtained via the catheter and a peripheral vein. To standardize our clinical laboratory assessment of children with long-term central venous catheters (Hickman, Broviac, and Port-a-Cath [Pharmacia Nu Tech, Piscataway, N.J.]) and possible catheter-related infections, we evaluated the DuPont Isolator 1.5 (Du Pont Co., Wilmington, Del.) microbial blood culture tube. The Isolator 1.5 is a commercially available blood culture system. It consists of a sterile, evacuated tube which contains saponin, a rapid cell-lysing agent which is nontoxic to microorganisms; propylene glycol, a foam retardant; and sodium polyanetholesulfonate, which neutralizes the bactericidal properties of blood and inhibits phagocytosis. It is familiar to many laboratory personnel, requires little additional processing in the laboratory, and provides for the quantitation of bacteria or fungi in blood. Additionally, the Isolator 1.5 has proven to be effective in the rapid isolation of organisms from mixed cultures and may be more sensitive than standard broth culture in detecting low levels of bacteremia caused by species of the family *Enterobacteriaceae* (2, 3).

We studied 13 patients with clinically suspected catheter-related infection at St. Jude Children's Research Hospital and LeBonheur Children's Medical Center. All the patients had long-term central venous catheters (12 Hickman, 1 Port-a-Cath) which were surgically placed for the administration of chemotherapy or parenteral nutrition. Catheter-related infection was suspected when patients developed fever without focal symptoms. Simultaneous blood samples were obtained via their long-term intravascular catheters and peripheral veins. Specimens were sterilely inoculated into DuPont Isolator 1.5 tubes and into bottles for routine broth culture. Aliquots (0.3 ml) of blood from the Isolator 1.5 tubes were subsequently placed on blood, chocolate, and MacConkey agar; specimens at St. Jude Children's Research Hospital were also inoculated on brain heart infusion agar with gentamicin (100 μg/ml) to facilitate the isolation of fungi. Colonies were counted after overnight incubation. Isolates were identified by standard clinical laboratory methods.

Blood samples from five patients were sterile. Eight patients had organisms isolated from blood obtained via their central venous catheters and inoculated into Isolator 1.5 tubes; for three of these patients, the same organisms were cultured from peripheral blood (Table 1). For all eight patients with blood isolates, the concentrations of bacteria or fungi in blood obtained via the catheter were more than fivefold higher than in peripheral blood, a finding considered diagnostic of catheter-related infection (1). Agar plates for a typical patient are shown in Fig. 1. All positive Isolator 1.5 cultures were associated with corresponding positive routine broth cultures with concordant organisms. However, one patient (patient 1) had no growth from the Isolator 1.5 sample of peripheral blood, but routine broth culture of peripheral blood grew *Klebsiella pneumoniae*, suggesting very low levels of bacteremia. A patient whose cultures were considered negative for the purposes of this study did have growth of *Histoplasma capsulatum* from peripheral blood cultured by using the Isolator 1.5 after 1 month of incubation.

Growth was evident on agar within 24 h for all eight of our patients with catheter-related infections. For four of these

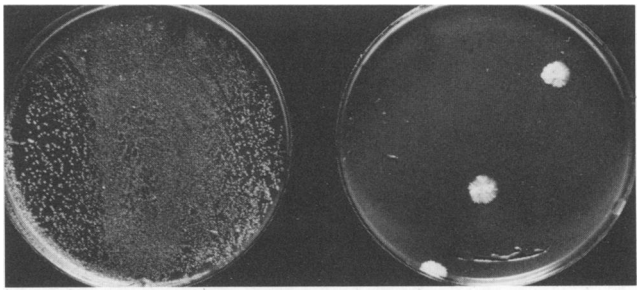

FIG. 1. Chocolate agar plates with 0.3 ml of blood obtained via the catheter (left) and from a peripheral vein (right) after 48 h of incubation. Note the typical colony morphology of *Candida albicans*. The smaller colony size on the plate with blood obtained via the catheter was presumably the result of crowding.

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TABLE 1. Quantitation and identification of bacteria or fungi isolated from Isolator 1.5 and broth cultures of eight patients with catheter-related infection

Patient no.	Organism growth[a] with:				Organism(s)
	Catheter blood		Peripheral blood		
	Isolator 1.5	Broth	Isolator 1.5	Broth	
1	190 CFU/ml	+	NG	+	*Klebsiella pneumoniae*[b]
2	Confluent	+	13 CFU/ml	+	*Candida albicans*
3	Confluent	+	10 CFU/ml	+	*C. albicans*
4	Confluent	+	20 CFU/ml	+	*Pseudomonas aeruginosa*
5	200 CFU/ml	+	NG	NG	Coagulase-negative staphylococci
6	20 CFU/ml	+	NG	NG	*Escherichia coli*
7	Confluent	+	NG	NG	Diphtheroids, gram-negative coccobacilli[c]
8	300 CFU/ml 300 CFU/ml	+	NG	NG	*Pseudomonas putida* *Acinetobacter lwoffii*

[a] +, Bacterial growth evident; NG, no growth. No growth on specimens cultured by using the Isolator 1.5 indicates ≤9 CFU/ml; no growth on those cultured by using routine broth indicates ≤3 CFU/ml.
[b] *K. pneumoniae* was also isolated from routine broth culture of peripheral blood but not of an Isolator 1.5 sample.
[c] Coccobacilli were fastidious and not identified further.

eight patients, the growth on Isolator 1.5 plates inoculated with blood obtained via the catheter was confluent, precluding precise quantitation of bacteremia. The remaining four patients had bacteremia ranging from 20 to 600 CFU/ml.

Failure of the Isolator to detect *K. pneumoniae* in the peripheral blood of patient 1 despite its isolation from routine broth culture was probably related to the very low level of bacteremia in this patient.

We effectively used the DuPont Isolator 1.5 to diagnose intravascular-catheter-related infection in pediatric patients with long-term central venous catheters. This method offers several advantages over routine broth cultures. By inoculating a standard amount of blood into the Isolator 1.5, quantitative cultures can be readily performed. Quantitation is not possible with routine broth cultures, because any number of viable organisms rapidly produce the maximal number of organisms that can be supported by the broth. Additionally, the Isolator 1.5 was familiar to our laboratory personnel, was available at all times, and did not require special processing by the medical staff. The technique is easily applicable to both pediatric and adult patients, since only 3.0 ml of blood is required, 1.5 ml each from the central venous catheter and a peripheral vein. In conclusion, we have shown that comparative central and peripheral blood cultures using the DuPont Isolator 1.5 microbial blood culture tube are a reliable and convenient means for diagnosing catheter-related bacteremia and fungemia.

This work was supported by the LeBonheur Children's Medical Center Small Grants Program and the American Lebanese Syrian Associated Charities.

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