Detection of Bacteriuria by Automated Electrical Impedance Monitoring in a Clinical Microbiology Laboratory

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An apparatus capable of rapidly detecting changes in electrical impedance was utilized for the continuous monitoring of bacterial growth in routine urine specimens in a clinical laboratory. In a trial study, 200 clinical specimens analyzed by the electrical impedance method resulted in an average detection time of 2.5 h for 41 clinically significant specimens, whereas conventional methods for bacterial isolation required overnight culture. Those specimens positive by the electrical impedance monitoring but negative by conventional bacteriological methods accounted for less than 2% of the total number of positive specimens, whereas electrical impedance-negative but conventional culture-positive specimens accounted for ca. 4%. Electrical impedance apparatus in clinical microbiology laboratories could provide rapid screening of clinical urine specimens as well as accurate detection of bacterial growth.

The rapid detection of microbial growth in clinical specimens is the primary goal of the diagnostic microbiology laboratory. The aid of mechanical equipment has significantly diminished detection time for many types of bacteria in clinical specimens (1, 4). Rapid detection procedures have been based on a variety of model systems, some of which depend upon radioisotopes (3), color changes (7), or chemical indicators (5). Recently an automated continuous electrical impedance monitoring apparatus (Bactometer 32) was developed for detection of bacterial growth in culture medium. The principal of the apparatus is essentially that of a wheatstone bridge that measures the ratio of electrical impedance between two chambers—one containing electrodes sampling a control culture medium without microorganisms and the other in culture medium with growing bacteria. This apparatus can continuously monitor 32 specimens and chart growth on a strip-chart recorder or a computer.

For the present study, the Bactometer was used to screen for bacteriuria in clinical samples in comparison to conventional bacteriological examination procedures with conventional media. In a trial study with 200 clinical specimens, analysis by the bacterial impedance technique resulted in an average detection time of 2.5 h for clinically significant positive specimens, whereas by conventional methods, overnight culture was required to detect the same positive specimens.

MATERIALS AND METHODS

Specimens. Specimens examined in this study were obtained in the normal manner from medical patients in Albert Einstein Medical Center, an 800-bed general hospital. Freshly voided, clean-catch urine specimens were submitted to the laboratory in 25-ml urine-culture tubes.

Electrical impedance monitoring. The Bactometer, made available from Bactomatic, Inc., Palo Alto, Calif., was utilized for continuous monitoring examinations. For culture in the Bactometer, a 0.5-ml urine sample was added to 0.5 ml of sterile Trypticase soy broth in one of 16 wells (5 by 4 by 4 mm) in the monitoring plate. One well contained 1.0 ml of growth medium alone as a control. As soon as the 32-specimen plate was filled (ca. 3 to 5 min), it was placed into the apparatus and maintained at 37°C, with normal room air as the atmosphere. The Bactometer was attached to a strip-chart recorder that monitored the ratio of electrical impedance between detecting wires in each well at 96-s intervals. Cultures were incubated for 18 to 20 h, and then samples were placed directly into bacteriological medium (see below) before being discarded, to ascertain that all impedance-negative specimens were indeed free of bacteria as assessed by conventional assays.

Bacteriological cultures. Each urine specimen was cultured by conventional means by plating 0.01- and 0.1-ml quantities on blood agar plates, phenylethyl alcohol, and MacConkey agar plates and incubating overnight at 37°C. In some cases urine samples were placed directly into thioglycolate broth or cultured on chocolate agar plates directly (2, 6). All specimens that were positive for bacterial growth after being cultured for 18 to 24 h were further

subjected to conventional bacteriological procedures to identify the organism(s). Similarly, the cultures that were positive in the Bactometer cups, as indicated by significant ratio changes by the electrical impedance apparatus, were immediately subcultured. If bacteria were detected, conventional methods were then utilized to determine the species to be sure the results were due to the same bacteria detected by the conventional method.

RESULTS AND DISCUSSION

Examination of 200 clinical specimens by both conventional bacteriological means and the electrical impedance apparatus indicated that both methods detected positive growth at a similar frequency, but the impedance apparatus showed the presence of microorganisms at only 2.5 h after culture initiation, on the average, if significant numbers of bacteria were present. Of the 200 specimens, 80 were positive for bacteria by impedance monitoring, with detection times always under 20 h. These specimens contained a variety of gram-positive and gram-negative bacteria (Table 1). A total of 99 individual bacterial species were recovered, with ca. 20% of the urine specimens from patients containing a mixture of microorganisms. Of the 80 positive specimens present at the 20-h cut-off time, 30 were positive in the range of 10^4 to 10^6 organisms per ml. An additional 11 specimens were found, representing detection of other microorganisms considered to be of clinical importance (i.e., 10^3 to 10^4 *Serratia*, coagulase-positive staphylococci, etc.). The mean detection time for these 41 clinically significant bacteria was 2.5 h. The remaining 39 positive specimens found by the electrical impedance apparatus were detected between 5 and 10 h after culture initiation. According to standard clinical interpretation used in this and most other laboratories, these were considered not clinically significant ($<10^4$ organisms per ml).

By using conventional colony count and plating techniques on solid medium, all of the positive organisms were detected upon initial examination only after overnight incubation. In nearly all cases, initial Gram staining of sedimented specimens of the same urine samples did not reveal the presence of bacteria. Other rapid screening techniques besides direct microscopic examinations are available, including colorimetric dye reduction assays, etc., as well as automated apparatus for detecting isotope release or metabolism, adenosine triphosphatase activity, etc. All of these methods have had some degree of success in various studies, but were not evaluated in this study.

There were some discrepancies between positive results observed by the conventional

method versus those detected with the impedance detection apparatus (Table 2). Approximately 4% of the bacteria detected by the conventional method was not found by the Bactometer, whereas 2% of the organisms that were detected by it were not detected by conventional methods (Table 2). Most of these discrepancies involved either yeast or low numbers of gram-positive cocci. This could reflect the differences in the atmospheric condition in the incubation chamber (i.e., lack of CO_2 enrichment in the Bactometer as compared to that used for conventional culture or absence of metabolite formation that could have affected the electrical

TABLE 1. *Organisms isolated upon detection by Bactometer method with urine specimens from 200 patients*

Organism	Total isolates
Gram-positive bacteria	
Diphtheroids	4
Enterococci	6
Micrococci	4
<i>Staphylococcus epidermidis</i> ^a	11
<i>Staphylococcus aureus</i> ^b	3
<i>Streptococcus</i> ^c	6
<i>Streptococcus</i> ^d	3
<i>Streptococcus</i> ^e	8
Gram-negative bacteria	
<i>Citrobacter</i>	3
<i>Enterobacter</i>	4
<i>Escherichia coli</i>	22
<i>Klebsiella</i>	5
<i>Proteus</i> species	10
<i>Pseudomonas</i> species	4
<i>Serratia</i>	2
Yeast	4

^a Coagulase negative.

^b Coagulase positive.

^c Alpha-hemolytic.

^d Beta-hemolytic.

^e Nonhemolytic.

TABLE 2. *Discrepancies between Bactometer and conventional screen methods for urine cultures*

Conventional negative, Bactometer positive	Conventional positive, Bactometer negative
Alpha-hemolytic <i>Streptococcus</i>	<i>Staphylococcus epidermidis</i> (10^2)
Nonhemolytic <i>Streptococcus</i>	Yeast and <i>Pseudomonas</i> (10^3)
Diphtheroids	<i>S. epidermidis</i> (10^3)
	Yeast (10^3)
	<i>S. epidermidis</i> (10^2)
	Nonhemolytic <i>Streptococcus</i> (10^2)
	Diphtheroids (10^2)

characteristics of the medium).

The results of the present study indicate that monitoring electrical impedance changes with the Bactometer appears to be an effective method for detecting bacteriuria in a short period of time, the average detection time for clinically significant bacteria being 2.5 h. This method shows promise as a rapid screen for urine specimens submitted to a clinical laboratory, with only positive specimens being plated and examined by conventional microbiological methods for identification and antibiotic susceptibility testing. The discrepancy between the detection of organisms by conventional means versus the electrical impedance screening method did not appear to be significant, since most of the false-negative specimens by the Bactometer method were associated with relatively low numbers of organisms (i.e., fewer than 10^2 or 10^3 bacteria per ml), which did not appear to reflect clinically important infections as determined by medical records. Rather, they may have actually been contaminants, since many microbiologists do not consider organisms present at a concentration of less than 10^4 or 10^5 bacteria per ml of clinical significance.

Utilization of a continuous monitoring system makes possible the initiation of a culture at almost any time, with results available on the strip-recorder chart when the first significant appearance of organisms occurs. The apparatus used for this study was so designed that initial indication of a significant change in the electrical impedance ratio occurred with 10^7 organisms per ml. This usually occurred within 2 to 3 h after incubation of 0.5 ml of a specimen that initially had 10^4 to 10^5 organisms per ml. The sensitivity of the apparatus may be altered so that much lower numbers of bacteria would result in significant changes within a few hours. However, at present it is felt that a 2- to 3-h incubation period with continuous monitoring is satisfactory for detecting significant numbers of clinically important aerobic organisms involved in urinary-tract infections.

A rapid, automated monitoring system for urine specimens, with results available within a few hours, should provide clinical laboratories with a valuable means of providing physicians with important information concerning bacteriuria so that antibiotic therapy, if necessary, could begin as soon as possible. With the availability of rapid antibiotic susceptibility procedures, it should also be possible to determine the appropriate antibiotic susceptibility within 8 h after receiving a specimen. This might eliminate the initial use of an inappropriate antibiotic by physicians unwilling to wait the usual 18 to 24 or more hours for results of bacteriuria from urine cultures.

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