

# Clinical Impact of Rapid In Vitro Susceptibility Testing and Bacterial Identification

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During the past decade, a variety of instrument-assisted bacterial identification and antimicrobial susceptibility test systems have been developed which permit provision of test results in a matter of hours rather than days, as has been the case with traditional overnight procedures. These newer rapid techniques are much more expensive than older methods. It has been presumed but not proven that the clinical benefits of rapid testing to patients with infection offset the added cost. The intent of this study was to objectively define the clinical impact of rapid bacterial identification and antimicrobial susceptibility testing. A 1-year study was performed in which infected, hospitalized patients in a tertiary-care, teaching, medical center were randomly assigned to one of two groups: patients for whom identification and susceptibility testing was performed by using a semi-automated, rapid, same-day procedure and those for whom testing was accomplished by using traditional overnight techniques. The two groups were compared with respect to numerous demographic descriptors, and then patients were monitored prospectively through the end of their hospitalization with the aim of determining whether there existed objectively definable differences in management and outcome between the two groups. The mean lengths of time to provision of susceptibility and identification test results in the rapid test group were 11.3 and 9.6 h, respectively. In the overnight test group, these values were 19.6 and 25.9 h, respectively ( $P < 0.0005$ ). There were 273 evaluable patients in the first group and 300 in the second group. Other than the length of time required to provide susceptibility and identification test results, no significant differences were noted between the two groups with respect to >100 demographic descriptors. With regard to measures of outcome, the mean lengths of hospitalization were also the same in both groups. Mortality rates were, however, lower in the rapid test group (i.e., 8.8% versus 15.3%). Similarly, statistically significantly fewer laboratory studies, imaging procedures, days of intubation, and days in an intensive or intermediate-care area were observed with patients in the rapid test group. Rapid testing was also associated with significantly shortened lengths of elapsed time prior to alterations in antimicrobial therapy. Lastly, patient costs for hospitalization were significantly lower in the rapid test group. The results of this study indicate the rapid same-day bacterial identification and susceptibility testing in the microbiology laboratory can have a major impact on the care and outcome of hospitalized patients with infection.

The identification of clinically significant bacteria in the laboratory and the performance of in vitro susceptibility tests provide information essential to the effective management of patients with infectious diseases (7). During the past two decades, a variety of instrument-assisted identification and susceptibility test methods have been developed which permit generation of test results in a period of 2 to 7 h, as opposed to the 15- to 24-h time frame previously required with traditional overnight methods. These newer techniques are often referred to as "rapid" methods and, in general, have been shown to provide test results nearly as accurate as those derived from traditional overnight tests. Rapid methods are, however, more expensive. Their added cost notwithstanding, these newer rapid methods have been widely adopted in United States clinical microbiology laboratories.

In view of the added cost of rapid identification and susceptibility test methods, the question arises, what is their clinical impact? Stated another way, can the added cost of these methods be justified on the basis of some definable contribution of the method to clinical care? It has been hypothesized that rapid susceptibility testing might lead to shortened re-

sponse times in cases where antibiotic therapy needs to be altered (2). Indeed, the results of two published studies indicate that rapid susceptibility tests significantly influenced clinician usage of antibiotics (3, 6). Other reports provide conflicting results (4). We are aware of no published investigations that have actually attempted to systematically assess the impact of rapid susceptibility testing on infectious disease outcome. Similarly, we know of no published studies that have examined the clinical impact of rapid bacterial identification. These were the objectives of the controlled, prospective, randomized study reported herein.

## MATERIALS AND METHODS

**Study design.** During a 1-year period, all specimens received in the University of Massachusetts Medical Center Clinical Microbiology Laboratories from hospitalized patients were assigned to one of two categories based on the first letter of the last name of the patient from whom the specimen had been obtained (A through K and L through Z). Previous experience indicated that roughly half of the laboratory's specimens came from patients in each group. Specimens were processed by standard methods. When bacteria were recovered and determined by standard laboratory criteria to merit identification and performance of in vitro susceptibility tests, such tests were performed by using a rapid 2- to 7-h instrument-assisted

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TABLE 1. Comparison of patient groups with respect to several characteristics

Category and subcategory <sup>a</sup>	Number (%) of patients in:		P <sup>b</sup>
	RAST group	ONAST group	
Service			
Medicine	111 (40.7)	133 (44.3)	NS
Surgery	105 (38.5)	107 (35.7)	NS
Pediatrics	30 (11.0)	32 (10.7)	NS
Others	27 (9.0)	28 (9.3)	NS
Disease <sup>c</sup>			
Nonfatal	115 (42.1)	147 (49.0)	NS
Possible fatal	99 (36.3)	100 (33.3)	NS
Rapidly fatal	21 (7.7)	32 (10.7)	NS
Ultimately fatal	34 (12.4)	21 (7.0)	0.027
Infection			
Community acquired	164 (60.1)	190 (63.3)	NS
Nosocomial	109 (39.9)	110 (36.7)	NS
Antibiotic allergy			
All antibiotics	43 (15.8)	33 (11.0)	NS
Penicillins	27 (9.9)	26 (8.7)	NS
Immunocompromised			
HIV <sup>c</sup> positive	5 (1.8)	5 (1.7)	NS
Autoimmune disorder	0	1 (0.3)	NS
Malignancy	29 (10.6)	31 (11.4)	NS
Steroid therapy	32 (11.7)	26 (8.7)	NS
Total	34 (12.5)	38 (12.6)	NS
Index positive culture			
Urine	100 (36.6)	125 (41.7)	NS
Blood	42 (15.4)	45 (15.0)	NS
Wound	60 (22.0)	63 (21.0)	NS
LRT	43 (15.8)	40 (13.3)	NS
Body fluid	26 (9.5)	26 (8.7)	NS
Other	2 (0.7)	1 (0.3)	NS

<sup>a</sup> HIV, human immunodeficiency virus; LRT, lower respiratory tract.<sup>b</sup> NS, not significant; i.e.,  $P > 0.05$ .<sup>c</sup> Disease categories are defined in the text.

test method, the Baxter-Microscan WALKAWAY-96 System (Baxter-Microscan, Sacramento, Calif.) (W/A), with commercially available reagents. The Microscan Rapids test panels employ fluorogenic enzyme substrates and fluorimetry as means for rapidly determining bacterial identification and susceptibility test results. Susceptibility tests were performed in a breakpoint broth microdilution format with results expressed in the form of susceptibility categories (resistant, intermediate, moderately susceptible, or susceptible). With patients in the A-K group, identification and susceptibility tests were initiated immediately upon recognition of bacterial growth, usually sometime between 8:00 and 11:00 a.m. As a result, test results were usually available on the same day. This group was referred to as the rapid antimicrobial susceptibility test (RAST) group. With patients in the L-Z group, identification and susceptibility tests were initiated between 9:00 and 10:00 p.m. on the evening of the day of recognition of growth such that test results were effectively not available until the following morning at ca. 8:30 a.m. The laboratory was not staffed during the third shift. This second group was referred to as the overnight antimicrobial susceptibility test (ONAST) group.

**Reporting of results.** The results of identification and susceptibility tests in both the RAST and ONAST groups were telephoned as soon as they became available by members of the laboratory's technologist staff directly to the physician who had requested the analysis with all isolates recovered from blood cultures, normally sterile body fluids, catheter tips yielding  $\geq 15$  colonies, specimens obtained in the operating

TABLE 2. Comparison of groups based on primary infectious disease problems

Infectious disease or condition <sup>a</sup>	Number (%) of patients in:		P <sup>b</sup>
	RAST group	ONAST group	
Uncomplicated UTI	70	87	NS
Complicated UTI	30	38	NS
Line-related bacteremia	21	15	<0.005
Urosepsis	5	9	NS
Endocarditis	1	0	NS
Bacteremia from other source	15	21	NS
Catheter site infection	2	1	NS
Cellulitis	10	10	NS
Postsurgical	22	21	NS
Chronic ulcer	12	13	NS
Other wounds	9	11	NS
Bone or joint infection	7	8	NS
Tracheobronchitis	12	7	NS
Pneumonia	31	33	NS
Pneumonia with empyema	2	0	NS
Intra-abdominal infection	20	25	NS
Meningitis	4	1	NS

<sup>a</sup> UTI, urinary tract infection.<sup>b</sup> See Table 1, footnoteb.

room, and selected other important specimens. All other test results were reported by using a computerized laboratory information system that had been in place for approximately 8 years. As soon as identification and susceptibility test results became available from the W/A instrument, they were transferred to the laboratory computer thereby becoming accessible to the clinical staff through use of an inquiry routine. In addition, hard copies of all test results were distributed to patients' medical records sometime between 2:00 and 5:00 a.m. the day after they first became available.

**Inclusion criteria.** Only patients from whom a clinically significant isolate of *Staphylococcus aureus*, non-aureus staphylococci, *Acinetobacter* spp., or a member of the *Enterobacteriaceae* had been recovered from a representative specimen were included in the study. The study was restricted to patients with infections due to these organisms since we believed that at the time this study was performed, only these organisms would yield reliable susceptibility test results with the W/A system when used in the rapid mode. The first specimen from which one or more of these organisms was recovered was defined as the index positive specimen. Immediately following enrollment in the study, patients were assigned to either a third-year clinical pathology resident (R.V.) or a third-year infectious disease fellow (M.G.) for evaluation and data gathering. All study patients were followed prospectively throughout their hospitalization in the context of numerous demographic descriptors (see Tables 1 to 4), with respect to antibiotic usage, numerous parameters of disease outcome, and cost of hospitalization (see Tables 5 to 7 and text). Information was tabulated by using the Fourth Dimension data base program on a Macintosh IIfx computer.

**Statistical analyses.** Paired *t* tests, chi square analysis, and Fisher's exact test were used for statistical analyses.

## RESULTS

There were 273 evaluable patients (52.0% males) in the RAST group and 300 evaluable patients (46.0% males) in the ONAST group. The mean age of patients in the RAST group

TABLE 3. Comparison of patient groups with respect to bacteria recovered from index positive culture

Organism	No. of organisms recovered in RAST/ONAST groups <sup>a</sup>						Total
	Blood	Body fluid	LRT	Urine	Wound	Other	
<i>Staphylococcus aureus</i>	12/13	4/3	30/17	3/3	36/40	1/0	86/76
Non-aureus staphylococcus	11/12	7/4		5/3	13/10	1/1	37/30
<i>Escherichia coli</i>	13/10	13/18	1/7	66/87	4/6		97/128
<i>Enterobacter</i> spp.	1/2	1/1	2/11	6/7	2/7		12/28
<i>Klebsiella</i> spp.	5/5	6/2	5/5	17/26	0/6		33/44
Other enterics	4/4	2/3	8/6	16/20	6/5		36/38
<i>Acinetobacter</i> spp.	2/2	1/0	3/5	1/1	1/6		8/14
Total	48/48	34/31	49/51	114/147	62/80	2/1	309/358

<sup>a</sup> Among the totals (both organism and specimen), results were statistically significantly different in only two cases, i.e. total numbers of isolates of *Staphylococcus aureus* ( $P = 0.047$ ) and *Enterobacter* spp. ( $P = 0.032$ ). LRT, lower respiratory tract.

was 51.3 years (range = 1 to 94; standard deviation [SD] = 25.0). In the ONAST group, the mean age was 53.7 years (range = 1 to 96; SD = 26.2). These differences were not statistically significant. When patient ages were analyzed by increments of 10 years as opposed to mean age, again no differences were seen. The two groups of patients were analyzed with respect to clinical service, severity of underlying disease, origin of the index positive infection (community acquired or nosocomial), presence or absence of antibiotic allergy, existence of immunocompromising condition (and if so, which one), and specimen source for their index positive culture (Table 1). Regarding severity of underlying disease, a modification of the criteria of McCabe (5) were employed in which four categories were defined: 1, nonfatal (conditions not expected to alter life span, with a  $\leq 5\%$  chance of hospital mortality [e.g., pneumonia in a healthy young adult, cellulitis, and urosepsis without shock, etc.]); 2, possibly fatal (conditions which were potentially treatable or curable [i.e., not rapidly or ultimately fatal] but which had the potential for altering life span and/or a 5 to 10% chance of hospital mortality [e.g., pneumonia in the elderly and complicated valve replacement, etc.]); 3, ultimately fatal (conditions with  $>80\%$  chance of mortality within 1 to 3 years regardless of intervention [e.g., cirrhosis with liver failure, metastatic cancer, and AIDS, etc.]); and 4, rapidly fatal (conditions with  $>80\%$  chance of death within 6 to 12 months regardless of intervention [e.g., end stage cancer or end-stage AIDS, etc.]). Significant differences between the two groups were noted for only one parameter: 12.4% of patients in the RAST group were judged to have an ultimately fatal underlying disease versus 7.0% of patients in the ONAST group. When antibiotic allergies were examined according to individual agents, no differences between the RAST and ONAST groups were noted (data not shown).

Patient groups were also analyzed from the perspective of the specialty or subspecialty service primarily responsible for an individual patient's management at the time of the index positive culture (data not shown). Again, no significant differences were found.

The primary infections patients were noted to have at the time of the index positive culture are depicted in Table 2. With one exception, no significant differences were noted between the RAST and ONAST groups. Significantly more patients (i.e., 21) in the first group had line-related bacteremia than in the second group (i.e., 15).

Table 3 lists those bacteria that were isolated from index positive cultures in the two patient groups. Only minor differences between the two groups were apparent. The number of isolates of staphylococci, *Acinetobacter* spp., and enteric gram-negative bacilli recovered from index positive cultures ex-

ceeded the number of actual specimens in most specimen categories. This reflects the fact that selected specimens yielded more than one organism. Table 3 lists only those bacteria recovered from index positive cultures upon which the rapid identification and susceptibility tests were performed. Selected other bacteria were also recovered from index positive specimens. These included aerobic diphtheroids, *Moraxella catarrhalis*, viridans streptococci, beta-hemolytic streptococci, *Streptococcus pneumoniae*, *Enterococcus* spp., *Haemophilus* spp., *Neisseria* spp., various anaerobes, *Pseudomonas aeruginosa*, and other miscellaneous gram-negative bacilli. The frequencies with which one or more of these bacteria were isolated from index positive specimens obtained from patients in the RAST group and the ONAST group, respectively, were as follows: blood cultures, 5 and 2; body fluids, 32 and 57; lower respiratory tract secretions, 29 and 18; urine specimens, 16 and 13; and wound specimens, 42 and 48.

In the RAST patient group, 230 of 273 patients (84.2%) were receiving antibiotic therapy at the time of the index positive culture; 277 of the 300 patients in the ONAST group (92.3%) were receiving antibiotics. These percentages were not statistically significantly different. Table 4 provides a comparison of patients in the two groups who were receiving antibiotics at the time of the index positive culture. No significant differences between the two groups were observed with respect to the reasons for therapy, routes of administra-

TABLE 4. Comparison of groups with respect to antibiotic therapy at the time of the index positive culture

Administration of antibiotic(s) directed against infection assessed by index positive culture	Route of administration <sup>b</sup>	Activity against presumed pathogen(s) from index positive culture	No. of patients with therapy in group <sup>d</sup>	
			RAST	ONAST
Yes	IV/IM	Yes	164	198
		No	11	10
	PO	Yes	38	52
No	IV/IM	No	3	2
		Yes	7	11
	PO	No	8	8
		Yes	2	3
		No	2	2

<sup>b</sup> IV, intravenous; IM, intramuscular, PO, oral.

<sup>d</sup>  $P$  values were not significant for any results.

TABLE 5. Comparison of patient groups based on length of hospitalization and mortality rates

Characteristic	Result for group		P
	RAST	ONAST	
Mean total length (days) of hospitalization (range [SD])	20.7 (2–129 [20.7])	20.1 (2–133 [20.0])	NS
Mean length of hospitalization (days) following index positive culture (range [SD])	14.7 (0–118 [17.6])	14.6 (1–118 [16.5])	NS
Total no. (%) of patient deaths	24 (8.8)	46 (15.3)	0.016
Total no. (%) of patient deaths attributable to infection	19 (7.0)	38 (12.7)	0.023

tion, and activity of the agents patients were receiving against their presumed infecting pathogens. Similarly, the RAST and ONAST patients were comparable in terms of those specific antibiotics patients were receiving at the time of the index positive culture and the percentage of patients who were receiving combination versus single-agent therapy (data not shown).

The mean length of time to positivity of index positive cultures in the RAST group, i.e., 24.8 h (range = 10.2 to 123; SD = 14.0) was nearly identical to that observed in the ONAST group, i.e., 23.9 h (range = 10.2 to 123; SD = 10.3). Statistically significant differences between the RAST and ONAST groups were, however, noted with respect to the mean length of time to a definitive identification of the presumed infecting pathogen(s) in the index positive culture and the average time period required before susceptibility test results were available. In the RAST group, these values were 11.3 h (range = 0.5 to 77; SD = 14.4) and 9.6 h (range = 4 to 68; SD = 13.2), respectively. In contrast, in the ONAST group, these values were 19.9 h (range = 0.5 to 101; SD = 15.5) and 25.9 h (range = 16 to 78; SD = 11.0), respectively. These differences were highly statistically significant ( $P < 0.0005$ ).

Having determined that the two patient groups were essentially comparable except for the much shorter period of time to provision of organism identification and susceptibility test results in the RAST group, it was of interest to compare and contrast the two groups in the context of various indicators of disease outcome, with respect to cost of hospitalization, and in terms of impact on antibiotic therapy.

The two patient groups were comparable when analyzed according to length of hospitalization, both total and that following the index positive culture (Table 5). Mortality rates, however, both overall and those attributable to infection, were significantly lower in the RAST group than in the ONAST group. The frequency with which microbiology tests were performed on study patients was assessed, as were the numbers of blood cultures obtained and the numbers of significant positive blood cultures (Table 6). Data were analyzed with respect to entire hospitalizations and for that specific period of hospitalization that followed the index positive culture. During both periods, statistically significantly fewer microbiology tests, blood cultures, and positive blood cultures were noted in the RAST group than in the ONAST group. The frequencies with which eight other laboratory tests were performed for the two

TABLE 6. Frequency with which various procedures were performed on patients in the two groups

Procedure <sup>a</sup>	RAST group			ONAST group			P
	Total no. of tests	Mean no. of tests/patient (range [SD])	No. (%) of patients getting test	Total no. of tests	Mean no. of tests/patient (range [SD])	No. (%) of patients getting test	
Microbiology tests							
During hospitalization	4,597	16.8 (0–98 [8.4])	273 (100)	5,833	19.4 (0–117 [9.0])	300 (100)	0.0006
Post-index positive culture	3,778	13.8 (0–74 [8.1])	273 (100)	4,830	16.1 (0–90 [11.2])	300 (100)	0.0054
Blood cultures							
During hospitalization	1,665	6.1 (0–28 [4.6])	212 (77.7)	2,649	8.8 (0–40 [4.0])	260 (86.7)	<0.0005
Post-index positive culture	1,338	4.9 (0–21 [3.2])	201 (73.6)	2,250	7.5 (0–29 [4.0])	238 (79.3)	<0.0005
Significant positive blood cultures							
During hospitalization	190	0.7 (0–8 [0.6])	56 (20.5)	343	1.1 (0–11 [1.0])	60 (20.0)	<0.0005
Post-index positive culture	148	0.5 (0–5 [0.9])	26 (9.5)	298	1.0 (0–7 [0.9])	31 (10.3)	<0.0005
Urinalysis	957	3.5 (0–38 [2.0])	248 (90.8)	1,176	3.9 (0–34 [2.1])	299 (99.7)	0.0199
Blood glucose	1,880	6.9 (0–98 [4.3])	245 (89.7)	2,660	8.9 (0–104 [4.8])	285 (95.0)	<0.0005
Electrolytes	2,503	9.2 (0–126 [7.1])	248 (90.8)	3,402	11.3 (0–140 [8.0])	292 (97.3)	0.0100
Chemical profile	1,229	4.5 (0–80 [4.2])	219 (80.2)	1,633	5.4 (0–66 [4.3])	270 (90.0)	0.0116
Complete blood count	5,675	20.8 (0–378 [18.3])	255 (93.4)	7,930	26.4 (0–578 [24.7])	300 (100)	0.0023
Differential	2,639	9.7 (0–178 [8.8])	245 (89.7)	3,448	11.5 (0–162 [8.9])	300 (100)	0.0153
Arterial blood gas	5,501	20.2 (0–660 [22.8])	164 (60.1)	8,630	28.8 (0–738 [40.6])	169 (56.3)	0.0021
Serum antibiotic assay	761	2.8 (0–32 [2.9])	140 (51.3)	1,515	5.1 (0–94 [4.5])	118 (39.3)	<0.0005
Electrocardiogram	1,355	5.0 (0–88 [4.9])	172 (63.0)	1,421	4.8 (0–52 [4.8])	223 (74.3)	NS
CT scan	325	1.2 (0–12 [1.0])	161 (59.0)	398	1.3 (0–18 [1.1])	125 (41.7)	NS
Chest X-ray	3,206	11.7 (0–37 [8.3])	180 (66.0)	4,243	14.1 (0–42 [7.9])	199 (66.3)	<0.0005
Abdominal X-ray	386	1.4 (0–8 [0.9])	82 (30.0)	531	1.8 (0–7 [0.8])	106 (35.3)	0.0006
Ultrasound	76	0.3 (0–4 [0.2])	56 (20.5)	107	0.4 (0–10 [0.3])	61 (20.3)	<0.0005
Days of intubation	1,482	5.4 (0–78 [6.4])	76 (27.8)	2,457	8.2 (0–93 [7.0])	96 (32.0)	0.0014
Days in an ICA	646	2.4 (0–41 [3.6])	48 (17.6)	1,010	3.4 (0–50 [4.2])	61 (20.3)	0.0024
Days in an ICU	1,320	4.8 (0–69 [5.0])	68 (24.9)	1,904	6.3 (0–81 [8.0])	80 (26.7)	0.0135

<sup>a</sup> ICA, intermediate-care area; ICU, intensive care unit.

TABLE 7. Comparison of costs incurred by patients in the two groups

Category	Cost (dollars) incurred per patient in:						<i>P</i> value
	RAST group			ONAST group			
	Mean	Range	SD	Mean	Range	SD	
Laboratory costs	4,732	178–98,314	5,650	6,074	24–169,700	7,111	0.0132
Microbiology costs	843	22–14,949	1,202	1,240	33–17,222	1,515	0.0006
Pharmacy costs	4,181	24–56,539	4,070	5,523	43–111,927	4,930	<0.0005
Antibiotic costs	1,063	28–8,260	809	1,354	33–31,179	1,077	0.0044
Other costs <sup>a</sup>	6,149	521–129,182	8,222	7,659	64–109,098	8,042	0.0269
Total	15,062	1,165–260,187	17,661	19,256	1,780–298,975	21,644	0.0118

<sup>a</sup> Room charges, radiology and nuclear medicine procedures, ventilatory assistance, and respiratory, physical, and nutritional therapy, etc.

groups were compared (Table 6). Again in all eight cases, the test frequency in the RAST group was significantly lower than in the ONAST group. Five different noninvasive diagnostic procedures were tracked (Table 6). The frequencies with which electrocardiograms and computerized tomography (CT) scans were performed were similar in the two groups; however, ultrasound, chest X-ray, and abdominal X-ray were performed significantly less frequently in the RAST group. Finally, days of intubation and days in an intensive or intermediate-care area were compared between the two groups (Table 6). In all three cases, values in the RAST group were statistically significantly lower than in the ONAST group.

Patients in the two groups were compared with respect to the impact of rapid testing on antibiotic therapy. Among the 230 patients in the RAST group who were receiving an antibiotic(s) at the time of the index positive culture, 105 (45.6%) had therapy altered within 24 h of receipt of susceptibility test results; in the ONAST group these figures were 110 of 277 patients (39.7%) ( $P = 0.2046$ ). All 43 patients in the RAST group and all 23 patients in the ONAST group who had not been receiving antibiotics at the time of the index positive cultures had therapy initiated within 24 h of receipt of susceptibility test results. The percentages of patients in both groups who had antibiotics switched, added, or dropped were equivalent (data not shown). So were the percentages of patients changed to oral therapy (data not shown). The frequencies with which changes in therapy appeared to have been predicated on in vitro test results, concerns for toxicity, and/or awareness of cost were not statistically significantly different in the two patient groups (data not shown). The only statistically significant difference related to antibiotic therapy was the mean length of time following recognition of growth in index positive cultures that passed prior to implementation of changes in therapy, i.e., 16.3 h in the RAST group versus 31.2 h in the ONAST group ( $P = < 0.0005$ ).

The results of an analysis of patient costs incurred during hospitalization in the two patient groups are depicted in Table 7. Costs were lumped into one of three categories; laboratory, pharmacy, and all others. In addition, laboratory costs specifically related to microbiology and pharmacy costs specifically related to antibiotics were determined. In all five cases, costs incurred by patients in the RAST group were statistically significantly lower than those in the ONAST group. The total mean cost of hospitalization in the RAST group (\$15,063) was significantly lower than the total mean cost of hospitalization in the ONAST group (\$19,257).

## DISCUSSION

The intent of the current study was to assess the clinical impact of rapid bacterial identification and in vitro susceptibility testing in the setting of an academic medical center referral hospital. We are unaware of previous published studies that have examined this issue. The study was prospective in design and benefitted from a control group of patients who were found to be nearly identical to patients in the study group with respect to numerous demographic characteristics. The single salient difference between the two groups was that patients in the study group had bacterial isolates processed by using a susceptibility and identification test system which generated information on the same day tests were initiated. In the control group, the results of susceptibility test and identification procedures were available on the day following performance of the test.

A routine result reporting scheme was employed whose general features, at least, are comparable to systems used in most tertiary-care hospitals. No effort was made to expedite result reporting. Clearly, the mechanism used to report laboratory results can have a major impact on how information is used (1, 4, 6). By using a routine, fairly typical, and widely applied result reporting scheme, we attempted to eliminate the influence of reporting as a variable on outcome. Furthermore, it was hoped that the results of this study would be generally applicable to other institutions of similar composition and scope of activities.

The two patient populations did not differ with respect to length of hospitalization. Mortality rates, however, both in general and mortality directly attributable to infection, were lower in the rapid test group than in the overnight test group. Length of hospitalization and mortality are extremely crude measures of outcome. In an attempt to examine clinical impact in a more refined manner, the frequencies of various procedures that might be related to disease outcome were compared between the two groups. Among a total of 19 different parameters, in only two cases, i.e., the frequency with which electrocardiograms and CT scans were performed, were the two patient groups found to be the same. In all other cases, significantly fewer procedures were performed among patients in the rapid test group versus those in the overnight test group. These included microbiology tests, subsequent significant positive blood cultures, various other laboratory studies, serum antibiotic assays, several imaging procedures, days of intubation, and length of time spent in either an intensive or intermediate-care area.

We also examined the impact of rapid microbiology testing on antibiotic usage. Interestingly, rapid tests were not found to influence physician selection of therapeutic agents in the context of any of the parameters we tracked. The only difference noted was that in patients in whom a change in therapy was made following performance of laboratory tests, i.e., ca. half of all patients in both groups, the change in therapy was instituted, on the average, ca. 15 h sooner in the rapid test group than in the overnight test group. The mean length of time to a change in therapy was 16.3 h in the former group and 31.2 h in the latter. This difference was highly statistically significant and was roughly comparable to the mean differences between the length of time required to generate test results in the rapid group versus the overnight group for both susceptibility tests and bacterial identification. In other words, the principal benefit of rapid tests on antibiotic therapy was provision of test information sooner so that changes in therapy, when indicated, could be implemented more quickly.

Perhaps not surprising in view of the foregoing, the costs of hospitalization for patients in the two groups varied significantly. Laboratory costs, pharmacy costs, and other general costs were significantly lower in the rapid test group than in the overnight test group. If we amortized the cost savings to patients over a 1-year period in our institution, the total savings would have been \$2,403,162.

Of interest in this study was the observation that despite an apparent impact of rapid microbiology tests on numerous parameters directly and indirectly related to disease outcome, we observed no effect on length of hospitalization. One possible explanation for this observation is that the parameters we assessed were largely related to the outcome of infectious diseases, and that in a tertiary-care teaching medical center where patient acuity is typically high, factors other than infectious disease problems have the greatest influence on length of hospitalization, the most obvious being the underlying diseases that caused patients to be hospitalized in the first place.

In conclusion, the results of the current study suggest that same-day in vitro susceptibility testing and bacterial identification can have a demonstrable clinical impact and are associated with significant cost savings for patients. In addition, rapid testing may be related to lower mortality rates in patients with infection.

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