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Frequency of Microbiologically Correct Antibiotic Therapy Increased by Infectious Disease Consultations and Microbiological Results

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In a prospective observational study of bacteremic patients we ascertained the influence of different parts of culture results on the correctness of empirical antibiotic therapy. Ninety-three bacteremic patients requiring antibiotic treatment were included. Patients who had consultations with an infectious disease consultation service before they became bacteremic received microbiologically correct empirical antibiotic therapy more often than those who did not have such consultations (75% versus 53%; $P = 0.03$). As a direct result of Gram staining, 92% of all patients received microbiologically correct antibiotic therapy.

Severe sepsis is a major health care problem, affecting millions of patients each year. The incidence of sepsis and septic shock is increasing, and the mortality rate is 25% (2). Byl et al. have shown that results of blood culture identification and susceptibility increase appropriate antibiotic treatment significantly, from 63% to 94%, and that empirical therapy is significantly more often correct if prescribed by infectious disease specialists (1).

We performed an observational prospective cohort study of positive blood cultures to determine which part of the culture results—Gram stain from positive blood cultures or identification or susceptibility of the microorganisms—was most influential on antibiotic treatment. Furthermore, the effect of infectious disease consultations on the correctness of empirical therapy was measured.

The Erasmus Medical Center (MC) is a 1,200-bed tertiary-care university medical center. The Department of Medical Microbiology and Infectious Diseases has its laboratory integrated with an active infectious disease (ID) consultation service run by a team of medical microbiologists and infectious disease specialists, including residents in training. This ID consultation service operates 24 hours a day, 7 days a week. The ID consultants actively trace the attending physician in case of a positive blood culture and recommend antibiotic treatment. ID consultants are also frequently consulted for advice on empirical treatment.

Blood cultures were processed with the Bactec system (Becton Dickinson, Sparks, MD). Identification and susceptibility testing were performed with the Vitek system (1 or 2; bioMérieux, Marcy l'Étoile, France). During the off-shift, no blood culture bottles were processed and no identification or susceptibility results were made available.

A total of 171 consecutive patients were included; patients could be included only once. A questionnaire was filled in by ID consultants at the time of consultancy, generated by each consecutive culture result. Collected data included the timing of consultation in relation to the culture result for each consultancy continuation or changing antibiotic therapy and whether there had been any previous consultation before determination of a positive blood culture. Information on microbiological culture results, age, sex, department of stay, underlying diseases, antibiotic use, and infections during the hospital stay was collected from the hospital information system or from the medical records. Infections were classified using the CDC definitions of health care-associated infections (3).

Microbiologically correct therapy was defined by comparing the susceptibility results with the given or advised antibiotics at the following time points: before any laboratory result was available, when the result of a Gram stain from a positive blood culture was available, when identification of the isolate was completed, and when its antimicrobial susceptibility profile was available. If the isolate was susceptible to the advised/given therapy, this therapy was considered microbiologically correct.

Advice on antibiotic therapy was grouped into one of seven categories: do not give antimicrobial therapy, start therapy, continue current therapy, streamline (change to smaller spectrum), broaden (change to broader spectrum), switch to a different regimen (change other than streamlining or broadening), and stop therapy.

Advice was classified as "followed up" when the antibiotic was changed, started, or stopped before the next microbiological result became available or within 24 h after susceptibility results were made available.

The study was part of a former study (4) and was approved by the Medical Ethics Committee of the Erasmus MC; therefore, no informed consent was required.

Patient characteristics, culture isolates, and infections were analyzed by Fisher's exact test (noncontinuous variables) and *t* tests (continuous variables) for differences between patients receiving prior ID consultations and patients without prior ID consultations (SPSS 16.0 for Windows). Differences in the percentage of correct antibiotic therapy were analyzed by chi-

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square tests between patients receiving prior ID consultations and patients without prior ID consultations (http://faculty.vassar.edu/lowry/VassarStats.html). Differences between empirical correct therapy and correct advised therapy after Gram stain results, when available, were analyzed by the McNemar test for paired samples. A P value of <0.05 was considered significant.

From January 2002 until May 2002, 171 questionnaires were distributed. Of these 171 patients, 93 patients had a bloodstream infection requiring antibiotic treatment, 16 had a bloodstream infection not requiring antibiotic treatment, 46 had no infection, and 16 did not fill in the questionnaire.

Table 1 shows the baseline patient characteristics at inclusion stratified by patients without and patients with prior ID consultation. Clearly, the two groups differed, with patients with severe underlying diseases having more often received a consultation from an ID physician.

From all 93 available Gram stain results, follow-up data were available for the advice given by the ID consultant. From 27 of 30 results of "identification only," follow-up data for advice were available (3 were lost to follow-up), whereas these data were available for 61 of 63 combined identification and susceptibility results (2 were lost to follow-up) and in 23 of 30 susceptibility-alone results (7 were lost to follow-up). Therefore, 204 advisories were available for analysis. After Gram stain results became available, advised therapy was found to be microbiologically correct in 86 of 93 results (92%). The difference with empirical therapy is statistically significant ($P < 0.001$). For identification alone, identification and susceptibility combined, and susceptibility alone, these percentages were 100%, 97%, and 100%, respectively. These percentages are not statistically different compared to the Gram stain result. Nine of the 204 advisories given were not followed. Empirical therapy without prior ID consultation was microbiologically correct in 26 of 49 (53%) cases compared to 33 of 44 (75%) cases with prior ID consultation ($P = 0.03$).

Figure 1 shows the categories of advice given after each laboratory result. The Gram stain accounted for 17/21(81%) of "start therapy" advisories given, 9/11 (82%) of "broaden therapy" advisories given, and 12/19 (63%) of "different therapy" advisories given.

Of the 204 advisories given based on microbiological results, 9 were not correct. In four patients, advice based on the Gram stain result did not cover resistant Gram-negative organisms; in addition, advice to withhold therapy was not correct for two patients who turned out to have *Staphylococcus aureus* bloodstream infection and for one patient with *Candida albicans* infection. After identification and susceptibility results became available in the case of one patient with an infection by a gentamicin-susceptible but amoxicillin-clavulanic acid-resistant *Escherichia coli* strain, the advice of an ID resident was to stop the gentamicin and continue the amoxicillin-clavulanic acid, advice which was later corrected by a supervisor, and one patient with *Klebsiella pneumoniae* thrombophlebitis was erroneously treated with vancomycin and a single dose of gentamicin.

This study has limitations. It is a single-center, observational study which excluded patients who died before Gram stain results were available. We chose to include only true infections requiring antibiotic therapy. The results were retrospectively assessed; therefore, mortality in relation to adequate antibiotic therapy could not be analyzed. The effect of prior infectious disease consultations on empirical therapy is confounded by the fact that some departments, including hematology and the intensive care unit, were visited routinely by the ID consultants and, therefore, empirical therapy was more likely to be based on advice given by the ID consultant. The number of patients included is too small to correct for this and other potential confounding factors.

TABLE 1 Patient characteristics

Characteristic	No. (%)[a] of patients with: No prior ID consultation ($n = 49$)	Prior ID consultation ($n = 44$)	P value
Mean age (yr) (±SD)	42 (15)	47 (15)	0.18
Male sex	35 (71)	30 (68)	0.74
Ward			0.23
Medicine	21 (43)	23 (52)	
Surgery	13 (27)	5 (11)	
Emergency department	10 (20)	8 (18)	
Intensive care unit	5 (10)	8 (18)	
Major clinical syndrome or sign			
Diabetes mellitus	2 (4)	10 (23)	0.011
Hematological malignancy	0 (0)	7 (16)	0.004
Solid malignancy	14 (29)	4 (9)	0.020
Solid organ transplantation	5 (10)	5 (11)	0.86
HIV positivity	0 (0)	2 (5)	0.22
Neutropenia	0 (0)	9 (20)	0.001
Ventilator support	1 (2)	11 (25)	0.001
McCabe score			0.80
Nonfatal	23 (47)	18 (41)	
Possibly fatal	19 (39)	21 (48)	
Ultimately fatal	6 (12)	5 (11)	
Rapidly fatal	1 (2)	0 (0)	
Type of infection			0.54
Urinary tract	12 (24)	9 (20)	
Intravenous catheter related	4 (8)	9 (20)	
Endocarditis	2 (4)	2 (5)	
Respiratory tract	3 (6)	2 (5)	
Intra-abdominal	14 (29)	7 (16)	
Skin	2 (4)	1 (2)	
Central nervous system	1 (2)	3 (7)	
Arthritis	1 (2)	0 (0)	
Bloodstream of unknown origin	10 (20)	11 (25)	
Type of microorganism			0.24
CoNS	1 (2)	6 (14)	
Staphylococcus aureus	6 (12)	2 (5)	
Streptococcus pneumoniae	2 (4)	4 (9)	
Enterococci	1 (2)	2 (5)	
Other Gram-positive organisms	9 (18)	4 (9)	
Enterobacteriaceae	22 (45)	19 (43)	
Nonfermentative bacilli	1 (2)	1 (2)	
Other Gram-negative bacilli	2 (4)	1 (2)	
Yeast	2 (4)	1 (2)	
Mixed infection	3 (6)	5 (11)	

[a] Values are no. (%) unless otherwise indicated.

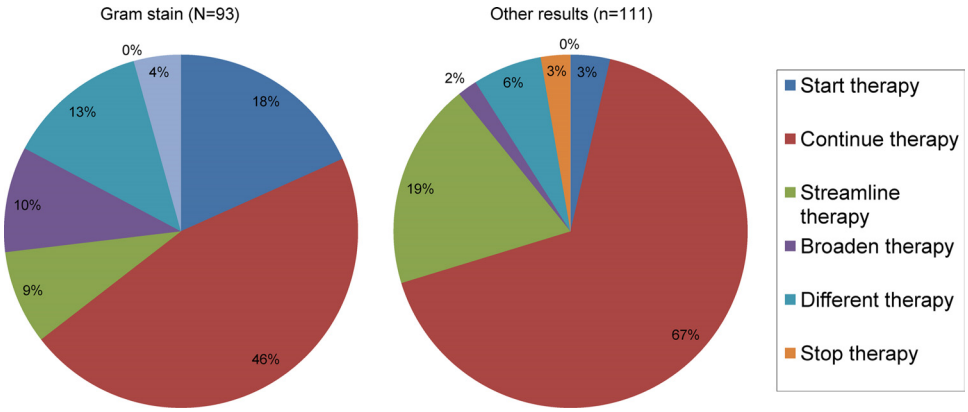

FIG 1 Antibiotic therapy changes as advised by ID consultants after laboratory results became available.

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REFERENCES

1. **Byl B, et al.** 1999. Impact of infectious diseases specialists and microbiological data on the appropriateness of antimicrobial therapy for bacteremia. Clin. Infect. Dis. **29**:60–66.
2. **Dellinger RP, et al.** 2008. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit. Care Med. **36**:296–327.
3. **Horan TC, Andrus M, Dudeck MA.** 2008. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am. J. Infect. Control **36**: 309–332.
4. **Kerremans JJ, et al.** 2008. Rapid identification and antimicrobial susceptibility testing reduce antibiotic use and accelerate pathogen-directed antibiotic use. J. Antimicrob. Chemother. **61**:428–435.