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Bacteremia After Genitourinary Tract Manipulation: Bacteriological Aspects and Evaluation of Various Blood Culture Systems

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A total of 300 patients undergoing various types of urological procedures was studied for incidence of bacteremia. An osmotically stabilized anaerobic broth with sodium polyanethol sulfonate (Liquoid) yielded more positive blood cultures than any other culture system and was also the best system by far for recovery of anaerobes. The membrane filter showed faster growth and, therefore, facilitated faster identification of the infecting organism. There was a 31% incidence of bacteremia in the patients having transurethral resection of the prostate, 17% in the cystoscopy group, 24% in the urethral dilation group, and 8% in the urethral catheterization group. The organisms found most frequently isolated in blood cultures were enterococci and *Klebsiella pneumoniae*. Notable were a relatively large number of anaerobes and two protoplasts. The major source of the bacteremia was previous urinary tract infection, but evidence is presented which indicates that the prostate gland and the normal urethral flora are other significant sources.

Even with the availability of a number of potent antibacterial drugs, the mortality in bacteremia is presently still 20 to 25%, and, when shock accompanies sepsis, the mortality rate is 60 to 80% (9, 10, 15, 21). The most common portal of entry for bacteremia is the genitourinary tract (10, 11, 14-18, 20). This is particularly true for gram-negative bacillary sepsis. Gram-negative bacteremia also carries a higher risk of shock and fatal outcome than does bacteremia due to gram-positive organisms. Various manipulations of the genitourinary tract, necessary for the diagnosis and management of infectious and noninfectious disease involving this system, may result in bacteremia.

There is evidence which indicates that the major factor which may lead to better recovery rates in bacteremia is early administration of appropriate antibacterial therapy. Therefore, it is imperative that one diagnose bacteremia and identify the infecting organism as rapidly as possible. Standard methods for recovery of bacteria from the blood are inadequate in that they usually require several days for growth and identification of the infecting agent. The results of previous studies in this laboratory indicate that a membrane-filter blood-culturing system expedites recovery and identification of bacteria and that the use of three systems (membrane filter, broth culture, and pour plate) increases the total yield of positives (7). Another study indicates that incorporation of an anticoagulant, sodium polyanethol sulfonate (Liquoid [LIQ]), in the broth leads to improved recovery, primarily by virtue of neutralizing normal antibacterial substances and certain antibiotics in the blood (8).

Previous studies on the incidence of bacteremia after urinary tract surgery or manipulation did not always use optimum bacteriological techniques (when the information given on methods used was adequate to make a decision on this point). Some workers used citrate for collection of the blood or in the broth itself; this compound is now known to be inhibitory to some organisms under certain conditions. The broths used would not be considered to be nutritionally adequate by current standards. There was not always adequate dilution of blood. The total volume of blood sampled never exceeded 15 ml and was only 5 ml in

some cases. LIQ was not used in any of these studies. In one case, it was mentioned that the blood was inoculated into broth within a few hours after it was obtained! Duration of incubation of cultures was not always adequate. In several cases, obvious contaminants such as coagulase-negative staphylococci or micrococci were counted as positive blood cultures without justification. Although pour plates were used by some groups, quantitative data was not always given. Concomitant premanipulation urine cultures were not always done.

Accordingly, the present study was undertaken to reassess the incidence of bacteremia after urological procedures and to attempt to determine the sources of this bacteremia.

MATERIALS AND METHODS

Patient selection. Four categories of genitourinary tract manipulation were studied. Of the total of 300 patients, 77 patients had transurethral resection (TUR) of the prostate, 81 had cystoscopy, 67 had urethral dilation, and 75 had urethral catheterization. Nineteen of the TUR prostate patients received antimicrobial prophylaxis and three patients from the catheterization group and two from the urethral dilation group were being treated with antimicrobial drugs at the time of the procedure. All patients were male and no patients were receiving corticosteroids, immunosuppressive drugs, radiation, or antineoplastic therapy.

It was not possible to do all cases consecutively, but patients for study were selected randomly.

Collection of specimens. A 10-ml amount of blood was collected immediately before the manipulation, and 30 ml was drawn immediately after the manipulation. The premanipulation specimen was inoculated into Trypticase Soy Broth (TSB) with 10% CO_2 and anaerobic broth with LIQ (0.05%) which had been osmotically stabilized with 16% sucrose and magnesium sulfate (OS with LIQ) (H. R. Attebery and S. M. Finegold. 1970. A new anaerobic blood culture system, p. 105. Proc. X Int. Congr. Microbiol. Mexico City, Abstr. Eg-8). Five milliliters of blood was placed into each bottle. The postmanipulation blood specimen was distributed in 5-ml portions to four types of broths—TSB, OS with LIQ, anaerobic broth without LIQ or osmotic stabilizers added (ANAER), and OS without LIQ (OS). All bottles contained 100 ml of broth. The other 10 ml of blood was injected into a vacuum tube containing a 0.5% solution of LIQ. This blood was used for a membrane-filter culture (5 ml) and for five 1-ml pour plates. Penicillinase and *p*-aminobenzoic acid were added to each system when indicated.

The blood was collected via a closed system (Fig. 1) which allowed for prompt transfer of blood from the patient to each unit of the culturing system. This system also minimized the risk of contamination and of entry of air.

Urine was obtained for quantitative culture prior to the manipulation. This specimen was collected through the resectoscope (TUR prostate patients), cystoscope (cystoscopy patients), through the filiform or by mid-stream voided collection (dilation patients), or by catheter (catheterized patients). We were unable to get urine specimens for culture from 2 TUR prostate patients, 2 cystoscopy patients, 19 dilation patients, and 1 patient in the catheterization group.

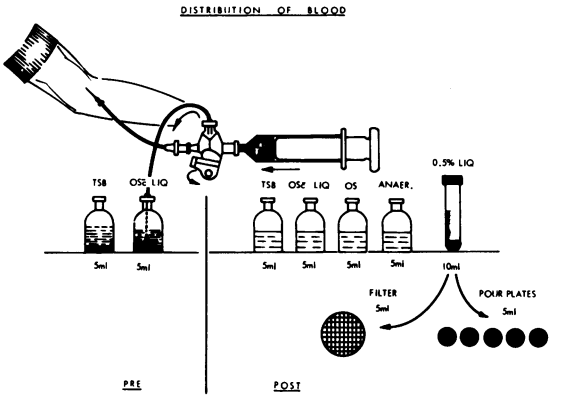

FIG. 1. *Scheme and setup for distribution of blood.*

Bacteriological methods. The broth bottles already contained the appropriate atmospheres and were therefore incubated in a conventional incubator.

A 5-ml amount was withdrawn from the vacuum tube and used for a membrane-filter culture. The blood was lysed and then filtered through a 90-mm, 0.45-μm membrane filter by using a vacuum of 20 to 25 inches. One hundred milliliters of normal saline was then aspirated through the filter to wash away normal antibacterial factors in the blood and antimicrobials the patient may have been receiving at the time of the culture. The filter was then cut in quarters and placed on the following media: blood-agar plate (BAP) in 10% CO_2, chocolate-agar plate in 10% CO_2, BAP aerobically, and eosin-methylene blue-agar (EMB) aerobically.

The remaining 5 ml of blood was used for pour plates. A 1-ml amount of blood was added to each of five tubes containing 19 ml of melted, cooled Brucella agar (Pfizer). The five pour plates were incubated as follows: two plates anaerobically, two plates in 10% CO_2, and one plate aerobically.

All setups were incubated at 37 C at the same time and were examined visually for growth after 18 to 24 hr of incubation and every 24 hr thereafter for 10 days. At the end of 21 days, the broth cultures were streaked out, incubated in various atmospheres, and discarded if negative. In the case of OS with LIQ, subcultures included osmotically stabilized agar plates.

Growth on filters and in pour plates was quantitated.

Coagulase-negative staphylococci or micrococci were considered contaminants except in two instances where significant counts of the same organ-

isms were recovered from urine cultures. Aerobic diphtheroids and *Propionibacterium acnes* were considered to be contaminants except for two cultures of *P. acnes* recovered as protoplasts. *Bacillus* species were regarded as contaminants.

A 0.001-ml loop was used for quantitating urine cultures. BAP, EMB, nutrient agar, and selective enterococcus agar (Pfizer) were the media employed. Only counts of 10^4 per ml or greater were considered to be significant.

Ten samples of irrigating fluid and 10 of various instruments were cultured. One milliliter of irrigating fluid was incorporated into 19-ml Brucella agar deeps (Pfizer), and pour plates were made. The instruments were streaked across the surface of BAP.

All organisms recovered were isolated and identified by conventional tests and schemes.

Gas chromatographic analysis. The OS broth culture was used for gas chromatographic studies in the hope of detecting bacterial metabolites before growth became apparent visually. Samples (2 ml) of this culture were taken at 0, 6, 18, 24, and 48 hr and were added to 0.2 ml of 10% H_2SO_4. After being mixed, the specimens were allowed to stand for 10 min and were then centrifuged for 30 min at 2,000 rev/min. The supernatant fluid was analyzed in Varian gas chromatographs with stainless-steel and Pyrex columns packed with 10% carbowax terminated with terephthalic acid on Chromosorb (60/80 mesh) and with 6% FFAP on Porapak Q (80/100 mesh) by using flame ionization, thermal conductivity, and electron capture detectors.

RESULTS

Five of the premanipulation blood cultures were positive (two in the TUR prostate group and one each in the other three groups). Organisms isolated were always identical to those in postmanipulation blood cultures and in urine cultures when these other sources were positive. All of the data presented subsequently are from postmanipulation blood cultures.

A comparison of the various blood culturing systems is given in Table 1. The OS broth is not listed because it was used primarily for chromatographic analysis. The anaerobic osmotically stabilized broth plus LIQ provided significantly more positives than any other system. The membrane filter gave faster growth in nine cases (and also facilitated more rapid identification of organisms since growth was first present in the form of colonies).

Tables 2–5 give the results of the postmanipulation blood cultures and of the urine cultures for each group studied. The correlation of positive blood and urine cultures was striking. There was a 7 to 52% chance of getting bacteremia, depending on the type of procedure, if a urinary tract infection was present. The two groups with the highest risk were the TUR prostate (52%) and dilation (40%).

TABLE 1. *Comparison of blood culturing systems*

System	Total no. of positives[a]	No. with faster growth[b]	No. positive only in this system[c]
Membrane filters	23	9	8
Pour plates	27	7	9
Trypticase Soy Broth with 10% carbon dioxide	24	1	8
Anaerobic broth	27	2	9[d]
Anaerobic broth osmotically stabilized plus Liquoid	43	2	20[e]

[a] In multiple bacteremia, each organism is counted as a positive.

[b] In case of tie, both systems with growth faster than a third system are counted.

[c] In cases of double bacteremia with one organism in one system and the other organism in a different system, both systems are counted.

[d] Includes one anaerobe.

[e] Includes eight anaerobes and two protoplasts of *P. acnes*. One additional anaerobe grew in both anaerobic broth and osmotically stabilized anaerobic broth and another grew in both of these plus Trypticase Soy Broth and a pour plate (incubated anaerobically).

Another factor contributing to the likelihood of bacteremia was the presence of prostatitis demonstrated histologically in the resected tissue of patients undergoing TUR prostate. Patients with bacteremia had a 60% incidence of prostatitis compared to patients without bacteremia, only 31% of whom showed prostatitis. This difference was significant statistically, with a P value of < 0.05.

Table 6 summarizes the frequency with which the various types of bacteria were found in the postmanipulation blood cultures. There were 16 instances of bacteremia with two or more organisms isolated from the same blood culture out of the total of 60 positive blood cultures. *Enterococcus* and *Klebsiella* were the most frequently encountered organisms. Of note was the recovery of 11 anaerobic or microaerophilic bacteria and of two protoplasts (of *Propionibacterium acnes*).

None of the irrigating fluids or instruments yielded any growth.

Although such end products of bacterial metabolism as volatile fatty acids and acetoin were detected in some positive blood cultures, in no instance were such compounds present before cultures were positive by gross inspection.

TABLE 2. *Incidence of bacteremia in patients undergoing transurethral resection of the prostate*

Determination	Total no.	No. of patients with positive urine and negative blood cultures	No. of patients with positive blood and negative urine cultures	No. of patients with different organisms in blood and urine cultures	No. of patients with same bacteria in urine and blood cultures	No. of patients on antimicrobial therapy or prophylaxis
Positive blood cultures	24 (31%)		7	2	15	5
Negative blood cultures	53	15				14
Total	77	15	7	2	15	19

TABLE 3. *Incidence of bacteremia in patients undergoing cystoscopy*

Determination	Total no.	No. of patients with positive urine and negative blood cultures	No. of patients with positive blood and negative urine cultures	No. of patients with different organisms in blood and urine cultures	No. of patients with same bacteria in urine and blood cultures	No. of patients on antimicrobial therapy or prophylaxis
Positive blood cultures	14 (17%)		6	3	5	0
Negative blood cultures	67	18				0
Total	81	18	6	3	5	0

TABLE 4. *Incidence of bacteremia in patients undergoing urethral dilatation*

Determination	Total no.	No. of patients with positive urine and negative blood cultures	No. of patients with positive blood and negative urine cultures	No. of patients with different organisms in blood and urine cultures	No. of patients with same bacteria in urine and blood cultures	No. of patients on antimicrobial therapy or prophylaxis
Positive blood cultures	16 (24%)		3[a]	4	5	0
Negative blood cultures	51	12				2
Total	67	12	3	4	5	2

[a] Four patients with positive blood cultures did not have urine cultures done.

DISCUSSION

The anaerobic broth osmotically stabilized with sucrose and magnesium sulfate plus 0.05% LIQ yielded the most positive cultures (a total of 43), 20 of which were positive only in this system. The membrane filter showed growth earliest more often than did the other systems and provided opportunities for more rapid identification of the infecting organism. It was also very useful in detection of multiple organism bacteremia (present in 26% of our positive cultures) and should be advantageous in blood cultures from patients who are receiving antimicrobial agents which cannot be inactivated.

The isolation of two organisms in the protoplast form is interesting although the significance of these particular isolates (which reverted to *P. acnes*) is uncertain. Of greater interest is the impressive yield of organisms (both aerobic and anaerobic) in the osmotically stabilized anaerobic broth with LIQ, as compared to the other systems. Unpublished data

TABLE 5. *Incidence of bacteremia in patients undergoing urethral catheterization*

Determination	Total no.	No. of patients with positive urine and negative blood cultures	No. of patients with positive blood and negative urine cultures	No. of patients with different organisms in blood and urine cultures	No. of patients with same bacteria in urine and blood cultures	No. of patients on antimicrobial therapy or prophylaxis
Positive blood cultures	6 (8%)		4	0	2	0
Negative blood cultures	69	13				3
Total	75	13	4	0	2	3

TABLE 6. *Significant organisms recovered*

Organism	No. of times present	No. of positive pour plates, filter, or both	Avg no. of cols./ml of blood when positive
Enterococcus	17	10	1.4
Klebsiella pneumoniae ...	14	6	84.3
Viridans streptococcus ..	6	2	0.8
Pseudomonas aeruginosa .	6	6	10.3
Proteus mirabilis	6	5	1.1
Escherichia coli	4	3	8.2
Group A β-hemolytic streptococcus	3	2	0.8
Anaerobic gram-positive cocci	3	0	
Peptostreptococcus	2	1	0.2
Coagulase-negative *Staphylococcus* or *Micrococcus*	2	2	0.2
Staphylococcus aureus ...	2	1	7.6
Protoplasts of *Propionibacterium acnes*	2	0	
Enterobacter aerogenes ..	1	1	0.2
Pseudomonas sp.	1	1	0.9
Flavobacterium	1	1	0.4
Unidentified non-fermenting GNR	1	1	0.2
Bacteroides melaninogenicus	1	0	
Bacteroides sp.	1	0	
Bifidobacterium adolescentis	1	0	
Propionibacterium avidum	1	0	
Veillonella parvula	1	1	0.2
Microaerophilic streptococcus	1	0	

in our laboratory indicate that the sucrose and magnesium sulfate, rather than the LIQ, account for the difference. This suggests that a number of bacteria in blood may have defective cell walls (even in the absence of antibiotic therapy) so that they are unable to survive in conventional (not osmotically stabilized) media on first isolation (although they will survive subculture to such media). However, it is also possible that entirely different reasons exist for better recovery of bacteria in this type of medium. Rosner (Symp. Bacteremia, Amer. Soc. Microbiol. Annu. Meet., Minneapolis, 1971) recently indicated that he has had comparably good results with media of high sucrose content.

Recovery of a relatively large number of anaerobes in these patients is consistent with the presence of these organisms in the normal urethral flora (6), particularly since 8 of the 11 anaerobic or microaerophilic isolates were recovered after urethral dilation. Mencher and Leiter (17) reported clostridial sepsis after urologic surgery. The use of special anaerobic broth media, made under prereduced conditions and bottled with a self-contained anaerobic atmosphere, undoubtedly facilitated recovery of these organisms. (They were found in only one instance in pour plates incubated anaerobically.)

The incidence of bacteremia in TUR prostate patients has varied from 1.6 to 66.7% in various series in the literature (2, 4, 5, 12, 13, 16); in our study it was 31%. In our series, the risk of bacteremia was 52% in patients with urinary tract infection, and the organisms found in the blood usually were the same as those in the urine. Strong correlation between urinary tract infection and bacteremia after prostate surgery has also been noted by others (2, 5, 12, 16) although the number of cases studied fully was very small, except in the series of Creevy and Feeney (5).

In the case of the other procedures, the incidence of bacteremia was lower in our study (8 to 24%), and underlying urinary tract infection was also important. The association was statistically significant in the urethral dilation

and cystoscopy groups, as it was in the TUR prostate group. There are fewer data in the literature on bacteremia after these other procedures, but urethral dilatation, in particular, has been noted to predispose to bacteremia (1, 19).

Aside from urinary tract infection and normal urethral flora, another potentially important source of organisms for bacteremia is the prostate gland itself in the case of prostatic surgery. Kidd and Burnside (12) have commented on this association; in two cases, they isolated the same organisms from resected prostatic tissue as were isolated from the blood (with urine cultures negative in both cases). A fourth potential source of organisms would be instruments and irrigating fluid; our cultures of these materials were negative. Buckle (3) and Miller et al. (16) also concluded that instruments, gloves, and external genitalia were unlikely sources of bacteremia.

It is unfortunate that gas chromatography did not prove useful in expediting detection of bacteremia in this study. Perhaps use of other media would give better results.

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