

Septicemia due to coagulase-negative *Staphylococcus* in a community hospital

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The experience with septicemia due to coagulase-negative *Staphylococcus* at a 623-bed primary care hospital between 1980 and 1984 was reviewed. A total of 38 episodes in 37 patients were documented; data were available on 37 episodes in 36 patients. The organism accounted for 3.8% of all cases of septicemia and 6.7% of cases of nosocomial septicemia and was associated with 0.03% of all admissions. The incidence remained stable over the 5 years. The rate of survival 28 days after the episode was 78%. Most of the episodes (31) originated from infected vascular access sites. Of the 37 isolates 15 (41%), all *S. epidermidis*, were slime producing. *S. epidermidis* accounted for 33 of the isolates; of the 33, 5 were methicillin-resistant and slime producing. Various in-vitro susceptibility testing methods and testing for β -lactamase production yielded conflicting results. Methicillin resistance, slime production and speciation as *S. epidermidis* were not confirmed as virulence markers. Five patients with methicillin-resistant organisms were treated with cephalosporins, and all recovered. These findings as well as examination of the literature do not support the recommendations that laboratories report such isolates as resistant to all β -lactam agents and that vancomycin be given in all such infections. The different case mix in community hospitals as compared with university centres results in different patterns of nosocomial infection. Since the community hospital patient population is much larger, more information on the patterns of infections in these centres is needed.

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Revue des cas de septicémie à staphylocoques coagulase-négatif survenus de 1980 à 1984 dans un hôpital général de 623 lits. On enregistre 38 faits chez 37 malades; pour 37 faits chez 36 malades on dispose de données suffisantes. Ce genre de microbe est en cause dans 3,8% de toutes les septicémies (6,7% des septicémies nosocomiales) et survient lors de 0,03% de toutes les hospitalisations. Cette fréquence reste égale sur les 5 ans. Le taux de survie 28 jours après le fait est 78%. La plupart des septicémies (soit 31) proviennent d'une sonde vasculaire infectée. Parmi les 37 souches microbiennes qui ont été isolées, on trouve 33 *S. epidermidis* dont 15 (soit 41% de l'ensemble) sont mucoides. Dans cinq cas le germe est à la fois méthicillino-résistant et mucöïde. Les diverses épreuves in vitro de sensibilité aux antibiotiques et de production de β -lactamase donnent des résultats divergents. Ni la méthicillino-résistance, ni le caractère mucöïde, ni la détermination spécifique d'un germe comme *S. epidermidis* n'en signe la pathogénicité. Les cinq porteurs de germes méthicillino-résistants, traités aux céphalosporines, guériront. Ceci, joint à une étude de la littérature, met en doute la sagesse de la pratique, dans certains laboratoires, de rapporter de telles souches comme résistantes à tous les β -lactames et justifiables d'un traitement par la vancomycine. Tout comme l'assortiment des cas, le génie des infections nosocomiales diffère selon qu'on se trouve dans un hôpital général ou dans un hôpital universitaire. Comme il y a beaucoup plus de malades dans les hôpitaux généraux, on a besoin de mieux y connaître ce genre d'infection.

Coagulase-negative *Staphylococcus* is increasingly recognized as an important pathogen,¹⁻³ accounting for up to 4% of nosocomial infections.⁴ A death rate of 46% has been reported among surgical patients.⁵ Two important

points have been emphasized. First, only two-thirds of patients with bloodstream infections due to coagulase-negative *Staphylococcus* are alive 28 days after the episode of sepsis.³ Second, all coagulase-negative *Staphylococcus* isolates resistant to methicillin should be considered resistant to all β -lactam antibiotics regardless of the results of in-vitro susceptibility testing, and patients with such infections should be treated with vancomycin.²

This picture of septicemia due to coagulase-negative *Staphylococcus* as a life-threatening disease necessitating aggressive therapy has emerged mainly from university hospitals. However, 72% of Ontario hospital beds are in community general hospitals (Ontario Hospital Association: personal communication). Toronto East General and Orthopaedic Hospital is a 623-bed primary care hospital that offers a full range of medical and surgical care but lacks specialized units (e.g., for cardiac surgery, neurosurgery and hemodialysis). Any differences noted in the pattern at our hospital are significant in that this information may better reflect the characteristics of a much larger patient population. The experience with septicemia due to coagulase-negative *Staphylococcus* over 5 years at this hospital was reviewed to compare it with published findings from teaching hospitals.

Methods

All blood cultures that yielded coagulase-negative *Staphylococcus* identified in the Toronto East General and Orthopaedic Hospital's diagnostic laboratory between 1980 and 1984 were reviewed for clinical significance. Septicemia was defined as a new clinical episode of serious infection accompanied by one or more positive blood cultures. Infections were considered to be nosocomial if the onset occurred at least 48 hours after admission.

Blood cultures were processed by means of the BACTEC radiometric method (Johnston Laboratories, Towson, Maryland). Organisms were identified with Taxo A bacitracin discs (Baltimore Biological Laboratories, Cockeysville, Md.), Microdase oxidase discs (Regional Media Laboratories Inc.,

Lenexa, Kansas), Staph Trac (DMS Laboratories Inc., Flemington, New Jersey) and Staph-Ident (Analytab Products, Plainview, New York).⁶ Slime production was tested by means of a tube method, as described by Christensen and colleagues.⁷ Testing for β -lactamase production was performed by means of the rapid paper iodometric method.⁸

Susceptibility testing was performed by means of the modified Kirby-Bauer method, agar dilution on Diagnostic Sensitivity Test agar (Oxoid Inc., Basingstoke, England) with an inoculum of 10^5 colony-forming units (cfu)/spot and microdilution (Micro-media panels [Beckman Instruments Inc., Carlsbad, California]) with an inoculum of 10^5 cfu/ml. All plates and panels were incubated at 35°C. *S. aureus* strains ATCC 29213 and ATCC 25923 were included as controls.

All isolates were further tested for methicillin resistance by plating 10^7 cfu of inoculum onto Mueller-Hinton agar containing 20 mg/L of methicillin. The plates were incubated at 35°C for 72 hours.

Results

Over the study period 38 episodes of septicemia due to coagulase-negative *Staphylococcus* were documented in 37 patients. All but two episodes were associated with more than one positive blood culture. The organism accounted for 3.8% of all cases of septicemia and 6.7% of cases of nosocomial septicemia and was associated with 0.03% of all admissions. There was no trend toward increasing incidence of this infection. Most of the episodes (34) were hospital acquired.

Data were available on 37 episodes in 36 patients, 24 men and 12 women with a mean age of 60.3 (extremes 25 and 84) years. Twenty-one patients were on surgical services and 15 on medical services; 10 (28%) were in critical care units. Three patients died within 48 hours; after 28 days 28 (78%) were still alive.

Most (31) of the episodes of septicemia originated from an infected vascular access site. The mortality associated with the various sources is shown in Table I.

Most of the isolates (33) were *S. epidermidis*; 3

Table I — Source of septicemia due to *Staphylococcus* in 37 episodes at a primary care hospital between 1980 and 1984

Source	Total no. of episodes	No. (and %) of episodes in which patient died within 28 days
Infected vascular access site	31	5 (16)
Central venous catheter	24	2 (8)
Swan-Ganz catheter	4	2 (50)
Temporary pacemaker	2	1 (50)
Peripheral intravenous cannula	1	0 (0)
Endocarditis (native valves)	2	1 (50)
Ascending cholangitis	1	0 (0)
Unknown	3	2 (67)

were *S. hominis* and 1 was *S. haemolyticus*. Slime production was detected in 15 isolates (41%), all *S. epidermidis*. Only one death was related to a slime-producing organism; the patient had had a massive myocardial infarction and died 13 days after the onset of septicemia. Only 5 of the episodes (14%) were caused by methicillin-resistant slime-producing strains of *S. epidermidis*.

With the microdilution method most isolates were found to be resistant to penicillin and ampicillin and about half to be resistant to semisynthetic penicillins, erythromycin and clindamycin (Table II). Only one isolate was resistant to cephalothin.

With methicillin susceptibility defined as complete absence of growth from a large inoculum on agar containing 20 mg/L of methicillin, 15 (42%) of 36 isolates were resistant (4 of the 15 produced fewer than four colonies). With this screen plate used as the standard, the plate containing oxacillin (2 mg/L) missed 6 (40%) of the 15, and microdilution missed 11 (73%) of the 15 at 24 hours and 5 (33%) of the 15 at 48 hours. However, eight isolates were found to be susceptible on the screen plate yet resistant to oxacillin with the Kirby-Bauer and agar dilution methods and to methicillin by microdilution (minimum inhibitory concentration greater than 16 mg/L).

With a cutoff point of 0.12 mg/L, 5 (56%) of 9 isolates susceptible to penicillin with the microdilution technique were found to produce β -lactamase. Raising the cutoff point to 0.25 mg/L made minimal difference: 8 (67%) of 12 isolates were found to produce β -lactamase. The agar

dilution method with a penicillin concentration of 0.075 mg/L classified all but 1 of 28 β -lactamase producers as resistant.

Five patients with organisms resistant to methicillin were treated with cephalosporin monotherapy, and all recovered; treatment consisted of cefazolin, 4 g/d for 2, 4 or 9 days, cephalothin, 12 g/d for 8 days, or cefoxitin, 12 g/d for 10 days. This treatment had been selected by the attending physicians on the basis of the clinical and laboratory findings available at the time. All isolates were inhibited in vitro by the drugs. In all five patients the septicemia had originated from an infected vascular access site.

Of the aminoglycosides, netilmicin and amikacin showed the greatest activity, 97% and 92% of the isolates respectively being susceptible, compared with 62% for gentamicin and 46% for tobramycin. Two (5%) of the isolates were susceptible only to netilmicin (Tables III and IV).

Discussion

Septicemia due to coagulase-negative *Staphylococcus* in this community hospital was associated with only 0.03% of admissions, compared with 0.07% in a large teaching hospital.³ The incidence remained stable over the 5 years of the study.

The survival rate after 28 days in the study, 78%, is almost identical to that reported by Ponce de Leon and Wenzel.³ The death rate at 1 week was also similar to that found by these authors (14% v 9%) and was close to that reported by Christensen and coworkers,¹ 15%. In my study 89% of isolates were identified as *S. epidermidis*; Sewell and associates⁹ found 93% of clinically

Table II — Proportion of the 37 isolates susceptible to selected antibiotics by the microdilution method

Antibiotic; concentration, mg/L	% of isolates susceptible	
	At 24 h	At 48 h
Penicillin		
≤ 0.12	24	22
≤ 0.25	32	30
Ampicillin, < 0.25	35	35
Methicillin		
≤ 8	59	46
≤ 16	68	51
Cephalothin		
≤ 2	97	92
≤ 4	97	97
Erythromycin, ≤ 1	41	43
Clindamycin, ≤ 1	43	46
Vancomycin, ≤ 2	100	100

Table IV — Aminoglycoside susceptibility patterns of the isolates

Pattern*	% of isolates
Susceptible to amikacin	92
Susceptible to gentamicin	62
Susceptible to tobramycin	46
Susceptible to netilmicin	97
Susceptible to all four	43
Susceptible to netilmicin only	5
Resistant to all four	3

*Concentration of gentamicin, tobramycin and netilmicin ≤ 4 mg/L, that of amikacin ≤ 16 mg/L.

Table III — Cumulative proportion of the isolates susceptible to selected aminoglycosides

Antibiotic	Concentration, mg/L; % of isolates												
	≤ 0.5	1	2	4	6	8	12	16	24	32	64	128	256
Amikacin	0	0	0	59	59	84	92	92	100				
Gentamicin	0	0	59	62	62	62	62	76	76	76	89	89	89
Tobramycin	0	0	0	46	49	49	49	59	59	59	76	76	76
Netilmicin	76	86	86	97	97	97	97	100					

significant isolates of coagulase-negative *Staphylococcus* to be *S. epidermidis*, but this species also accounted for 78% of nonpathogenic isolates.

Much interest surrounds slime production. In this study, only 41% of all cases of septicemia and 72% of cases of septicemia that originated from vascular access sites were caused by slime-producing isolates. Christensen and colleagues⁷ reported that 63% of such strains were slime producing. Needham and Stempsey¹⁰ found no association when examining pathogenic strains from a variety of sources. Conversely, Ishak and collaborators¹¹ found a significant correlation when comparing pathogens detected on blood culture with contaminants and determined that the combination of slime production and *S. epidermidis* had a predictive value for pathogenicity of 87%. Recently, Christensen and associates¹² examined strains for adherence using five methods and found virulent strains to be consistently more adherent than contaminants. The relation between slime production and adherence requires further study. Whether these properties prove to be virulence factors and whether testing for them proves to be of value in diagnostic laboratories remain to be seen.

The interpretation of results of susceptibility tests remains problematic. Christensen and colleagues¹³ found that 12% of β -lactamase-producing isolates were apparently susceptible to penicillin and ampicillin with the disc diffusion method. My results revealed the agar dilution method with a very low concentration of penicillin (0.075 mg/L) to be more reliable than the microdilution technique, but disc diffusion was not performed. Since clinical correlation between β -lactamase production and failure of therapy with penicillin or ampicillin is lacking, the value of testing for β -lactamase production remains uncertain.

Plating large inocula onto media containing methicillin has been recommended as the best way of determining methicillin resistance.² In my study the results of this method correlated poorly with those of the other methods. Extensive evaluation and clinical correlation are needed before this test can be recommended.

Many coagulase-negative *Staphylococcus* isolates are resistant to semisynthetic penicillins; vancomycin has been recommended because of the high failure rates associated with β -lactam agents.² However, vancomycin has never been required for infection due to this organism at my centre. A close examination of the literature shows that few such treatment failures are well documented. In three such cases neutropenia was present.^{14,15} Of the patients with prosthetic valve endocarditis described by Karchmer and associates,¹⁶ only two received single-drug treatment without surgery (vancomycin in one case and a β -lactam in the other), and treatment failed in both cases. In contrast, a good rate of response to cefazolin has been reported among patients despite immunosuppressive therapy: in four of five cases of septicemia treated with cefazolin, removal of Hickman-type

catheters was not required; unfortunately, neither the source of the septicemia nor how many of these isolates were resistant to methicillin is stated.¹⁷ In another report three of five patients undergoing continuous ambulatory peritoneal dialysis who had peritonitis due to methicillin-resistant coagulase-negative *Staphylococcus* responded clinically to intraperitoneal administration of cephalothin.¹⁸ In my study the in-vitro results for cephalosporins correlated with clinical success.

Amikacin has been found to be more active than gentamicin or tobramycin.¹⁹ My results confirmed this finding and showed netilmicin to be even more active. These two agents should be considered preferable for the empiric treatment of nosocomial sepsis.

Microbiology laboratories have an obligation to report results of susceptibility testing in a way that protects patients from ineffective antimicrobial therapy. Recent reports of widespread heteroresistance to cephalosporins among methicillin-resistant coagulase-negative *Staphylococcus* (as with *S. aureus*) imply that, when significant, these isolates should be reported as resistant to all β -lactam agents.² Such a policy would lead to administration of vancomycin, a drug with considerable toxicity, to large numbers of patients. Scrutiny of the literature and my findings do not support this recommendation except in cases of profound neutropenia and perhaps when infection involves permanent prosthetic devices. Since my study was retrospective and the numbers were small, definitive conclusions cannot be drawn. It does seem reasonable, however, to at least consider a safe drug such as cefazolin for the treatment of infections associated with devices that are removed.

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Removal of esophageal foreign bodies with a Foley balloon catheter under fluoroscopic control

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Between 1982 and 1985 removal of a nonorganic, smooth, radiopaque foreign body in the esophagus with a Foley balloon catheter under fluoroscopic control without sedation was attempted in 38 children. An ultra-low-dose fluoroscopic unit was used. In 35 children the foreign body (a coin) was either easily removed (in 29 cases) or advanced into the stomach (in 6). No complications of the procedure were observed. In three children the foreign body could not be removed by this means; it was subsequently removed by endoscopy (in two cases, both of coins) or esophagotomy (in one, of a stone). When carefully performed, removal of blunt, recently ingested esophageal foreign bodies with a Foley catheter under fluoroscopic control is a safe mode of treatment.

Entre 1982 et 1985 nous avons tenté chez 38 enfants l'ablation d'un corps étranger oesophagien non organique, moussé et radio-opaque par le cathéter à ballon de Foley sous radioscopie à très faible dose; dans 35 cas nous avons réussi

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aisément et sans complication. Il s'agissait chaque fois d'une pièce de monnaie, qui a été enlevé soit par voie haute (29 fois), soit poussée dans l'estomac (6 fois). Des trois autres cas, deux pièces de monnaie ont été enlevées par endoscopie, et un caillou a été enlevé par oesophagotomie. Si elle est bien faite, l'ablation d'un corps étranger oesophagien moussé d'ingestion récente par le cathéter de Foley sous radioscopie est sécuritaire.

Ingestion of a foreign body as a cause of acute esophageal obstruction is most common among children.¹ Most of the objects are smooth (e.g., coins). Extraction with a rigid endoscope, although the accepted method of treatment,^{2,3} is associated with a morbidity rate of 0.34% and a death rate of 0.05%.⁴ Removal with a flexible endoscope in young children requires special expertise and general anesthesia⁵ or adequate sedation.⁶ Removal of smooth, nonorganic foreign bodies lodged in the esophagus with a Foley catheter under fluoroscopic control has previously been described.⁷⁻⁹ We report our experience with this procedure.

Methods

Thirty-eight patients (20 girls and 18 boys)