Bacteraemia in children in the south-western Cape

A hospital-based survey

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Summary

During 1989, of the 8 524 children admitted to the paediatric wards of Tygerberg Hospital, 165 (1,96%) had bacteraemia. The incidence of community-acquired bacteraemias was 1,6% and that of nosocomial bacteraemias 0,5%. The most important community-acquired isolates were *Streptococcus pneumoniae, Staphylococcus aureus* and *Neisseria meningitidis*. The most important nosocomial isolates were *Klebsiella* and *Salmonella* spp. Both bacteraemia (relative risk (RR) = 2,08) and severe malnutrition (RR = 3,01) were more common in black patients. Overall, severe malnutrition was more common than mild malnutrition or a normal nutritional status in bacteraemic patients (odds radio (OR) = 3,17). Nineteen patients with bacteraemia died, there was a significantly higher case-fatality rate in patients with extreme malnutrition (P = 0,03; OR = 3,7). Gram-negative bacilli were found more commonly in patients with extreme malnutrition (OR = 5,4) and patients with nosocomial bacteraemia (OR = 4,6). Three of 39 patients (7,6%) with nosocomial bacteraemia had suppurative thrombophlebitis.

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Bacteraemias are associated with severe morbidity and mortality.[1,2] There is at present little information on paediatric bacteraemias in southern Africa, the only comprehensive survey having been carried out at Baragwanath Hospital in 1982.[1]

The present study was undertaken in order to document the spectrum of organisms, their antibiotic-sensitivity patterns, underlying diagnoses and outcome of both community-acquired and nosocomial bacteraemias in children seen at Tygerberg Hospital, a teaching hospital in the south-western Cape. This region has a mediterranean climate, with hot, dry summers and cold, wet winters.

Patients and methods

The paediatric department consists of an outpatient department, an 'overnight' ward (84 beds), 4 general wards (133 beds) and an intensive care unit (7 beds).

All patients between 1 month and 13 years of age admitted to these wards from 1 January to 31 December 1989 were eligible for the study. Bacteraemias occurring within 72 hours of admission were considered community-acquired and beyond 72 hours to be nosocomial in origin.[3] Bacteraemias occurring within 72 hours of transfer from another hospital were also considered nosocomial. Death occurring within 14 days of a positive culture being obtained was regarded as being due to the bacteraemia.[1]

All positive blood culture isolates and their antibiotic sensitivity patterns were recorded prospectively. Patients with nosocomial bacteraemia were assessed clinically for a possible source of infection by one of the authors (M.F.C.). Information on nutritional status, underlying diagnoses and outcome was collected prospectively in these patients and retrospectively from the medical records of patients with community-acquired bacteraemias. Nutritional status was determined using US National Child Health Survey standards. Patients with marasmus, kwashiorkor and marasmic kwashiorkor were regarded as being severely malnourished, while nutritional dwarfs were considered to be mildly malnourished.[4] Information on the total number of admissions was obtained from the computer service of Tygerberg Hospital.

The standard procedure for blood culture consisted of the physician washing his hands with antiseptic soap (chlorhexidine gluconate and 4% isopropyl alcohol), sterilising the skin with chlorhexidine 0,5% in 70% ethanol and then with 10% povidone iodine solution before venous blood (± 2 ml) was taken from a patient and inoculated into an aerobic culture bottle. No note was taken of whether the above precautions were strictly adhered to in every instance. An automated radiometric blood culture system (BACTEC 640) was used to process specimens. Organisms were identified using standard microbiological techniques and antibiotic sensitivity was evaluated using the disc method of Stokes.[5] All *Staphylococcus epidermidis* isolates were considered contaminants unless 2 positive cultures with the same antibiogram were obtained from a patient. Statistical analysis was done using the χ^2-test with Yates' correction factor for discrete variables when there were either 50 or fewer patients in a group or only 1 degree of freedom. Student's t-test was used for continuous variables. A P-value less than 0,05 was considered significant.

The χ^2-test, relative risks (RR), and odds ratios (OR) were calculated using the Epi-info software program distributed by the Center for Disease Control in Atlanta, Georgia, USA. RR was calculated for comparisons between bacteraemic patients and all admissions and OR for comparisons within the bacteraemic group.

Results

During the study period 8 524 paediatric patients were admitted to Tygerberg Hospital. A total of 171 cases of bacteraemia were documented (2,02/100 admissions) in 165 patients (1,96/100 admissions). One patient had 3 episodes of bacteraemia and 4 patients had 2 episodes (3 during the same and 1 on separate admissions). There was no polymicrobial bacteraemia.

Of the bacteraemias, 132 were community-acquired (1,6/100 admissions) and 39 were nosocomial (0,5/100).

The male:female ratio for patients with bacteraemia was 1,8:1 and 1,3:1 for all admissions (χ^2 = 0,3; P = 0,6). The mean age of bacteraemic patients was 2,4 ± 3 years. There was no significant age difference between those with community-acquired and nosocomial bacteraemia (1,8 ± 2,5 v. 2,5 ± 3,2

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years; $t = 1,3$; $P > 0,05$). Nineteen patients with bacteraemia died (case-fatality rate 11%). Bacteraemias were found more commonly in black children than in children of other racial groups ($\chi^2 = 15$; $P = 0,0001$; RR = 2,08 (1,45 — 2,98 at 95% confidence level)). Similarly, severe malnutrition was also more common in black children ($\chi^2 = 67,7$: $P = 10^{-7}$; RR = 3,01 (2,3 — 3,94 at 95% confidence level)). Overall, 13 patients (9,8%) with community-acquired and 10 patients (25,6%) with nosocomial bacteraemia were severely malnourished, therefore severe malnutrition was significantly more common in bacteraemic patients ($\chi^2 = 73$; $P = 10^{-7}$; OR = 3,17 (2,26 — 3,68 at 95% confidence level)). Bacteraemic patients with severe malnutrition were far more likely to die than those who were well nourished or mildly malnourished (OR = 3,7: inexact — 12,3 at 95% confidence level). The influence of nutritional status on mortality is shown in Table I.

TABLE I. RELATIONSHIP BETWEEN NUTRITIONAL STATUS AND CASE FATALITY RATE IN BACTERAEMIC PATIENTS

Nutritional status	Deaths No.	Deaths %	No. of patients
Normal (1)	**9**	**8,2**	**110**
Mild malnutrition (2)	**4**	**12,5**	**32**
Severe malnutrition (3)	**6**	**26,1**	**23**

1 v. 2 v. 3: $\chi^2 = 6,7$; $P = 0,035$
3 v. 1 + 2: $\chi^2 = 4,47$; $P = 0,03$.

The organisms isolated and nutritional status of both community-acquired and nosocomial bacteraemias are shown in Fig. 1. By far the most common community-acquired isolate was *Streptococcus pneumoniae* (33%) followed by *S. aureus* (13,6%) and *Neisseria meningitidis* (11,4%). The most common nosocomial isolates were *Klebsiella* sp. (18%) followed by *Salmonella* sp. (13,4%), *S. pneumoniae* (10,3%) and *S. aureus* (10,3%). *S. typhi* was isolated in 3 patients with community-acquired salmonellosis.

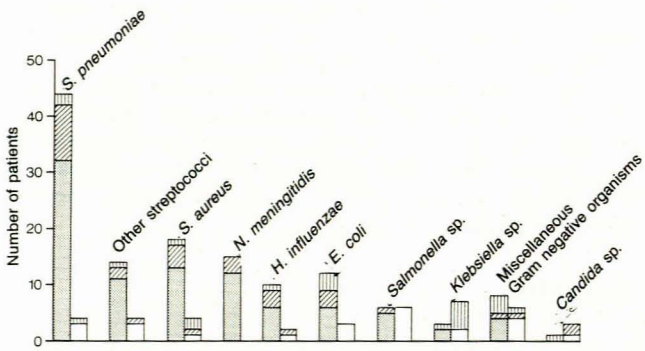

Fig. 1. Spectrum and nutritional status of children with community-acquired and nosocomial bacteraemias (▨= community-acquired; □ = nosocomial; ▨ = mild malnutrition (nutritional dwarfs); ▩ = severe malnutrition (marasmus, kwashiorkor, marasmic kwashiorkor). Other streptococci (α-haemolytic 12, β-haemolytic 4, *S. faecalis* 2). Miscellaneous Gram-negative bacilli (*Acinetobacter* sp., *Pseudomonas* sp. 2; *Alcaligenes* sp. 1).

Six of 7 *Salmonella* isolates were serotyped as group C_1 and arose from a nosocomial outbreak that began in the neonatal wards. One study patient died. The outbreak was controlled by strict isolation of all patients with positive stool cultures.

TABLE II. SITE OF DISEASE v. ORGANISMS ISOLATED

	No. of patients	*S. aureus* No.	*S. aureus* %	*S. pneumoniae* No.	*S. pneumoniae* %	Other streptococci No.	Other streptococci %	*N. meningitidis* No.	*N. meningitidis* %	*H. influenzae* No.	*H. influenzae* %	*Klebsiella* sp. No.	*Klebsiella* sp. %	*E. coli* No.	*E. coli* %	Misc. Gram – organisms No.	Misc. Gram – organisms %	*Salmonella* sp. No.	*Salmonella* sp. %	*Candida* No.	*Candida* %
Respiratory	**72**	**7**	**9,7**	**32**	**44,4**	**9**	**12,5**	**-**	**-**	**7***	**9,7**	**7†**	**9,7**	**1**	**-**	**7**	**9,7**	**1**	**1,4**	**1**	**1,4**
Central nervous system	**26**	**-**	**-**	**8**	**30,8**	**1**	**3,9**	**11**	**42,0**	**5**	**19,2**	**-**	**-**	**-**	**-**	**1**	**3,9**	**-**	**-**	**-**	**-**
Occult	**22**	**1**	**4,5**	**5‡**	**22,7**	**2**	**9,1**	**4‡**	**18,2**	**-**	**-**	**1**	**4,5**	**-**	**-**	**2**	**9,1**	**4§**	**4,5**	**3**	**13,6**
Gastro-intestinal (gastro-enteritis in 17)	**24**	**2**	**8,3**	**3¶**	**12,5**	**2**	**8,3**	**-**	**-**	**-**	**-**	**-†**	**-**	**8**	**33,3**	**2**	**8,3**	**7**	**29,2**	**-**	**-**
Orthopaedic	**8**	**7**	**87,5**	**-**	**-**	**1**	**12,5**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Oncology	**7**	**2**	**28,6**	**-**	**-**	**3**	**42,9**	**-**	**-**	**-**	**-**	**-**	**-**	**2**	**28,7**	**-**	**-**	**-**	**-**	**-**	**-**
Renal	**4**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**4**	**100**	**-**	**-**	**-**	**-**	**-**	**-**
Thrombophlebitis	**3**	**1**	**33,3**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1**	**33,3**	**-**	**-**	**1**	**33,3**	**-**	**-**	**-**	**-**
Other (trauma in 2, subcutaneous infection in 3)	**5**	**3**	**60,0**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1**	**20,0**	**-**	**-**	**1**	**20,0**	**-**	**-**	**-**	**-**

* 1 patient had epiglottitis.
† 3 patients had gastro-enteritis in addition to pneumonia.
‡ 3 patients with *S. pneumoniae* and 2 with *N. meningitidis* presented with febrile convulsions.
§ 3 of 4 patients had typhoid.
¶ Peritonitis in 1 and gastro-enteritis in 2.

Enterobacteraceae (E. coli, Salmonella sp., *Klebsiella* sp., *Enterobacter* sp., and *Proteus* sp.) and miscellaneous Gram-negative bacilli (*Acinetobacter* sp., *Pseudomonas* sp. and *Alcaligenes* sp.) occurred more commonly in severely malnourished children than those with mild or without malnutrition (χ^2 = 12,8; P = 0,0004) (OR = 5,4: 2 — 15,3 at 95% confidence level).

The comparison of organisms isolated and organ systems most involved is shown in Table II. Most isolates came from patients with respiratory disease, where 44,4% of isolates were *S. pneumoniae. S. epidermidis* was considered a true pathogen in 1 patient with congenital heart disease and infective endocarditis.

Six of 7 patients with *S. aureus*-related pneumonia had community-acquired infections. One of them was later diagnosed as having cystic fibrosis. Only 1 had a chest radiograph suggestive of an *S. aureus* infection. He had pneumatocele formation. Suppurative thrombophlebitis was the probable source of bacteraemia in 3 of 39 patients (7,6%) with nosocomial bacteraemia. All had chronic gastro-enteritis and were receiving intravenous fluid, 2 having had 'cut-downs'. The organism was cultured from the blood and vein in all 3. In total, 12 of 39 patients (30%) with nosocomial bacteraemia had an underlying diagnosis of chronic gastro-enteritis. Surprisingly, the intensive care unit accounted for only 5 nosocomial bacteraemias (12%). Patients from the oncology service were regarded as a separate group and accounted for 6 nosocomial bacteraemias (15,4%).

Four nosocomial bacteraemias were acquired at the referring hospital. These included 2 children with pneumonia from convalescent hospitals (*S. pneumoniae* in 1 and *H. influenzae* in 1), 1 with salmonellosis and 1 with *Enterobacter*-associated thrombophlebitis.

The oldest patient with pneumonia due to *H. influenzae* was 2,2 years of age while 9 patients (10,8%) with *S. pneumoniae*-related respiratory disease were older.

Thirty-one per cent of Gram-positive isolates occurred in the 1st year of life, 34,5% in the second and 34,5% thereafter. Fifty-three per cent of Gram-negative isolates occurred in the 1st year (60% of Enterobacteraceae isolates) 21,8% in the second and 23,1% thereafter.

Enterobacteraceae and miscellaneous Gram-negative organisms were found significantly more commonly in nosocomial than community-acquired bacteraemias (χ^2 = 15,5; P = 0,00008) (OR = 4,6; 2,0 — 6,5 at 95% confidence level).

The antibiotic sensitivity patterns of most common isolates are shown in Table III. All *S. pneumoniae* isolates from both community-aquired and nosocomial bacteraemias and all *N. meningitidis* isolates were penicillin-sensitive. All community acquired *H. influenzae* isolates were sensitive to both ampicillin and chloramphenicol. One of 2 nosocomial isolates (from a patient with pneumonia) was resistant to both, but sensitive to co-trimoxazole. All *E. coli* isolates were resistant to both ampicillin and co-trimoxazole. Sixteen of 18 community-acquired (89%) *S. aureus* isolates and 2 of 4 nosocomial isolates (50%) were sensitive to cloxacillin. All community-acquired *Salmonella* isolates were sensitive to both co-trimoxazole and ampicillin and all nosocomial isolates were resistant. In addition, only 1 of 6 hospital-acquired isolates (16,3%) was susceptible to gentamicin and tobramycin, while all were sensitive to amikacin and second-generation cephalosporins.

Discussion

We have documented for the first time the pattern of bacteraemia in hospitalised children in the south-western Cape Province. Our data are compared with those from Baragwanath Hospital and Denver, USA, in Table IV.[1-2] The

TABLE III. ANTIBIOTIC SENSITIVITY PATTERNS OF COMMON COMMUNITY AND NOSOCOMIAL ISOLATES

	Community-acquired														Nosocomial											
	Pen.		Amox.		Co-t.		Eryth.		Clox.		Fusi.		Van.		Pen.		Amox.		Co-t.		Eryth.		Clox.		Fusi.		Van.	
Gram-positive	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
S. pneumoniae	38/38	100	38/38	100	29/29	100	-	-	-	-	-	-	-	-	3/3	100	3/3	100	0/1	-	2/2	100	-	-	-	-	-	-
S. aureus	0/18	-	-	-	15/16	94	12/13	92	16/18	89	18/18	100	18/18	100	0/4	-	-	-	2/4	50	2/4	50	2/4	50	3/4*	75	4/4	100
Gram-negative	Gen.		Tob.		Net.		Ami.		Cefx.		Amox.		Co-t.		Gen.		Tob.		Net.		Ami.		Cefx.		Amox.		Co-t.	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Entero-bacteriaceae	23/24	96	19/24	90	22/24	92	24/24	100	12/14	86	7/21	33	10/24	43	7/18	39	7/16	44	12/17	71	18/18	100	11/11	100	2/17	12	2/15	13
Miscellaneous organisms	5/5	100	5/5	100	5/5	100	5/5	100	1/3	33	2/4	50	3/3	100	3/3	100	3/3	100	3/3	100	3/3	100	1/3	33	1/2	50	2/3	66

*1 isolate initially sensitive to fusidic acid, subsequently resistant after 5 days of oral fusidic acid and rifampicin.
Miscellaneous organisms = *Pseudomonas* sp.; *Alcaligenes* sp.; *Acinetobacter* sp.; Pen. = penicillin; Amox. = amoxycillin; Co-t. = co-trimoxazole; Eryth. = erythromycin; Clox. = cloxacillin; Fusi. = fusidic acid; Van. = vancomycin; Gen. = gentamicin; Tob. = tobramycin; Net. = netilmycin; Ami. = amikacin; Cefx. = cefoxitin.

increased incidence and case fatality rate seen at Baragwanath Hospital can probably be explained by their study population including only patients ill enough to be admitted to the general wards whereas ours included patients admitted to a short-stay 'overnight' ward. Nevertheless, we found that black patients were twice as likely as children from other racial groups to develop bacteraemia and were also three times as likely to be severely malnourished.

TABLE IV. COMPARISON OF THREE STUDIES OF BACTERAEMIA

	Tygerberg Hospital	Baragwanath Hospital	Denver, Colo., USA
Incidence (%)	**2,02**	**5,84**	**2,72***
Case-fatality rate (%)	**11**	**23,2**	**13**
Mean age (mo.)	**28**	**19**	**—**
Number of isolates	**172**	**315**	**189**
***S. pneumoniae* (%)**	**25,6**	**24**	**18**
***S. aureus* (%)**	**11,6**	**6,7**	**11,6**
***S. enteritidis* (%)**	**5,2**	**17,8**	**2,7**
***S. typhi* (%)**	**1,7**	**4,1**	†
***E. coli* (%)**	**8,2**	**13,7**	†
***Klebsiella* sp. (%)**	**4,7**	**7,0**	†
***N. meningitidis* (%)**	**8,8**	**5,1**	**2,1**
***H. influenzae* (%)**	**7,0**	**14,9**	**39**

* Percentage of positive blood culture isolates over a 2-year period.
† Enterobacteriaceae (5,8%).

Overall, *S. pneumoniae* was by far the most important isolate, being the most common in both South African studies and the second most common in Denver. In contrast, *H. influenzae*, while accounting for 39% of bacteraemias in Denver, was relatively less important here. *S. enteritidis* was common at Baragwanath Hospital reflecting poor sanitation in surrounding areas and was an important nosocomial isolate at our hospital. Our relatively high incidence of *N. meningitidis* in comparison with other studies has been documented previously in the south-western Cape.[6]

Malnutrition has already been documented as both an important risk factor in the development of both community-acquired and nosocomial bacteraemia and in influencing mortality.[1,3,7,8] As in previous studies, Gram-negative bacilli, particularly Enterobacteraceae, were the most frequently isolated organisms in patients with extreme malnutrition.[1,7,8] In contrast to previous studies of nosocomial bacteraemia, we found that Gram-negative bacilli were significantly more common than Gram-positive isolates.[1,3]

Thrombophlebitis as a cause of nosocomial bacteraemia has been underemphasised, although its presence in children has recently been stressed.[9] It was responsible for 7,6% of nosocomial bacteraemias in our study. Current recommendations include either excising the infected segment of vein or incision and drainage where perivenous abscess formation has occurred.[9]

Antibiotic resistance, especially among nosocomial isolates, is a problem here as elsewhere.[3] All *S. pneumoniae* isolates in the present study were penicillin-sensitive, although 2 of 28 isolates were resistant in a survey between 1984 and 1986.[10] A nosocomially acquired *H. influenzae* isolate resistant to both ampicillin and chloramphenicol was isolated here for the first time, although previously documented elsewhere in South Africa,[3,11] including Cape Town.[12] Our finding that all *E. coli* isolates were resistant to both ampicillin and co-trimoxazole is particularly disturbing and suggests that these agents are unlikely to be of value even for community-acquired urinary tract infections. This was confirmed by a 74% incidence of resistance to ampicillin and 45% to co-trimoxazole from *E. coli* urinary isolates in 1989 (P. J. Burger — personal communication).

In our department, amikacin remains the aminoglycoside of choice, since the Gram-negative bacilli were susceptible, in keeping with a recently published study.[13]

Conclusions

We documented the spectrum of paediatric bacteraemias seen in hospitalised children in the south-western Cape over a 1-year period and confirmed the importance of pathogens such as *S. pneumoniae, H. influenzae, S. aureus, N. meningitidis, E. coli* and *Salmonella* sp.

For patients with community-acquired respiratory, central nervous system and orthopaedic infections antimicrobial agents, such as penicillin, ampicillin and cloxacillin, remain the drugs of choice. Unfortunately, in our area co-trimoxazole and ampicillin are ineffective for urinary tract infections. Alternative agents, such as nalidixic acid, nitrofurantoin or oral cephalosporins, should be used.

The importance of adequate Gram-negative cover both for malnourished patients and those with nosocomial bacteraemia was confirmed. The choice of antibiotic, however, depends on local sensitivity patterns.

We have also shown that infective thrombophlebitis is an important cause of nosocomial bacteraemia and its presence needs to be actively sought in all hospitalised patients with fever.

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REFERENCES

1. Berkowitz FE. Bacteremia in hospitalised Black South African Children. *Am J Dis Child* 1984; **138:** 551-556.
2. Winchester PD, Todd JK, Roe MH. Bacteremia in hospitalised children. *Am J Dis Child* 1977; **131:** 753-758.
3. Cotton MF, Berkowitz FE, Berkowitz Z, Becker PJ, Heney C. Nosocomial infections in black South African children. *Pediatr Infect Dis J* 1989; **8:** 676-683.
4. Wellcome Trust International Working Party. Classification of infantile malnutrition. *Lancet* 1970; **2:** 302-303.
5. Stokes EJ. *Clinical Bacteriology*. 4th ed. London: Edward Arnold, 1975: 203-261.
6. Donald PR, Burger PJ, Becker WB. Paediatric meningitis in the Western Cape. *S Afr Med J* 1986; **70:** 391-395.
7. Scragg JS, Appelbaum PC. Septicaemia in kwashiorkor. *S. Afr Med J* 1978; **53:** 358-359.
8. Smythe PM, Campbell JAH. The significance of the bacteraemia of kwashiokor. *S Afr Med J* 1959; **33:** 777.
9. Berkowitz FE, Argent AC, Baise T. Suppurative thrombophlebitis — a serious nosocomial infection. *Pediatr Infect Dis J* 1987; **6:** 64-67.
10. Donald PR, Kuhn SH, Cotton MF, Van Schalkwyk HJS, Burger PJ. Die kliniese kenmerke van *S. pneumoniae* en *H. influenzae* infeksies by kinders. *Geneeskunde* 1989; **31:** 14-17.
11. Peer AK, Thejpal R, Naidoo D, Van den Ende J. Failure of infection control measures to limit the carriage of resistant *H. influenzae* type b in paediatric patients (Abstract 02). Congress of the Infectious Diseases Society of South Africa, Durban, 14 Oct 1987.
12. Forder A, Roditi D, Olver S, De Goveia C. Antibiotic resistance in *H. influenzae* in Cape Town. (Abstract 03), Congress of the Infectious Diseases Society of South Africa, Durban, 14 Oct 1987.
13. Hesseling PB, Mouton WL, Henning PA *et al.* A prospective study of long-term use of amikacin in a paediatrics department. *S Afr Med J* 1990; **78:** 192-195.