

# Septicaemia in a general hospital

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**ABSTRACT:** Over a three-year period, 6102 blood cultures were performed in a large general hospital. Each year, septicaemia was diagnosed in about 0.5% of patients. Detailed examination of one-year records showed that the largest proportion was from the surgical wards, followed by the emergency admitting ward, with smaller numbers from the adult medical, renal and paediatric areas. The organism most frequently responsible was *Staphylococcus aureus* followed by *Escherichia coli*. The mortality rate rose from 16% in those

treated with one antibiotic, to 58% in those given three or more. Nosocomial infections accounted for 39% of all episodes, with a mortality rate of 29%. At least five cases of these, with two deaths, were attributable to intravenous cannulae. Neutropenia and concurrent immunosuppressive drug therapy were associated with a worse prognosis, but the body temperature and leucocyte count had no prognostic significance.

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SEPTICAEMIA is a significant hazard in hospitals. We report the experience of The Royal Newcastle Hospital, a district general hospital with 25 000 admissions annually, which serves an industrial area of 300 000 people.

## Subjects and methods

The records of 6102 blood cultures performed during 1976-79, 1337 of which gave positive results, form the basis of the study. For the year 1978-79, we also analysed the associated clinical features in detail. We defined septicaemia as the positive result of a blood culture in the presence of systemic symptoms of infection. Where the evidence of systemic infection was slight or absent, and an organism of doubtful or nil pathogenicity was isolated, we regarded the culture as contaminated. In a minority of instances, the significance of an isolate, on the basis of its potential pathogenicity and the clinical features, was indeterminate. We diagnosed nosocomial infection if the patient developed it later than three days after admission to hospital and there was clear clinical evidence that it was hospital-acquired. Immunosuppressive diseases were the disorders associated with severe impairment of the immune response, such as lymphomas, leukaemias, marrow disorders with leucopenia, severe renal failure and cirrhosis of the liver. Immunosuppressive drugs were corticosteroids, alkylating agents, anti-metabolites, plant alkaloids and the antimetabolic antibiotics.

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## Results

About 2000 blood samples were taken, and septicaemia was diagnosed in about 120 patients each year. Over the three years, the rate of positive culture results fell from 31% to 23% in the third year, due entirely to a fall in the proportion of contaminated or non-significant blood cultures (Table 1). The proportion of contaminated cultures fell from 19% to 7%.

A detailed analysis of the year 1978-1979 showed that 121 patients had 135 septicaemic episodes; 241 blood cultures were performed in these patients with 77% of bottles showing growth. The sexes

**TABLE 1: Three-year analysis of blood cultures: positivity, significance, and contamination rate**

	1976-77	1977-78	1978-79
Total number of blood cultures	2301	1903	2168
Total number of positive blood cultures	626 (31%)	435 (23%)	290 (13%)
Significant positive cultures	195 (10%)	231 (12%)	135 (6%)
Number of patients with significant cultures	110	121	121
Number of non-significant positive cultures	415	191	155
Undetermined significance	16	13	0
Percentage of contaminated cultures*	19%	11%	7%

\* Percentage contaminated =  $\frac{(\text{non-significant} + \text{undetermined}) \times 100}{\text{total blood cultures}}$

TABLE 2: Hospital units, distribution of drugs, and comparative mortality rates

	Number of patients					Mortality rate
	Single drug	2 drugs	≥ 3 drugs	No drugs	Total	
Emergency ward	11	11	4	2	28	36%
Renal unit	11	6	2	1	20	18%
Paediatric	9	9	1	—	19	5%
Medical	8	12	1	—	21	47%
Surgical	10	22	2	3	37	23%
Intensive care	—	4	2	1	7	71%
All units	49	64	12	7	132*	27%
Mortality rate	16%	22%	58%	72%	27%	—

\* In two patients (three septicaemic episodes) antibiotic treatment could not be determined from inpatient clinical records.

Comparing 1 and 2 drugs:  $\chi^2=0.23$ ;  $P>0.6$ .

Comparing ≥ 3 and no drugs:  $\chi^2=0.01$ ;  $P=0.9$ .

Comparing 1 or 2 drugs with 3 drugs:  $\chi^2=7.1$ ;  $P<0.01$ .

were equally affected with a similar mortality rate. The largest contribution came from the surgical wards (35 episodes), followed by the emergency ward with 28 episodes representing most of the community acquired infections. General adult medical, renal and paediatric areas each contributed similar numbers (Table 2). The highest mortality rate (71%) was in the intensive care unit.

A wide variety of organisms was encountered, the largest groups being *Staphylococcus aureus* (33 episodes), *Escherichia coli* (26 episodes) and the pneumococcus (12 episodes). With the exception of *Haemophilus influenzae* (six episodes), meningococcus (two episodes) and *Staph. epidermidis* (eight episodes), the remaining 64 isolates were almost exclusively those of bowel flora. Seven of the eight cases of *Staph. epidermidis* septicaemia were nosocomial. All these patients had an indwelling intravenous polyethylene catheter, with three septicaemic episodes being definitely attributed to these. We classified the remaining 93 *Staph. epidermidis* isolates as contaminants after reviewing the clinical data.

The likelihood of a particular organism being found depended upon the area of the hospital in which the patient was situated (Table 3). In 28 isolates from the emergency ward, the largest groups of organisms were *E. coli* (seven isolates), pneumococcus (six isolates), and *Staph. aureus* (four isolates). By contrast, 13 of 22 isolates from the renal ward were due to *Staph. aureus*; this included all the infected shunts (10 episodes) and dialysis-associated septicaemias (12 episodes), and only seven isolates were those of Gram-negative organisms, of which five were coliforms. In the medical wards, the largest group of organisms isolated was the coliforms. This was also the case in the surgical wards, which

presented a remarkable variety of organisms headed by enterobacteria (eight episodes), *Klebsiella* and *Staph. aureus* with seven episodes each and, in five patients, *Staph. epidermidis* was considered pathogenic. Of the 20 cases found in the Paediatric Department (including the nurseries), the largest groups were *H. influenzae* (five episodes) and pneumococcus (four episodes). The age distribution was bimodal, with peaks at 0 to nine years and at 60 to 79 years. By contrast, the highest mortality rate, of about 40%, was in the age group 40 to 79 years.

#### Microbiology

The microbiology department reviews the clinical summary on the request form together with its findings, and then comments whether the infection is significant or not. Of the true septicaemias, it had classified 87 as significant, 12 as not significant, and made no comment on 39. Of the contaminated cultures, it had classified two as significant, 84 as not significant, and made no comment on 69.

#### Antibiotic use

We found adequate records for 132 of the 135 episodes. At the time of blood culture, 19 patients were already receiving antibiotics; in 99 episodes, antibiotic therapy was commenced at the time of venepuncture; and in eight episodes, antibiotics were not given for a variety of reasons. Only in six episodes were antibiotics withheld until receipt of microbiology reports.

The antibiotic regimens showed no consistent pattern. The most frequently used drugs were gentamicin, ampicillin/amoxycillin,

TABLE 3: Organism, origin and mortality rate

	Number of patients							Mortality rate
	Emergency	Renal	Medical	Surgical	Paediatric	Intensive care	Total	
<i>Staph. aureus</i>	4	13*	5	7	2	2	33	12%
<i>E. coli</i>	7	4	8	6	1	—	26†	23%
<i>Klebsiella</i>	—	—	—	6	1	2	9	56%
Enterobacteria	2	1	2	8	—	—	13	46%
Pneumococci	6	1	1	—	4	—	12	42%
<i>Staph. epidermidis</i>	—	1‡	2	5	—	—	8	13%
Mixed growth	3	1	—	—	1	—	5	40%
<i>H. influenzae</i>	1	—	—	—	5	—	6‡	17%
<i>Pseudomonas</i>	—	1	1	—	2	3	7	26%
<i>Strep. viridans</i>	2	—	—	2	—	—	4	0
Enterococci	2	—	2	3	2	—	9	22%
Micrococci	1	—	—	—	1	—	2	50%
<i>Acinetobacter</i>	—	—	—	1	—	—	1	0
Total	28	22	21	38	19	7	135	27%

\* Twelve of the 13 patients on dialysis (one — peritoneal infection with positive growth in aspirate).

† 73% genitourinary in origin.

‡ On dialysis.

§ Four cultures grew predominantly Gram-negative bacilli (*Pseudomonas*, *Proteus*); one grew enterococci and one grew enterococci with coliforms.

cloxacillin and the cephalosporins. We could draw no conclusions concerning the relative effectiveness of the various antibiotic regimens. Forty-nine episodes were treated with one, 64 with two and 12 episodes with three or more antibiotics. The mortality rates did not differ significantly between those treated with one and those treated with two antibiotics (16% and 22% respectively), and between those treated with three or more antibiotics and those treated with none (58% and 72% respectively) (Table 2). But those treated with three or more drugs fared significantly worse than those receiving only one or two drugs.

#### Nosocomial infection

There were 52 episodes of nosocomial infection with a mortality rate of 29%. The surgical wards contributed the largest proportion (52%), followed by the medical wards (19%); the rest were fairly evenly distributed amongst renal unit (10%), intensive care (12%) and paediatric areas (8%). Twenty-eight episodes followed a procedure of some form; 39 patients had indwelling intravenous cannulae, to which in five cases (with two deaths) the infection was attributable. Fourteen patients had indwelling urinary catheters, to which in six cases (with two deaths) the infections were attributable. Nine patients had immunosuppressive diseases, five were receiving immunosuppressive drugs, and two had both. The most common infecting organisms were *Staph. aureus* (12 episodes), *E. coli* (nine episodes), *Klebsiella* (seven episodes), and *Staph. epidermidis* (seven episodes).

One hundred and fifty-five cultures were regarded as contaminated; 60% grew *Staph. epidermidis*, 12% mixed organisms, 6% each produced diphtheroids and *Bacillus* species, 5% micrococcus, and 3% each enterobacter and *E. coli*. *Staph. aureus* was classified as a contaminant in seven (5%), forming 18% of all *Staph. aureus* cultures.

#### Immunosuppression

There were 73 episodes in patients considered to have altered immune responses; 40 of these had immunosuppressive disease, 20 were receiving immunosuppressive drugs, and 13 shared both characteristics. The mortality rates were 25%, 50%, and 46% respectively. Use of immunosuppressive drugs was associated with poorer prognosis ( $0.1 > P > 0.05$ ), which was not worsened by concurrent immunosuppressive therapy. Both in immunodeficient and in immunosuppressed patients, 25% of infections were nosocomial. All of the immunosuppressed patients and 70% of the immunodeficient patients had indwelling intravenous polyethylene cannulas at the time of infection, but none had indwelling urinary catheters.

#### Clinical indices

An analysis of the white cell count and body temperature at the time of blood culture produced some disturbing findings. In 115 episodes, the result of a white cell count done within a short time of blood culture was available; 74 had leucocytosis, in 36 the white cell count was within normal range; and five, who had neutropenia, died (white blood cell infusions were not available at the time). The survival rate in those with normal or elevated white cell count did not differ significantly in any subgroup. The body temperature also provided no prognostic help; four of 10 patients who were clearly normothermic or hypothermic died, a similar proportion to those who were febrile.

#### Discussion

One of the major difficulties in a study such as this is to define the problem. Septicaemia as a topic tends to recur in textbooks without an overview or definition, which seems assumed to be "evidence of systemic infection with a positive blood culture result". This is the definition we employed. We accept the view that organisms of low virulence such as *Staph. epidermidis* may sometimes be pathogenic, although in the older literature they were generally regarded as being of no consequence. In a comprehensive review of bacteraemia in the Boston City Hospital (1935-1965), Finland omitted all *Staph. albus* cultures from consideration.<sup>1</sup> It seems

likely that such organisms can produce infection not only in prosthetic and damaged heart valves but also from indwelling venous appliances. We found 101 cultures which grew *Staph. epidermidis*, and regarded eight as pathogenic; in some others, the significance was unclear and, in most, the organisms were contaminants of no consequence. We regarded one patient as having died from *Staph. epidermidis* septicaemia; when infection can be fatal, instances of less severe infection must occur.

Bacterial contamination of blood cultures is frequent, and its interpretation can be difficult. It is interesting to compare our study with the 10-year experience of St Bartholomew's Hospital, London.<sup>2</sup> While we were perturbed at the high prevalence of contamination (19% initially, falling to 7% in the third year), similar figures were found at St Bartholomew's and elsewhere.<sup>3,4</sup>

Does contamination occur at phlebotomy or in the laboratory? Strict attention to asepsis at the bedside is important in the investigation of suspected septicaemia. A study from Dundee<sup>5</sup> may shed some light on this. The authors found bacterial colonisation in almost half the plastic cannulae in place for less than 48 hours, rising to 78% in those *in situ* for longer. *Staph. epidermidis* alone was present in 76% of cultures, and in many of the others in a mixed growth. It would be interesting to determine if a correlation exists between *Staph. epidermidis* in blood cultures and the presence of an indwelling plastic cannula.

The fall in contamination rate over the three-year period reported here requires comment. Since a review in 1974 by one of us,<sup>6</sup> attention has been focused in the hospital on the need for changing cannulae each 48 hours; this is a possible explanation for the observed fall in the rate of contamination.

A number of other lessons emerge from our study. The likelihood of a particular organism being present depends upon the area of the hospital in which the culture was taken. *Escherichia coli* was the major organism (25%) found in "acute" patients admitted to the emergency and medical wards (29%). This is a remarkable change from several decades ago, when Gram-positive cocci were reported to be the outstanding organisms.<sup>7,8</sup> A great variety of enterobacteria were the major contributors in surgical wards (56%). These findings are significant when the appropriate antimicrobial regimen has to be commenced in ignorance of the causal agent. As assumed by Williams *et al.*,<sup>2</sup> and found by McGregor *et al.*,<sup>3</sup> our experience was that *Bacillus* sp., diphtheroids, and *Micrococcoccus* sp. were only found as contaminants, and that *E. coli*, pneumococcus, *Klebsiella*, *Pseudomonas* sp., *H. influenzae*, *Streptococcus viridans*, and the meningococcus were only found in true septicaemias. Pneumococci, *H. influenzae*, meningococcus and enterobacteria, *Citrobacter freundii* and *Aeromonas*, were never found as nosocomial infections.

Clearly, nosocomial infections are of increasing importance and 39% of the septicaemias reported here developed in hospital—a rate similar to that found at the Boston City Hospital over 12 selected years between 1935-1972,<sup>7</sup> and more recently.<sup>4</sup> At least five patients (10% of all nosocomial infections<sup>5</sup>) developed septicaemia while receiving intravenous therapy, which could be regarded as of aetiological significance.<sup>9,12</sup> This proportion is nearly double that of McGowan *et al.*<sup>4</sup> Seven of the eight *Staph. epidermidis* septicaemias (7% of all *Staph. epidermidis* positive cultures) were associated with intravenous therapy, consistent with the findings of McGregor *et al.*<sup>3</sup> Of the nosocomial infections, 54% followed major surgical intervention. The medical wards received 89% of the community acquired infections and of these *E. coli* and pneumococcus together accounted for one third, similar to the results of McGowan *et al.*<sup>4</sup>

A number of prognostic features emerged. The mortality rate increased to the age of 40 years, and then levelled off at about 40%, whereas other authors showed increasing mortality with age.<sup>8,13</sup> As at the Boston City Hospital,<sup>7</sup> bacteraemia was most frequent in the young and the old. The type of organism also plays a role in the outcome—Gram-negative organisms, causing one half of infections, accounted for two-thirds of deaths.

Immunosuppressive therapy doubled the mortality rate (50%), compared to immunocompetent patients (27%) and patients with immunodeficiencies (25%). That the mortality rate rose with the number of antibiotics administered is disturbing. A plausible explanation is that the patients with severe illness received multiple drugs and died from causes other than septicaemia. It also suggests that polypharmacy may not help.

The absence of any prognostic significance in the body temperature is at variance with the findings of Kreger *et al* in Gram-negative bacteraemia.<sup>13</sup> Conventional wisdom might hold that hypothermic patients could have a higher mortality rate because of the association with Gram-negative organisms and, likewise, the presence of a high fever should represent an increased immune response by the patient, but our data failed to support this.

### Conclusion

Septicaemia is important and life-threatening, affecting 0.5% of patients admitted to one large general hospital. The diagnosis is difficult and is rendered more so by frequent contaminated cultures. The use of multiple antibiotics is not associated with a fall in mortality rate. A greater awareness of the frequency of the syndrome in a large modern hospital, and a closer collaboration between clinician and microbiologist, seem to be important.

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## Toxocariasis

### A possible cause of the Palm Island mystery disease

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**ABSTRACT:** Toxocariasis may have been the cause of the outbreak of a hepatitis-like illness amongst residents of the Palm Island community in 1979. Baby fruit bats on the island were infected with *Toxocara pteropodis*, and many eggs of this worm were recovered from mangoes. The lifecycle of

*T. pteropodis* is described and compared with that of *T. canis*. If *T. pteropodis* was responsible, the infection could be prevented by washing the mangoes before eating them.

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BYTH described an outbreak of a hepatitis-like syndrome which occurred on Palm Island in November, 1979.<sup>1</sup> The symptoms suggested toxocariasis<sup>2,3</sup> as the cause, and this possible aetiology was investigated at the time of the outbreak; the results are presented here.

### Methods and Results

Because of the explosive nature of the outbreak, it seemed unlikely that the well-known causes of human toxocariasis, *Toxocara canis* of the dog or *T. cati* of cats, could be involved. But there are species of *Toxocara* in other hosts which may be zoonotic, and can be expected to cause similar symptoms in humans. A feature common to all the patients was that they had eaten locally grown mangoes, which could have provided the entry route for the eggs of a *Toxocara*, or a related genus, from fruit bats which are common in the area.

Fourteen fruit bats, *Pteropus alecto* collected at nearby Townsville early in December, 1979, were examined. Three suckling young

were infected with a *Toxocara* sp., subsequently identified as *T. pteropodis*, and were passing viable eggs in their faeces. Three males, four females and four other juveniles were uninfected. Examination of bats caught in Brisbane early in January, 1980, also showed that suckling young were infected, while the adults were not. Furthermore, a second species of fruit bat, *P. poliocephalus*, was found infected with a *Toxocara* sp. and an egg-excreting baby caught on January 17, 1980, continued to excrete eggs until January 27, when at least one of the adult worms was spontaneously expelled in the faeces. After this, no more eggs were produced. The gut was empty of worms, which normally lie in the upper part of the small intestine, when the bat was killed on July 23, 1980.

*Toxocara pteropodis* was originally described from specimens collected from the alimentary canal of a suckling fruit bat, *Pteropus geddiei*, at Hog Harbour, Espiritu Santo, New Hebrides.<sup>4</sup> It had not previously been recorded in Australia.

Thirteen mangoes, collected on December 13, 1979, on Palm Island after they fell from the trees, were washed and the washings examined for eggs. Many hundreds of viable eggs of *T. pteropodis* were present. These eggs are readily distinguishable from those of *T. canis* which could be expected to be present in small numbers on the ground. At the same time, washings of a sample of privately

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