COMMUNITY ACQUIRED BACTERAEMIA; A PROSPECTIVE SURVEY OF 239 CASES.

SUBMISSION FOR THE M. MED PART III.

BRIAN L. RAYNER, M.B.Ch.B., F.C.P.(S.A.).

SUPERVISOR : PAUL A. WILLCOX, B.Sc.(Hons), M.B.Ch.B., M.R.C.P.(U.K.).

DEPARTMENT OF MEDICINE, UNIVERSITY OF CAPE TOWN.

This study was published in part in the Quarterly Journal of Medicine: B.L. Rayner, P.A. Willcox. Community acquired bacteraemia; a prospective survey of 239 cases. Q J Med Nov 1988.

INTRODUCTION

The incidence and epidemiology of bacteraemia has been widely reported in the United States and Europe [1-13] but little data is available from Southern Africa. In addition, most studies have concentrated on the overall incidence of bacteraemia, on individual organisms, or clinical situations. [14-19] and it is difficult to interpret the data from these studies with regard to community acquired bacteraemia. From a retospective survey of summaries from a single medical ward at Groote Schuur Hospital it was estimated that bacteraemia accounted for about 4% of the total admissions. It was therefore thought useful to provide clinicians particularly at Groote Schuur Hospital with information about community acquired bacteraemia to improve overall patient management. With this in mind it was decided to undertake a comprehensive prospective study of community acquired bacteraemia at Groote Schuur Hospital.

PATIENTS AND METHODS

Between 1st February 1986 and 31st January 1987 all positive blood cultures from the Groote Schuur Hospital Bacteriology Laboratory were reported to the investigators (Dr. Paul Willcox and myself) and were analysed prospectively to determine the incidence, patient profile and outcome of community acquired bacteraemia.

1) BLOOD CULTURE TECHNIQUE

3 - 5 mls of blood was innoculated into a 7D anaerobic and 6B aerobic BACTEC blood culture bottles (Johnson Laboratories)

respectively. Each contained 30 mls of volume enriched tryptic soy broth, anticoagulant and ^{14}C labelled substrate. Aerobic 6B bottles were incubated at 37 °C and tested on the BACTEC 460 twice on the first day and once daily for 7 days. Anaerobic 7D bottles were incubated at 37 C and tested daily from days 2 - 7. A growth index of 35 or more and 20 or more for aerobic and anaerobic bottles respectively was considered positive. A gram stained slide was then prepared on positive bottles and appropriate identification and antibiotic sensitivity testing performed.

2) DEFINITIONS

(1) Community acquired bacteraemia

An episode of bacteraemia was considered to be community acquired if the culture was obtained within 48 hours of admission unless it was related to a procedure after admission or it was considered a contaminant. Other exclusion criteria were that the patient was 12 years or younger since most paediatric cases are admitted elsewhere; had an indwelling catheter; and was involved in trauma prior to admission.

(2) Statistical analysis

All statistical testing was done by X^2 test, Fisher's exact test or student "t" test.

(3) Outcome

This was only analysed during the hospital stay and patients dying after discharge were considered to have survived for purposes of the study.

EPIDEMIOLOGY

RESULTS. During the study period blood cultures were taken from 4595 patients and a positive growth was obtained in 626. Two hundred and thirty nine of these were considered to have community acquired bacteraemia. The remaining 387 patients had either hospital acquired bacteraemia or contamination of the blood culture. In the same period 53,208 patients were admitted to Groote Schuur Hospital and the overall prevalence of community acquired bacteraemia was 4.5/1000 admissions.

DISCUSSION. The prevalence of community acquired bacteraemia appears to be low but many admissions to hospital are for elective surgical procedures, trauma or inpatient investigation and it is difficult to determine the exact prevalence in relation to acute hospital admissions. However it probably can be inferred that it is a important problem in emergency medicine.

Interestingly the prevalence of 4.5/1000 admissions closely correlates with the community acquired data of a recent comprehensive study of bacteraemia from the United Kingdom.[1]

PATIENTS

RESULTS. Of the 239 episodes 117 occured in females and 122 in males with a mean age of 48 years (range 13 - 90). There were 142 mixed race, 52 white, 44 black and 1 Asian patient. The overall mortality was 29.2% (70 patients). There was no statistical difference in mortality in relation to sex or race of the patients. Figure 1 shows the relationship of mortality to age. Mortality was significantly higher in patients > 30 years (7,6% versus 35,6%; p<0,00004).

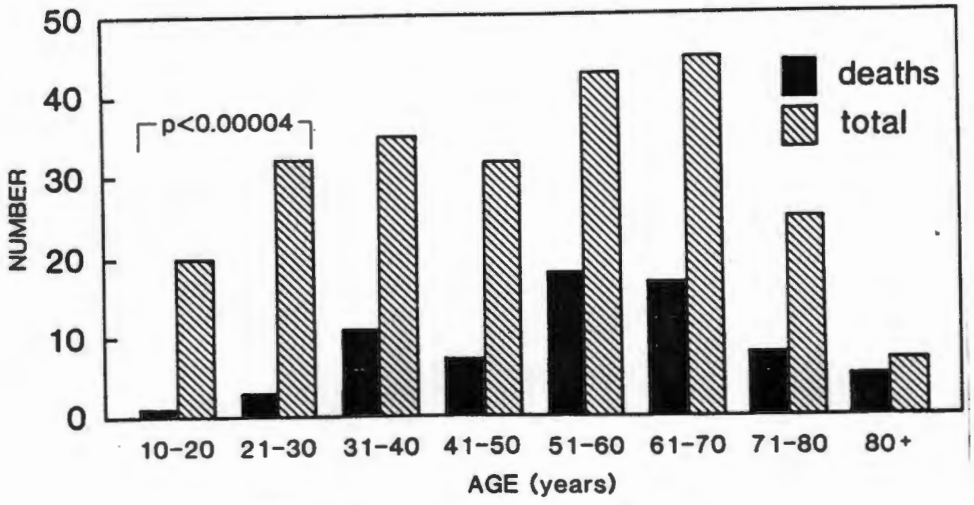

FIG. 1. Mortality related to age of patient.

DISCUSSION. The overall mortality for the study was 29.2% which is considerable. This figure is comparable to earlier studies and despite the development of newer and more powerful antibiotics and modern intensive care support mortality is high. Later in depth discussion of particular aspects of the study will try and elucidate the reasons for this.

Surprisingly mortality rose sharply after the age of 30 years and remained relatively constant.(Figure 1) There was no significant difference in outcome between the under and over 65's in a recent survey (D. Whitelaw personal communication) This is an important clinical observation as it is not just elderly patients who are at high risk.

ORGANISMS

1) OVERALL.

RESULTS. The distribution of organisms and their relationship to mortality is shown in Table 1. There were 108 episodes of gram negative bacteraemia and 131 gram positive with very similar mortalities (26.8 versus 29.5%,NS). The most common isolate was

Escherichia coli (E.Coli) followed by Streptoccus pneumoniae (S. pneumoniae) and Staphylococcus aureus (S. aureus). Mortality was highest in the haemolytic streptococci (72.7% p<0,003) and Klebsiella group (61% p<0,005). The lowest mortality was recorded in the Viridans streptoccal group (0% p<0,02) and E.coli (18.8% p<0,04). Polymicrobial bacteraemia accounted for ten episodes with only a 20% mortality. (N.S.)

TABLE 1 INFECTING ORGANISMS AND MORTALITY

	EPISODES	%	DEATHS	%	
GRAM NEGATIVE					
E. coli	69	28.9	13	18.8	p<0,04
Klebsiella sp.	18	7.5	11	61.1	p<0,005
Salmonella typhi	4	1.6	0	0	
N. meningitides	4	1.6	0	0	
H.Influenza	3	1.2	1	33.3	
Salmonella sp.	2	0.8	1	50	
Pseudomonas sp.	2	0.8	2	100	
Miscellaneous	6	2.5	1	16.6	
TOTAL	108	45	29	26.8	
GRAM POSITIVES					
S.pneumoniae	51	21.3	17	33.3	
S. aureus	29	12.1	12	41.3	
Viridans Strepto-cocci	14	5.8	0	0	p=0,02
Haemolytic Strepto-cocci (A,B,& C)	11	4.6	8	72.7	p<0,003
Peptococcus	5	2	0	0	
Miscellaneous	11	4.6	2	14.2	
TOTAL	121	50.6	39	29.5	
POLYMICROBIAL	10	4.2	2	20	
GRAND TOTAL	239	100	70	29.2	

DISCUSSION. The most common organisms found in the study were E. coli, Klebsiella sp, S. pneumoniae and S. aureus which is what

has been described from other centres.[1,2,6,7,9,10,12] H. influenzae was not a common isolate due to the exclusion of paediatric patients from our study. Opportunistic organisms had a low incidence. Analysis of mortality data showed no difference between gram negative and positive organisms or polymicrobial infection unlike other series.[1,3] Although gram negative sepsis has historically a worse outcome it would appear that better management has contributed to the decline in mortality. Two specific organisms were associated with a particularly high mortality, namely the Klebsiella and haemolytic streptoccal group which contrasted with the low rates for the E. coli and S. viridans group. The clinical features and outcome of the common and important organisms in the study will be dicussed in detail below.

2) **E.COLI**

RESULTS. E. coli was the most common organism in the study occurring in 69 patients (29%). The clinical features of this group are shown in table 2.

TABLE 2. CLINICAL FEATURES OF E. COLI. BACTERAEMIA.

	EPISODES	%	DEATHS	%
NUMBER	69	29	13	19
SEX				
Males	18	26	5	28
Females	51	74	8	16
SITE				
Urinary tract	46	67	6	13
Undetermined	15	22	5	33
Biliary	5	7	0	0
UNDERLYING DISEASE				
Diabetes	28	41	8	29
Nil	9	13	1	11
Malignancy	7	10		
COMPLICATIONS				
Acute renal failure	18	26	5	28
Respiratory failure	6	9	3	50
Hepatic dysfunction	9	13		
D.I.C.	4	6		
Shock	7	10	2	29
CAUSE OF DEATH				
Bacteraemia	10	77		
Nosocomial sepsis	1	8		
Miscellaneous	2	15		

DISCUSSION. E. coli is a normal commensal of the gastro-intestinal tract. It is responsible for over 90% of community acquired urinary tract infections (UTI's) and a common pathogen in gastro-intestinal and biliary infection.[20] It is therefore not surprising that the most common source of infection was the urinary system in 46 patients (67%) and the major predisposing factors are the female sex and diabetes mellitus in 74% and 41% of cases respectively. Fifteen patients had no primary site identified but in many of these cases mid-stream urines were not sent for culture prior to starting antibiotics.

Interestingly the mortality for the group was significantly

lower compared to the rest of the bacteraemic patients (19% versus 34%, p <0.04) which is rather surprising for a serious gram negative bacteraemia. This may be because bacteraemia arising from the urinary tract represents a less serious invasion of the body defence mechanisms compared to infection arising from the lungs (see Klebsiella and S. aureus infection) or E. coli is inherently less virulent.

The most common complication was acute renal failure (ARF) probably due to a combination of pyelonephritis and bacteraemia. Other major complications of bacteraemia shock and respiratory failure had a relatively low incidence and in an addition a low mortality compared with other bacteraemias.

3) KLEBSIELLA

RESULTS. Klebsiella bacteraemia accounted for only 18 episodes of bacteraemia but nevertheless formed an important subgroup of patients. The clinical features are shown in table 3.

TABLE 3. CLINICAL FEATURES OF KLEBSIELLA BACTERAEMIA.

	EPISODES	%	DEATHS	%
NUMBER	18	7.5	11	61
SEX				
Females	3	17	1	33
Males	15	83	10	67
SITE				
Respiratory	10	56	8	80
Urinary tract	6	33	1	17
Miscellaneous	2	11	2	100
UNDERLYING DISEASE				
Diabetes	5	28	2	40
Malignancy	2	11	1	50
Nil	6	33	5	83
COMPLICATIONS				
Acute renal failure	8	44	5	63
Respiratory failure	11	61	7	64
Hepatic dysfunction	4	22		
D.I.C.	4	22		
Shock	6	28	6	100
CAUSE OF DEATH				
Bacteraemia	10	91		
Miscellaneous	1	9		

DISCUSSION. Klebsiella infection is an important cause of nosocomial sepsis, and a less common cause of community acquired pneumonia and urinary tract infection.[20] In this survey the mortality of Klebsiella bacteraemia was significantly higher than the rest of the group (61% versus 27%, $p<0.005$). The majority of deaths occured if the primary site of infection was the lungs compared to a negligible mortality if this was the urinary tract (80% versus 17% respectively). A similar observation was made by Montgomerie.[15] The reason for the difference in mortality was probably due to the high incidence of chronic alcoholism in the former group suggesting that aspiration may have been the precipitating event. These patients were all extremely ill often requiring urgent admission to an intensive care unit for respiratory support. None of the patients received combination

antibiotics (a cephalosporin and an aminoglycoside) initially. This regimen has been recommended for serious Klebsiella infection [20] and may have helped reduce mortality.

Because of the very poor outcome of Klebsiella pneumonia it is extremely important that clinicians recognise this condition before cultures are available so that aggressive, early and appropriate treatment can be instituted. It should be suspected in any male alcoholic with pneumonia particularly if complicated by respiratory failure.

3). S. PNEUMONIAE.

RESULTS. Pneumococcal bacteraemia formed the second most common isolate in the survey. The clinical features are shown on Table 4.

TABLE 4. CLINICAL FEATURES OF S. PNEUMOMONIAE BACTERAEMIA.

	EPISODES	%	DEATHS	%
NUMBER	51	21	17	33
SEX				
Male	32	63	9	28
Female	19	37	8	42
ALCOHOLISM	14	27	7	50
SITE				
Respiratory	43	84	14	33
Undetermined	3	6	1	33
Miscellaneous	5	10	2	40
UNDERLYING DISEASE				
Nil	20	39	3	15
Diabetes	5	10	2	40
Chronic lung disease	8	16	5	63
COMPLICATIONS				
Acute renal failure	12	24	7	58
Respiratory failure	8	16	6	75
Hepatic dysfunction	5	10		
D.I.C.	2	4		
Shock	8	16	7	88
CAUSE OF DEATH				
Bacteraemia	10	59		
Pulmonary embolus	2	12		
Miscellaneous	5	29		

DISCUSSION. S. pneumoniae is the most common form of community acquired bacterial pneumonia and is complicated by bacteraemia in 1/3 of cases. Mortality depends on the serotype involved and can range from 10 - 50%. No serotype analysis was done in our patients. Mortality in this survey was 33 % which is extremely high and leaves no room for complacency in the treatment of this disorder. Patients with the worst outcome usually had underlying chronic lung disease or alcohol abuse (63% and 50% mortality respectively) although the numbers are small to draw definitive conclusions.

Interestingly not all deaths were due to bacteraemia. In 3 patients the cause of death was not established and 2 died of pulmonary emboli. It is uncertain if the death rate for pneumococcal bacteraemia can be reduced as most patients were treated appropriately. Even admission to the intensive care seems to have limited impact on mortality.

4) VIRIDANS STREPTOCOCCAL BACTERAEMIA.

DEFINITION. This group included Streptococcus mitior, salivarius, and sanguis.

RESULTS. This organism accounted for a small number of cases in this survey but was important because of its significantly reduced mortality. (0/14, $p<0.02$). The clinical features are shown in table 5.

TABLE 5. CLINICAL FEATURES OF S. VIRIDANS BACTERAEMIA.

	EPISODES	%	DEATHS	%
NUMBER	14	6	0	0
SEX				
Male	7	50		
Female	7	50		
ALCOHOLISM	4	29		
SITE				
Cardiac	6	43		
Undetermined	4	29		
Miscellaneous	4	29		
UNDERLYING DISEASE				
Nil	3	21		
Diabetes	1	7		
Cardiac	6	43		
COMPLICATIONS				
Acute renal failure	0	0		
Respiratory failure	0	0		
Hepatic dysfunction	1	7		
D.I.C.	0	0		
Shock	0	0		

DISCUSSION. This group of organisms are usually normal commensals of the oropharynx but cause significant morbidity due to dental caries and local sepsis. Transient bacteraemias may follow dental manipulation and endocarditis may occur in susceptible individuals with underlying valvular or congenital heart disease. This is well borne out by the survey as 6 patients (43%) had underlying endocarditis complicating rheumatic or congenital heart disease. No relationship could be found to previous dental work. The source of infection was unknown in 4 cases.

Despite a high incidence of endocarditis in this group the mortality was zero suggesting that this organism is not particularly virulent and / or extremely susceptible to antibiotics. This is also readily apparent by the complete absence of complications save 1 case of jaundice.

5) HAEMOLYTIC STREPTOCOCCI GROUP A,B,C,E.

RESULTS. This was a small but important group because of a significantly increased mortality. (73%, $p<0.003$) The clinical features are shown in table 6.

TABLE 6. CLINICAL FEATURES OF β HAEMOLYTIC STREPTOCOCCAL BACTERAEMIA.

	EPISODES	%	DEATH	%
NUMBER	11	5	8	73
SEX				
Male	4	36	2	50
Female	7	64	6	86
SITE				
Skin	6	55	5	83
Undetermined	4	36	3	75
Miscellaneous	1	9		
UNDERLYING DISEASE				
Nil	1	9		
Diabetes	5	45	4	80
Cancer	4	36	3	75
COMPLICATIONS				
Acute renal failure	4	36	4	100
Respiratory failure	2	18	2	100
Endocarditis	2	18	2	100
Shock	2	18	2	100
CAUSE OF DEATH				
Bacteraemia	6	55		
Cancer	1	18		
Miscellaneous	1	9		

DISCUSSION. Group A B haemolytic streptococci are common pathogens in man causing tonsillitis and skin infection. Other groups can cause gynaecological sepsis and neonatal bacteraemia. In the antibiotic era little attention has been paid to haemolytic streptococcal bacteraemia. A few reports have suggested that this has a high mortality; underlying malignancy is a predisposing factor; and infection usually arises from the

skin or subcutaneous tissues. In this group (although the numbers are small) diabetes and underlying cancer appeared to be predisposing factors. The skin was the most common primary site but was undetermined in 4 cases. Any of the major complications of bacteraemia were serious harbingers of death and interestingly 2 patients developed endocarditis. Most deaths were due to the bacteraemia and only one due to the underlying malignancy.

6) S. AUREUS.

RESULTS. The clinical features of S. aureus bacteraemia are shown on Table 7.

TABLE 7. CLINICAL FEATURES OF S. AUREUS BACTERAEMIA.

	EPISODES	%	DEATH	%
NUMBER	29	12	12	41
SEX				
Male	22	76	7	32
Female	7	24	5	71
SITE				
Respiratory	6	21	5	83
Undetermined	9	31	4	44
Skin	5	17	0	0
Bone/Joint	2	7	0	0
Cardiac	3	10	1	33
Urinary tract	2	7	1	50
ENT	2	7	1	50
UNDERLYING DISEASE				
Nil	4	14		
Diabetes	2	7		
Rheumatoid arthritis	2	7		
COMPLICATIONS				
Acute renal failure	6	21	5	83
Respiratory failure	2	7	2	100
Hepatic dysfunction	1	4		
Cerebral embolus	2	7	2	100
Shock	1	4	1	100
CAUSE OF DEATH				
Bacteraemia	6	21		
Cerebral embolus	2	7		
Miscellaneous	4	14		

DISCUSSION. S. aureus is a ubiquitous skin parasite in man causing skin and subcutaneous infection. It occasionally causes serious infection in joints, bones, lungs and on heart valves often with high morbidity and mortality. Staphylococcal bacteraemia is rising in incidence but most of this is related to nosocomial sepsis. Nonetheless community acquired bacteraemia is still an important problem. Males outnumber females by 2 to 1 and confusion is an important presenting symptom in 30 - 40%. Fifteen to thirty percent of cases are associated with osteitis and shock is rare. Primary pneumonia usually occurs post influenza and has an poor prognosis with a mortality of up to 50% in adults.[20]

In the survey group there were 29 cases with a mortality of 41% which is slightly higher than the expected mortality of 30%. The male to female preponderance reported by others was confirmed. The primary site of infection was quite varied and not unexpected although in 9 this was undetermined. Primary osteitis however had a very low incidence probably due to the exclusion of paediatric patients. Although the numbers are small primary S. aureus pneumonia associated with bacteraemia had a 83% death rate (considerably higher than the usually quoted mortality) which contrasts with the absence of death if the primary site of infection was the skin. This is somewhat similar to the difference in mortality between Klebsiella pneumoniae and urinary tract infection. The reason for this high mortality in the former group was unclear as all cases were recognised clinically and appropriate anti-staphylococcal antibiotics were prescribed

usually intravenous cloxacillin alone.

Diabetes mellitus is usually considered a predisposing factor for the development of S. aureus infection but in this series it was only seen in 7% which is considerably lower than for all bacteraemic patients. Despite the high mortality for the group shock occurred in only 1 patient which confirms previous observations. Other complications like ARF and respiratory failure were more common and ominous markers of death in contrast. Interestingly bacteraemia was the direct cause of death in only 50% and cerebral embolus was an important factor in 2 patients with endocarditis. In 3 cases the cause of death was unknown.

SOURCE OF INFECTION

DEFINITION

The source of bacteraemia was defined as clinically known if there was an obvious source of infection or the same organism was isolated from the blood and the local site of infection.

RESULTS

The respiratory and urinary tracts were the most common primary sites of infection but in 19.2% it was unknown. (Table 8). The mortality of primary pneumonia with bacteraemia was significantly higher ($p<0.005$) than the rest of the group contrasting with the significantly lower mortality for urinary tract infection ($p<0.04$). Only 1 patient out 13 died if the source of infection was the genital tract (in most cases due to a spontaneous septic abortion) but this was not statistically significant.

TABLE 8 MORTALITY RELATED TO SOURCE OF INFECTION

SOURCE	EPISODES	%	MORTALITY	%	
Respiratory system	64	26.8	28	44	p<0,005
Urinary tract	58	24.2	10	17	p<0,04
Unknown	46	19.2	17	37	
Skin	16	7	5	31.2	
Genital tract	13	5.4	1	7.7	
Gastro-intestinal tract	13	5.4	4	31	
Cardiovascular system	13	5.4	2	15.5	
Biliary tract	8	3.3	1	13	
Miscellaneous	8	3.3	2	25	
TOTAL	239	100	70	29.2	

DISCUSSION

The marked difference in mortality between the 2 most common sources of bacteraemia i.e. the respiratory and urinary tracts was probably due to the extremely high mortality for primary S. aureus and Klebsiella pneumonia and the low mortality for E. coli infection which is the most common cause of urinary tract infection (46/58 cases). Inherent differences between the urinary and respiratory tract may also have a role if one looks at differences in outcome in the Klebsiella group.

There was a low mortality related to underlying endocarditis which also has been observed by Ispahani.[1] The genital tract also had a low mortality and this was probably due to the a combination of early aggressive combination antibiotic therapy, surgical evacuation of the septic products of conception (as most cases were septic abortions) and the young age of these patients.

ANTIMICROBIAL TREATMENT

DEFINITION

Treatment was considered appropriate if the infecting organism was susceptible to standard in vitro testing and was recommended by standard clinical practice guides. Antimicrobial treatment was considered inappropriate if the organism was resistant to in vitro testing and the treatment regimen was inferior to recommended standard practice. Prompt treatment was defined as an appropriate antimicrobial given within 12 hours of admission and delayed if given after this period.

RESULTS

In 7 patients (2.9%) no antimicrobial therapy was prescribed and 6 of these patients died (85.7%) (Table 9). In a further 9, inappropriate antibiotics were prescribed with a 88.8% mortality. Eighteen patients had delayed but appropriate treatment with a 55.5% mortality. Comparing this outcome to those patients with those receiving prompt antimicrobial therapy there was a highly significant difference in outcome ($p<0,000001$).

Table 10 refers to in vitro resistance to commonly used antibiotics. E. coli and Klebsiella had a high resistance to ampicillin (59.7% and 94.7 respectively) and to a lesser extent cotrimoxazole (37.5% and 44.4% respectively). S. aureus was generally resistant to penicillin but a significant proportion (21.8%) were methicilin resistant. All strains of S. pneumoniae were sensitive to penicillin.

27 Patients received oral antibiotics prior to admission. There were 5 deaths (18.5% N.S.)

TABLE 9 MORTALITY RELATED TO ANTIMICROBIAL TREATMENT

TREATMENT	NUMBER	%	MORTALITY	%	
Nil	7	2.9	6	85.7	
Inappro-priate	9	3.7	8	88.8	p<0,000001
Delayed	18	7.5	10	55.5	
Prompt	205	85.8	46	22.3	

TABLE 10 ORGANISM RESISTANCE TO STANDARD IN VITRO TESTING

	E. coli %	Klebsiella %	S. aureus %	S. pneumoniae %
Penicillin	–	–	81.2	0
Ampicillin	59.7	94.4	–	0
Cotrimoxazole	37.5	44.4	–	–
Cloxacillin	–	–	21.8	–
Cefotaxime	0	0	–	–
Amikacin	0	0	–	–

DISCUSSION

Initiation of early appropriate anti-microbial therapy was an important factor in outcome which has been observed in other series on bacteraemia [1,3,10]. Only 2 out of 18 patients survived if no or inappropriate anti-microbials were administered. Furthermore over 50% of patients died who had delayed but appropriate treatment. Taking these factors together this had a highly significant bearing on outcome ($p<0,000001$) and for this reason antibiotics should be administered promptly after taking appropriate blood cultures in patients with suspected bacteraemia. The choice of antibiotics should be judged by local sensitivities of organisms. In our study the overwhelming

majority of gram negative organisms were sensitive to Cefotaxime or an aminoglycoside and the majority of non-staphylococcal gram positive organisms were sensitive to Pencillin or Cefotaxime. It would therefore seem appropriate that initial treatment should consist of either Cefotaxime (or similar third generation cephalosporin) alone or a combination of Penicillin and aminoglycoside until appropriate sensitivities are available. The only weakness of this regimen would be the limited staphylococcal cover and if this organism is suspected a specific anti staphylococcal agent should be added. One perturbing factor is the 21.8% cloxacillin resistance which may influence selection of an anti-staphylococcal agent.Resistance to cotrimoxazole and particularly ampicillin was very high amongst gram negative organisms and either agent should not be used as first line therapy alone.

CLINICAL VARIABLES

DEFINITIONS

Symptoms prior to admission were recorded with special reference to fever, rigors, sweats, confusion, vomiting and diarrhoea. The admission temperature, total leucocyte count, platelets,liver and renal function, pulse and blood pressure were recorded. Underlying disease was categorised as rapidly fatal (e.g.adults with acute leukaemia or blastic relapse of chronic leukaemia), ultimately fatal (disease likely to be fatal in 5 years), non fatal (disease unlikely to be fatal in 5 years), and none (previously fit).[4,5,20] A patient was considered to be alcoholic if this was stated in the case records.

1) SYMPTOMS

RESULTS

Patients symptoms are recorded in Table 11.Forty seven patients reported none of these symptoms and only 18 (7.5%) fever,rigors and sweats. Confusion only was noted in 26 and this was associated with a 58% mortality (p=<0,002).

TABLE 11 SYMPTOMS OF BACTERAEMIA

SYMPTOM	NUMBER	%
Sweats	48	20
Fever	103	43
Rigors	69	29
Above 3	18	7.5
Confusion	64	27
Vomiting	55	23
Diarrhoea	27	11
Confusion only	26*	11
None of above	47	20

*Mortality 58% p<0.002.

DISCUSSION

Interestingly classical symptoms of bacteraemia were not reported with a very high frequency. Fever occurred in only 43% and the combination of fever,rigors and sweating in 7.5%. Clinicians should be therefore alerted to unusual presentations of bacteraemia. This is well borne out in the patients who presented with confusion alone. In this group there was a significantly higher mortality.(58%, p<0.002) In over 50% this was related to a failure to recognise bacteraemia by the attending physician resulting in a delay or failure to institute antimicrobial therapy. This may represent only the tip of the iceberg as the performance of a blood culture suggests that bacteraemia was considered as a possible diagnosis but not treated because of a low index of suspicion. In the majority of

cases this was in the >65 age group. It is possible that patients are dying without blood cultures being performed particularly in elderly persons. Gleckman[26] also stressed this point that in elderly patients with a change in mental status who may not be febrile bacteraemia should always be considered as a possible diagnosis.

2)FEVER, PULSE AND BLOOD PRESSURE.

RESULTS

The highest temperature in the first 24 hours after admission was recorded in 228 patients (Figure 2) with a mean of 38.4 C (range 33 - 41.2). Failure to mount an adequate febrile response (temperature > 37 C) occurred in 24 patients with a 54% mortality (p=0,01). One hundred and twenty eight had a fever > 38.5 with a 24% death rate (p=0,052).

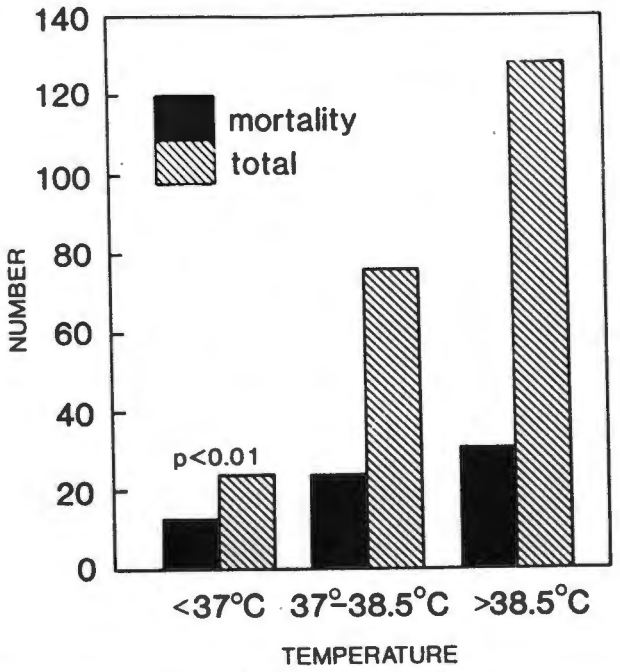

FIG. 2. The highest initial temperature in relation to mortality.

DISCUSSION

This study also confirmed the often noted fact that patients with bacteraemia do not necessarily mount a febrile response in the first 24 hours after admission and this was associated with a significantly poorer outcome (p=0,01).[1,12]

3) UNDERLYING DISEASE

RESULTS (Table 12 and 13)

Sixty one patients were previously fit with a mortality of 23% (N.S). Over 50% were categorised as non fatal disease with a mortality of 27% (N.S). There were 38 patients with ultimately fatal disease with a significantly higher mortality (p=0,04). The numbers in the rapidly fatal group were too small for analysis.The most prevalent underlying diseases are shown in Table 7. There was no significant differences in mortality.

TABLE 12 MORTALITY RELATED TO UNDERLYING DISEASE CATEGORY					
DISEASE CATEGORY	NUMBER	%	DEATHS	%	
Rapidly fatal	5	2.1	2	40	
Ultimately fatal	38	15.9	17	45	P=0,04
Non fatal	135	56.4	37	27	
None	61	25.6	14	23	

TABLE 13 MORTALITY RELATED TO MAJOR UNDERLYING DISEASE				
UNDERLYING DISEASE	NUMBER	%	DEATHS	%
Diabetes mellitus	57	23.5	21	37
Alcoholism	51	21.3	20	39
Immunosuppression	29	12.1	9	31
Nil	61	25.1	14	23.3

DISCUSSION

The underlying pre-existing disease had a small but significant factor in influencing outcome. Not unexpectedly a worse outcome was seen in patients with ultimately fatal disease. Patients without underlying disease did not fare significantly better. There was a high incidence of diabetics in the series (23,5%) which has not been described in previous studies of bacteraemia although it is not surprising that it should occur due to diabetics susceptibility to infection. Diabetics had a slightly worse outcome but not significantly so. Other major underlying diseases were alcoholism in 51 and immunosuppressive treatment in 29 but these patients did not do significantly worse.

4) LEUCOCYTES AND PLATELETS

RESULTS

The mean leucocyte and platelet counts were 14,500μ/l (range 400 - 7500) and platelets 220,000μ/l (range 900 - 721,000) respectively (Table 14 & 15). There was significant increase in mortality if the leucocyte count was below 2,500μ/l (p=0,01) and the platelet count below 100,000μ/l (p=0,002). The clinical features of patients with severe leukopaenia not on prior treatment with cytotoxics or immunosuppressive agents are shown in Table 16.

TABLE 14 OUTCOME RELATED TO THE TOTAL PERIPHERAL LEUKOCYTE COUNT

CELL COUNT (μ/L)	NUMBER	DEATHS	%	
<2,500	15	9	60	p=0.01
2,500 - 9,999	63	19	30	
10,000 - 20,000	94	23	25	
> 20,000	43	12	28	

Mean count 11,500 (range 400 - 75,000)

TABLE 15 OUTCOME RELATED TO TOTAL PERIPHERAL PLATELET COUNT

CELL COUNT (μ/L)	NUMBER	DEATHS	%	
<100,000	36	19	53	p<0.002
>100,000	176	43	23	

Mean count 220,000 (range 9,000 - 721,000)

TABLE 16. CLINCAL FEATURES OF PATIENTS WITH LEUKOPAENIA NOT NOT DUE TO IMMUNOSUPPRESSION.

	EPISODES	%	DEATHS	%
NUMBER	11	5	8	73
SEX				
Males	8		5	63
Females	3		3	100
ORGANISMS				
Klebsiella	6	55	4	67
S.aureus	2	18	2	100
S. pneumoniae	2	18	2	100
PRIMARY SITE				
Respiratory	7	64	6	86
Miscellaneous	4	36	2	50
ALCOHOLISM	5	45	4	80
COMPLICATIONS				
Acute renal failure	7	64	5	71
Respiratory failure	8	73	6	75
Shock	3	27	3	100
D.I.Coagulopathy	2	18	1	50

DISCUSSION

Initial laboratory data was obtained in the majority of patients. The presence of leukopaenia (WCC <2,500) which incidentally was usually due to bacteraemia and not immunosuppressive or cytotoxic agents and a thrombocytopaenia <100,000 u/l were significantly associated with a poor outcome. The cause of such of severe leukopaenia in bacteraemia is not well established. It may be due to peripheral consumption e.g. a severe lobar pneumonia, as part of a disseminated intravascular coagulopathy, due to an underlying disease process e.g. hypersplenism or due to cytotoxic drug therapy. In analysing the clinical features of patients with severe leukopaenia not on immunosuppressives these features are borne out to some extent. Pneumonia was common but not disseminated intravascular coagulation. Interestingly the most common organism was Klebsiella but the reasons for this are not entirely clear.

5) LIVER FUNCTION

DEFINITIONS

Liver function tests were analysed on admission. Patients with biliary sepsis were excluded from analysis and the remainder were divided into patients with (i) no underlying liver disease or alcoholism, (ii) prexisting liver disease and no alcoholism, (iii) alcoholism. Jaundice was defined as a conjugated bilirubin > 20 umol/l.

RESULTS

Admission liver functions are shown in Table 17. Comparing the alcoholic and non alcoholic group the serum albumen, aspartate and alanine transaminases (AST and ALT respectively) were similar but the alcoholic group had higher levels of bilirubin and gamma-glutamyl transferase (GGT) and lower levels of alkaline phosphatase. Patients in group (ii) numbered only 1 and were too small to analyse.

Fifteen patients without underlying liver disease or alcoholism (Table 18) were jaundiced on admission. There were 10 males and 5 females in this group and organisms isolated included S. pneumoniae (6), E. coli (5), Klebsiella (1), haemolytic Streptococcus (1), S. aureus (1) and Salmonella typhi (1). Complications included acute renal failure (4), respiratory failure (5), shock (4), and disseminated intravascular coagulopathy (2). Mortality was 40%(6/15 N.S.) and most deaths were due to overwhelming bacteraemia. The mean transaminases, alkaline phoshatase and bilirubin were elevated 2-3 times the upper limit of normal and the GGT 5 times (figure 3).

TABLE 17 LIVER FUNCTION OF PATIENTS ON ADMISSION WITHOUT BILIARY TRACT SEPSIS

	TOTAL		ALCOHOLICS		NO LIVER DISEASE OR ALCOHOLISM	
	NUMBER	MEAN	NUMBER	MEAN	NUMBER	MEAN
Albumen g/l	191	29 (14 - 45)	45	27 (14 - 44)	146	30 (15 - 45)
AST u/l	175	48 (3 - 330)	40	64 (7 - 216)	134	43 (3 - 330)
ALT u/l	163	51 (1 - 530)	33	60 (5 - 530)	129	49 (1 - 375)
GGT u/l	169	99 (1 - 897)	42	168 (9 - 897)	126	77 (1 - 605)
Alk Phos Units	191	155 (16 - 638)	44	137 (17 - 381)	146	161 (16 - 638)
Bilirubin umol/l	191	25 (2 - 298)	44	48 (5 - 298)	146	18 (2 - 218)
C. Bilirub umol/l	191	11 (0 - 113)	44	23 (0 - 113)	146	7 (0 - 80)

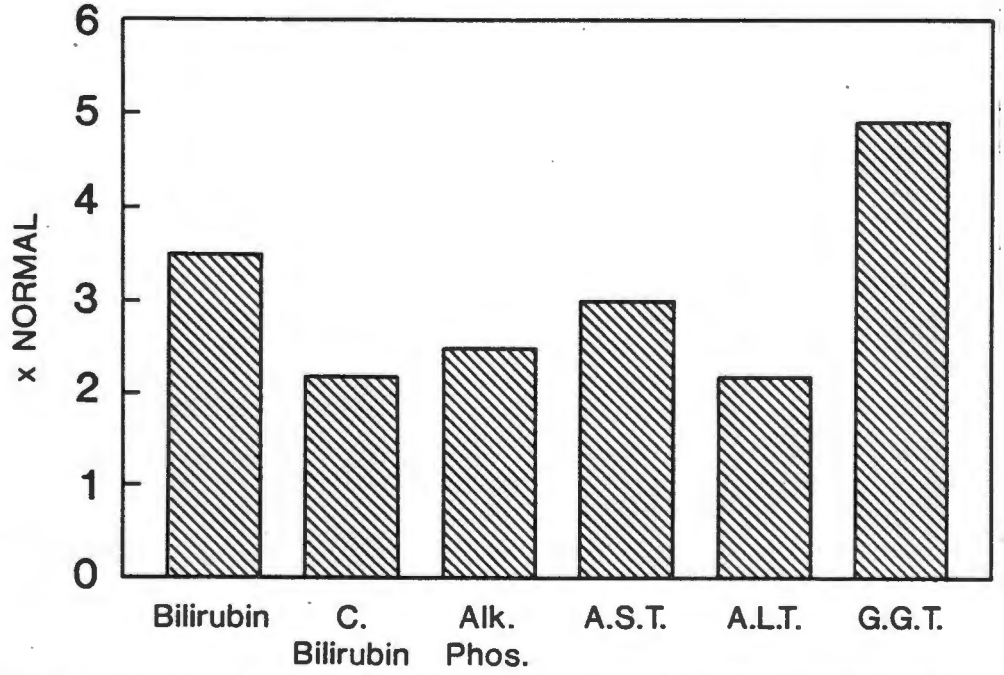

FIG. 3. Liver function in jaundiced patients expressed as a multiple of the upper limit of the normal level.

TABLE 18 LIVER FUNCTION TESTS OF JAUNDICED PATIENTS WITHOUT ALCOHOLISM,LIVER DISEASE OR BILIARY SEPSIS.

		NUMBER	MEAN	RANGE
Bilirubin	(umol/l)	15	59	36 - 118
Conj.bilirubin		15	37	21 - 80
Albumen	(g/l)	15	28	15 - 36
AST	(u/l)	14	119	25 - 330
ALT	(u/l)	14	116	22 - 335
GGT	(u/l)	14	244	34 - 605
Alk Phos	(units)	15	284	78 - 638

DISCUSSION

An interesting aspect of the study was the documentation of liver function in the majority of patients excluding those with underlying biliary sepsis. Not surprisingly the alcoholic patients had a marked elevation in the mean gamma glutamyl transferase with a lesser elevation of alkaline phosphatase and bilirubin. The group without liver disease or alcoholism interestingly had a greater elevation of alkaline phosphatase but the mean gamma glutamyl transferase was just outside the normal range and significantly lower than the alcoholic group.

Fifteen patients had jaundice on admission without a satisfactory explanation except on the basis of bacteraemia(Table 10). This complication has been the subject of several reports and the incidence has ranged from 0,6% to 34%.[27-33] The causes of the jaundice are unknown but is probably related to endotoxin or other bacterial toxins.[34] The jaundice has been reported to be cholestatic in nature and Hoofnagle[35] in pooling data from 7 series showed a picture of hyperbilirubinaemia often marked with marginal elevation in the liver enzymes.[27,30] Liver histology has shown intrahepatic cholestasis with minimal or no hepatocyte

necrosis. Miller[27] suggested that this picture was due to a selective defect in excretion of bilirubin rather than intrahepatic cholestasis. All these studies are flawed by problems in patient selection and definition of jaundice.

This survey probably represents the only one that has documented liver function in patients with bacteraemia in a prospective manner. The incidence of jaundice on admission was 7.8% and there was no significant increase in mortality. In contrast to others the mean levels of transaminases and alkaline phoshatase were elevated in proportion to serum bilirubin but the gamma-glutamyl transferase showed a greater rise (Figure 3). This suggests a more hepatocellular cause for the jaundice which is not changed by the exclusion of the patient with typhoid (a known cause for reactive hepatitis). It is however interesting to note that 3 patients demonstrated the finding of disproportionate rise in bilirubin compared to liver enzymes. This suggests that the pattern of jaundice occurring in bacteraemia is variable and may have a multifactorial aetiology.

COMPLICATIONS

1) OVERALL

RESULTS. The major complications of bacteraemia are listed in Table 19.

TABLE 19 OUTCOME RELATED TO COMPLICATIONS OF BACTERAEMIA.

COMPLICATIONS	EPISODES	%	MORTALITY	%	
None	109	46	11	10	p<0.000001
Acute Renal failure	58	24	31	53	p<0,001
Respiratory failure	39	16	26	67	p<0,000001
Shock	36	15	24	67	p<0,000001
Liver dysfunction	25	10	6	24	
D.I.C	16	7	9	56	p<0,02
Endocarditis	7	3	4	57	

DISCUSSION. It is not surprising that the major complications of bacteraemia particularly acute renal failure, shock and respiratory failure are highly significantly associated with a poor noutcome. Further discussion will focus on the latter complications particularly acute renal failure.

2) ACUTE RENAL FAILURE

DEFINITIONS

ARF was defined as a doubling or more in serum creatinine from baseline. These patients were further subdivided into those who had recovery of renal function in the first 24 hours after admission determined by a progressive fall in serum creatinine without dialysis and those who had persistent elevation or a rising serum creatinine and / or required dialysis. These 2 groups were labelled Group 1 and 2 respectively.

RESULTS

During the 1 year study period 239 cases of community acquired bacteraemia were identified of which 58 (24%) had ARF.

PATIENTS

Of the 58 cases 30 occured in male and 28 in female patients.

The mean age was 54 years (range 17 - 85).The overall mortality was 53% (31 patients) compared with 22% for bacteraemic patients without ARF (p<0,001).Older patients (>65 years) had a significantly worse outcome (79% versus 45%, p<0,05). Mortality was not influenced by sex or race of the patient.

ORGANISMS

The distribution of organisms and associated mortality for ARF and bacteraemic patients without ARF is shown in Table 20. There was a greater number of gram negative than gram positive organisms in the ARF group (53% versus 38%) compared with bacteraemic patients without ARF. The mortality due to gram positive organisms in the ARF group was significantly higher than gram negatives (73% versus 42%, p<0,05). The relative incidences of the most common organisms i.e. E.coli, Klebsiella sp.,S pneumoniae, S aureus, and β Haemolytic streptococci were very similar in each group. Infection due to E. coli had a significantly better outcome (p=0,01) in the ARF group but S. aureus and B haemolytic streptococci had an almost uniformly fatal outcome.

TABLE 20. INFECTING ORGANISMS AND MORTALITY.

ORGANISM	NO RENAL FAILURE				ACUTE RENAL FAILURE			
	EPISODES	%	DEATHS	%	EPISODES	%	DEATHS	%
GRAM NEGATIVE								
E. coli	51	28	8	16	18	31	5	28
Klebsiella sp.	10	6	6	60	8	14	5	63
Salmonella typhi	4	2	0	0	0	0	0	0
N. meningitides	4	2	0	0	0	0	0	0
Miscellaneous	8	4	2	25	5	9	3	60
TOTAL	77	43	16	21	31	53	13	42
GRAM POSITIVE								
S. pneumoniae	39	17	10	33	12	21	7	58
S. aureus	23	13	7	30	6	10	5	83
B Haemolytic Streptococci(A,B,C)	7	4	4	57	4	7	4	100
S. mitior	11	5	0	0	0	0	0	0
Miscellaneous	19	16	2	11	0	0	0	0
TOTAL	99	55	23	23	22	38	16	73
POLYMICROBIAL	5	2	0	0	5	9	2	40
GRAND TOTAL	181	100	39	22	58	100	31	53

SOURCE

The most common sources of infection were very similar to bacteraemic patients wihout ARF i.e. the respiratory and urinary tract and undetermined sources. In addition the trend to a higher mortality for respiratory infection and lower for urinary infection was confirmed. Undetermined sources formed an important subgroup.Other sources of infection are listed in Table 21.

TABLE 21. MORTALITY RELATED TO SOURCE OF INFECTION.

	NO RENAL FAILURE				ACUTE RENAL FAILURE			
	EPISODES	%	DEATHS	%	EPISODES	%	DEATHS	%
SOURCE								
Respiratory	49	27	18	37	15	26	10	67
Urinary tract	40	22	4	15	18	31	6	33
Undetermined	31	17	9	29	15	26	8	53
Skin	12	7	3	25	4	7	2	50
Genital tract	12	7	0	0	1	2	1	100
Gastro-intestinal tract	10	6	2	20	3	5	2	67
Cardiovascular	13	5	2	16	0	0	0	0
Biliary	7	4	0	0	1	2	1	100
Miscellaneous	7	4	1	14	1	2	1	100
TOTAL	181	100	39	22	58	100	31	53

ANTIMICROBIAL THERAPY

The failure to administer appropriate antimicrobials or a delay in their use in all bacteraemic patients was associated with a high mortality. This trend was confirmed in the ARF group with all 9 of these patients dying from bacteraemia or complications thereof ($p<0,0005$).

CLINICAL VARIABLES

The mean temperature, plasma creatinine, white cell count (WCC) and platelets for the study were 37.9 ℃ (range 33 - 41,2), 368 umol/l (91 - 1470), 15,900 µl (0,7 - 65,000) and 177,000 µl (9 - 605,000) respectively. The mean WCC, serum creatinine and platelet counts for the 2 subgroups are listed in table 22. The most important pre-existing disease was diabetes mellitus occuring in 35% of the ARF group compared with 20% for bacteraemic patients without ARF ($p<0,05$). Ten patients had no underlying disease. Diabetics did not have a significantly worse

outcome. Nine patients had severe ARF i.e. an initial serum creatinine >500umol/l and only 4 died. 16 patients were admitted to the intensive care unit (of whom 11 were ventilated) and only 4 survived (p<0,04).

TABLE 22. COMPARISON BETWEEN GROUP 1 AND GROUP 2 PATIENTS.

	GROUP 1	GROUP 2	
NUMBER	30	28	
AGE(mean)	50	57	
MORTALITY	6(20%)	25(89%)	p<0,000001
CREATININE(mean)	385	351	
W.C.C.(mean) ul	17,9	13,7	
PLATELETS(mean) ul	185	168	
TYPE OF ORGANISM			
E. coli	13	5	NS
Klebsiella	3	5	
H. streptococci	0	4	
S. aureus	2	4	
COMPLICATIONS			
Shock	9	13	NS
Resp. failure	6	12	NS
PRIMARY SITE			
Resp. tract	5	10	NS
Urinary tract	11	7	NS
CAUSE OF DEATH			
Bacteraemia	5	20	
Nosocomial sepsis	0	2	
Miscellaneous	1	3	

COMPLICATIONS

The most frequent complications of bacteraemia associated with ARF were shock, respiratory failure, disseminated intravascular coagulopathy, and hepatic dysfunction occurring in 22, 18, 10 and 11 patients. (Table 23) Shock and respiratory failure were associated with a statistical significant increase in mortality to 73% and 78% ($p<0.02$ and $p<0.002$ respectively).

TABLE 23. CONDITIONS COMPLICATING BACTERAEMIA AND ARF.

COMPLICATIONS	EPISODES	DEATHS	%	
Resp. failure	18	14	78	p<0,002
Shock	22	16	73	p<0,02
D.I.C.	10	5	50	
Hepatic dysfunction	11	5	45	

RESOLUTION OF ARF

In group 1 where early recovery of renal function occurred there were 30 patients with a 20% mortality. In contrast in group 2 where there was failure of initial recovery or a requirement for dialysis there were 28 patients with a 89% mortality (p<0,000001). Nine of these patients were dialysed and only 2 survived. No patient died of factors attributable directly to renal failure, hyperkalaemia, metabolic acidosis, and/or volume overload. Most of these patients died before dialysis was indicated. The overall characteristics of the 2 groups are listed in table 22 and serial renal function is shown in figures 4 and 5. Group 2 tends to have more markers of adverse outcome such as shock, respiratory failure, lower WCC and platelet counts than

group 1.

FIGURE 4

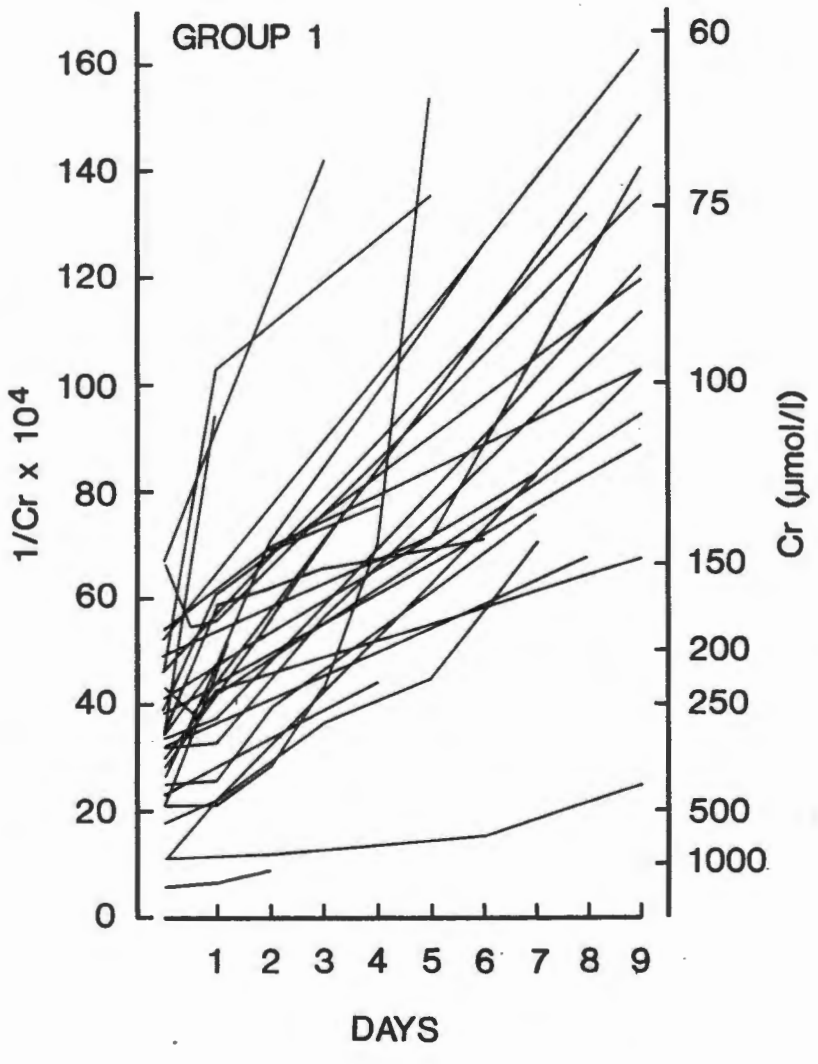

Fig. 4. Time (x axis) versus reciprocal of creatinine (y axis). Corresponding creatinine in µmol/ℓ on the right hand side.

FIGURE 5.

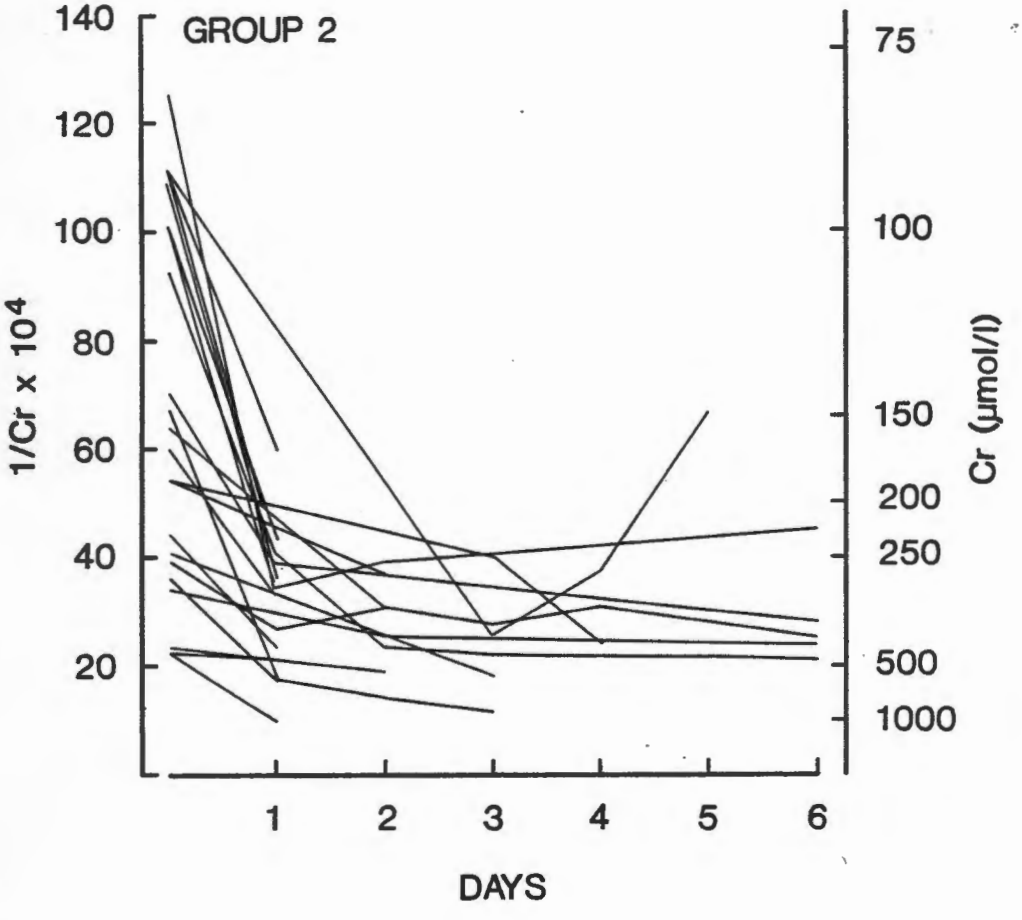

Fig. 5. Time (x axis) versus reciprocal of creatinine (y axis). Corresponding creatinine in µmol/ℓ on the right hand side.

DISCUSSION

The prevalence and outcome of ARF due to bacteraemia is not well defined.[36-41] In this survey the prevalence of ARF was 24% and was shown to be a significant marker of high mortality in bacteraemia despite the inclusion of patients with mild ARF by all criteria. Early resolution of ARF (group 1 patients) with treatment of the underlying bacteraemia was associated with a 20% mortality which is lower than the overall mortality for all bacteraemic patients (29%). In contrast group 2 patients had a highly significantly worse outcome with a mortality of 89% ($p<0,000001$). The reason for this marked diference is not well explained. Although group 2 had more markers for adverse outcome of bacteraemia no factor reached any statistical or clinical significance. Another noteworthy point is the small role for dialysis in this survey. In all, only 9 patients were dialysed out of a total of 58 and only 2 of these patients survived (<5% of the total) but it is unknown if the early institution of dialysis would have improved survival.

The mortality was not influenced by race or sex but those over the age of 65 had a significantly worse outcome which has been noted by some[37,38] but not all[39,42]. Diabetes mellitus was found to predispose to the development of ARF.

A greater number of patients had gram negative bacteraemia in the ARF group compared with bacteraemic patients without ARF but of particular interest was the high mortality of gram positive (73%) compared to gram negative (42%, $p<0,05$) bacteraemia and ARF. This was due to a 90% mortality for B haemolytic

streptococcal and S. aureus bacteraemia.

Another important finding of the study is the 100% mortality associated with the delay or use of inappropriate antimicrobials in patients with ARF. In over half of these instances the delay was due to a failure to suspect bacteraemia as a cause for the ARF. The importance of early, aggressive and appropriate antimicrobial therapy is stressed and it should be commenced as soon as suitable cultures have been obtained.

Not surprisingly the presence of any of the other major complications of bacteraemia i.e. shock and respiratory failure was associated with a high mortality. Interestingly patients with severe acute renal failure (plasma creatinine concentration >500 umol/l) did not do any worse than the other patients.

2) RESPIRATORY FAILURE

DEFINITIONS.

Respiratory failure was defined for the purposes of the study as the requirement for mechanical ventilation and / or a PaO_2 of < 8 kPa.

RESULTS.

The clinical characteristics of patients with respiratory failure are shown in Table 24. The cause of the respiratory failure was not recorded but in most instances it was probably due to the adult respiratory distress syndrome. Four patients died of respiratory failure without being ventilated.

TABLE 24. CLINICAL FEATURES OF PATIENTS WITH RESPIRATORY FAILURE.

	EPISODES	%	DEATHS	%	
NUMBER	39	16	26	67	
SEX					
Males	28	72	18	64	
Females	11	28	8	73	
ORGANISMS					
Gram negative	12	31	11	91	
Gram positive	24	62	14	58	p<0.05
Klebsiella	11	28	7	64	
S.aureus	3	8	3	100	
S. pneumoniae	7	18	6	86	
E. coli	6	15	3	50	
Miscellaneous	12	31	7	58	
PRIMARY SITE					
Respiratory	19	49	15	79	
Other	20	51	11	55	p<0.002
ALCOHOLISM	14	36	10	71	
COMPLICATIONS					
Acute renal failure	17	44	13	76	
Shock	19	49	17	90	p<0.04
D.I.Coagulopathy	6	15	4	67	

DISCUSSION.

Respiratory failure is a well recognised complication of bacteraemia particularly gram negative endotoxaemia. This complication has not been well documented in previous studies of bacteraemia. In this survey the prevalence was 16% with a significantly increased mortality of 67% compared to patients without respiratory failure. These results approximate those obtained by Kaplan [43] who studied patients with gram negative bacteraemia. The mortality in that study was probably higher due to inclusion of patients with nosocomial sepsis.

Interesting points to arise from the data are : 1) The preponderance of patients with Klebsiella infection; 2) The very

high mortality if the primary site of infection was the lungs compared to other sites (79% versus 55%, $p<0.002$); Gram positive bacteraemia was almost uniformly fatal compared to gram negative (92% versus 58%, $p<0.05$). The reasons for this is unclear but certainly the trend of the study is for Klebsiella infection to be associated with serious complications and the very high mortality for gram positive bacteraemia to have an ominous prognosis if complicated by renal failure , respiratory failure or shock.

One perturbing point was the 4 deaths due to respiratory failure which occurred without the institution of ventilatory support. The reason for this appeared to be a failure to recognise clinically that the patient was severely hypoxaemic, delays in obtaining blood gas results and /or failing to act on these results.

3) SHOCK

DEFINITION.

Shock was defined as a systolic blood pressure of < 90mmHg in a clinically euvolaemic patient.

RESULTS.

The clincal details of patients with shock are shown in Table 25.

TABLE 25. CLINICAL FEATURES OF PATIENT WITH SHOCK.

	EPISODES	%	DEATHS	%	
NUMBER	36	15	26	72	
SEX					
Males	20	56	16	80	
Females	16	44	10	63	
ORGANISMS					
Gram positive	13	36	12	92	
Gram negative	21	58	13	62	
Klebsiella	8	22	7	88	
S.aureus	2	6	2	100	
S. pneumoniae	8	22	7	88	
E. coli	7	19	2	29	
Miscellaneous	11	31	8	73	
PRIMARY SITE					
Respiratory	13	36	13	100	p<0.002
Other	23	64	13	57	
ALCOHOLISM	6	17	5	83	
COMPLICATIONS					
Acute renal failure	22	61	16	73	
Respiratory failure	18	50	15	83	
D.I.Coagulopathy	6	17	3	50	

DISCUSSION.

Shock is a well recognised complication of bacteraemia particularly gram negative endotoxaemia. In this survey the prevalence was 15% and was associated with a significantly increased mortality. (72%) Gram negative organisms predominated but mortality for gram positive bacteraemia with shock was much higher (92% versus 62%) although the numbers are small to make definitive conclusions. Patients with pneumonia and shock had a significantly increased mortality compared with those who had a other primary sites of infection (100% versus 57%, p<0.002).

FACTORS IN DEATH

RESULTS

The majority of deaths were directly related to the original bacteraemia (Table 26) and a much smaller number due to nosocomial sepsis and the underlying disease process. Secondary complications directly or indirectly related to the underlying bacteraemia accounted for a further 17 deaths. These included massive pulmonary embolus (2),respiratory failure (4), cerebrovascular accidents (2), mycotic aneurysms (2),endocarditis (1),sudden death (3),hyperkalaemia (1), and unknown (2).

TABLE 26 FACTORS IN DEATH

CAUSE OF DEATH	NUMBER	%
Bacteraemia	46	66
Nosocomial sepsis	4	6
Underlying disease	3	4
Secondary or unrelated	17	24
TOTAL	70	100

DISCUSSION

In the majority of patients death was due to the original bacteraemia or complications thereof with the underlying disease and secondary nosocomial sepsis having minor roles. It is therefore imperative that therapy be directed aggressively and appropriately to eradication of the bacteraemia. Previous data presented in this paper suggested that the use of inapproriate or no antibiotics was a highly significant factor in determining outcome and to improve mortality in community acquired bacteraemia prompt and appropriate antibiotics should be administered after taking appropriate cultures. For example if the 70.5% mortality for the group with delayed, no or

inappropriate antibiotics was reduced to the overall mortality for the study ie 29%, 13 patients may have survived and the overall death rate reduced to 19%. Other factors that may have been prevented were the 4 deaths due to respiratory failure who died without the institution of ventilatory support.

CONCLUSIONS

1) Community acquired bacteraemia is a common acute medical problem which continues to have a high mortality.

2) The most common organisms encountered in the study were E. coli, S. pneumoniae, and S. aureus. Organisms associated with a poor prognosis were B haemolytic streptococci and Klebsiella whilst E. coli and Viridans streptococci had a relatively good outcome.

3) The most common sources of infection were the urinary and respiratory tracts whilst there were a large number without an identifiable primary site. Outcome was significantly better if the primary source was the urinary tract but worse if it was the lungs.

4) Inappropriate, delayed or no antibiotic therapy was significantly associated with an adverse outcome. The commonest reason for inappropriate therapy was the failure to consider mental confusion alone as a symptom of bacteraemia particularly in elderly patients.

5) E. coli, the commonest gram negative pathogen, was resistant to ampicillin and cotrimoxazole in 59.7% and 37.5% of cases respectively.

6) Clinical factors predicting a poor outcome were confusion; failure to mount a febrile response; patients with ultimately fatal disease; a WCC < 2,500u/l or platelet count < 100,000 u/l respectively; and any of the major complications of bacteraemia like acute renal failure, respiratory failure, shock and disseminated intravascular coagulation.

7) The analysis of liver function and jaundice formed an important aspect of the study.

ACKNOWLEDGEMENTS

I wish to thank my supervisor, Dr. Paul Willcox, for his invaluable assistance in this project and his considerable help in obtaining all the clinical information. I would also like to thank the the Department of Microbiology (Dr. Roditi) for supplying us with positive blood culture results; Mrs Carmen Stoter for typing the manuscript, Ms Lillian Harris for additional secretarial assistance , Mr Sedick Isaacs for statistical and computer advice; Sue Abrahams for art work; and Dr. Mike Pascoe for his advice on the section on acute renal failure.

REFERENCES

1. Ispahani P, Pearson NJ, Greenwood D. An analysis of community and hospital acquired bacteraemia in a large teaching hospital in the United Kingdom. Q J Med 1987; 63: 427-440.

2. Scheckler WE. Septicemia in a community hospital 1970 through 1973. J A M A 1977; 237: 1938-1941.

3. Setia U, Gross PA. Bacteremia in a community hospital. Spectrum and mortality. Arch Intern Med 1977; 137: 1698-1701.

4. Du Pont HL, Spink WW. Infections due to gram-negative organisms: an analysis of 860 patients with bacteremia at the University of Minnesota Medical Centre, 1958 - 1966. Medicine (Baltimore) 1969; 48: 307-332.

5. Kreger BE, Craven DE, Carling PC, McCabe WR. Gram negative bacteremia III. Reassessment of etiology, epidemiology and ecology in 612 patients. Am J Med 1980; 68: 332-355.

6. Williams GT, Houang ET, Shaw EJ Tabaqchali S. Bacteraemia in a London teaching hospital 1966 - 75. Lancet 1976; 2: 1291-1293.

7. Hassain Qadri SM, Evans LJ, Wende RD, Williams RP. Texas Med 1977; 73: 59-66.

8. Watt PJ, Okubadejo OA. Changes in incidence and aetilcgy of bacteraemia arising in hospital practice. Brit Med J 1967: 1: 210-211.

9. McGowan JE, Barnes MW, Finland M. Bacteraemia at Boston city hospital: occurrence and mortality during 12 selected years (1935 - 1972), with special reference to hospital acquired cases. J Inf Dis 1975; 132: 316-335.

10. Jansson E. A 10 year study of bacteremia. Scand J Infect 1971; 3: 151-155.

11. Skansberg P, Belfrage S, Ericson C, Renmarker K. Bacteremia: the significance of outside versus inside hospital origin. Scand J Infect Dis 1975; 7: 29-33.

12. Weinstein MP, Barth Reller L, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. Rev Infect Dis 1983; 5: 35-70.

13. Hable KA, Horstmeier C, Wold AD, Washington JA. Group A B-haemolytic streptococcemia. Bacteriologic and clinical study of 44 cases. Mayo Clin Proc 1973; 48: 336-339.

14. Nolan CM, Beaty HN. Staphylococcus aureus bacteremia. Current clinical patterns. Am J Med 1976; 60: 495-500.

15. Montgomerie JZ, Ota JK. Klebsiella bacteraemia. Arch Intern Med 1980; 140: 525-527.

16. Gruer LD, McKendrick MW, Geddes AM. Pneumococcal bacteraemia - a continuing challenge. Q J Med 1984; 210: 259-270.

17. Grandsen WR, Eykyn SJ, Phillips I. Staphylococcus aureus bacteraemia: 400 episodes in St Thomas's hospital. Br J Med 1984; 288: 300-303.

18. Madden JW, Croker JR , Beynon GPJ. Septicaemia in the elderly. Postgrad Med J 1981; 57: 502-506.

19. Klastersky J, Weerts D. Recent experience with bacteremia in patients presenting with cancer. Europ J Cancer 1973; 9: 69-76.

20. Mandell GL, Douglas RG, Bennett JE. Principles and practice of infectious disease. John Wiley and sons, New York. 1979.

21. Grandsen WR, Eykyn JE, Phillips I. Pneumococcal bacteraemia: 325 episodes diagnosed at St. Thomas's hospital. Br Med J 1985; 290: 505-508.

22. Ruben FL, Norden CW, Korica Y. Pneumococcal bacteremia at a medical/surgical hospital for adults between 1975 and 1980. Am Med 1984; 77: 1091-1094.

23. Hook EW, Horton CA, Schaberg DR. Failure of intensive care unit support to influence mortality from pneumococcal bacteremia. JAMA 1983; 249: 1055-1057.

24. Henkel JS, Armstrong D, Blevins A, Moody MD. Group A B-hemolytic streptococcus bacteremia in a cancer hospital. JAMA 1970; 211: 983-986.

25. Gallagher PG, Watanakunakorn C. Group B Streptococcal bacteremia in a community teaching hospital. Am J Med 1985; 78: 795-800.

26. Gleckman R, Hibert D. Afebrile bacteremia. A phenomemon in geriatric patients. JAMA 1982; 248: 1478-1481.

27. Miller DJ, Keeton GR, Webber BL, Saunders SJ. Jaundice in severe bacterial infection. Gastroenterology 1976; 71: 94-97.

28. Miller DF, Irvine RW. Jaundice in acute appendicitis. Lancet 1969; 1: 321-323.

29. Borges MAG, DeBrito T, Borges JMG. Hepatic manifestations in bacterial infections of infants and children. Clinical features, biochemical data and morphologic hepatic changes (histological and ultrastructural). Acta Hepato Gastroenterol 1972; 19: 328-344.

30. Fahrlander H, Huber F, Gloor F. Intrahepatic retention of bile in severe bacterial infections. Gastroenterology 1964; 47: 590-599.

31. Eley DF, Hargreaves T, Lambert HP. Jaundice in severe infections. Br Med J 1965; 2: 75-77.

32. Vermillon SE, Gregg JA, Bagenstoss AH, Bartholomew LG. Jaundice associated with bacteremia. Arch Intern Med 1969; 124: 611-618.

33. Franson TR, Hierholzer WJ, LaBrecque DR. Frequency and characteristics of hyperbilirubinemia associated with bacteremia. Rev Infect Dis 1985; 7: 1-9.

34. Utili R, Abernathy CO, Zimmerman HJ. Cholestatic effects of Escherichia coli endotoxin on the isolated perfused rat liver.Gastroenterology 1976; 70: 248-253.

35. Zimmerman HJ, Fang M, Utili R, Seeff LB, Hoofnagle J. Jaundice due to bacterial infection. Gastroenterology 1979; 77: 362-374.

36. Brezis M, Rosen S, Epstein FN. Acute renal failure. In: Brenner BM, Rector FC, eds. The kidney (3rd edition). Philadelphia: WB Saunders, 1986: 735-799.

37. Stott RB, Cameron JS, Ogg CS, Bewick M. Why the persistently high mortality in acute renal failure? Lancet 1972; 2: 75-79.

38. Kennedy AC, Burton JA, Luke RG, et al. Factors affecting the prognosis in acute renal failure. A survey of 251 cases. Q J Med 1973; 42: 73-86.

39. Beaman M, Turney JH, Rodger RSC, McGonigle RSJ, Adu D, Michael J. Changing pattern of acute renal failure. Q J Med 1987; 62: 15-23.

40. Zech P, Bouletreau R, Moskovtchenko JF, Beruard M, Favre-Bulle S, Blanc-Brunat N, Traeger J. Adv Nephrol 1971; 1: 231-258.

41. Baslov JT, Jorgenson HE. A survey of 499 patients with acute anuric renal insufficiency. Causes, treatment, complications and mortality. Am J Med 1963; 34: 753-764.

42. Kumar R, Hill CM, Mc Geown G. Acute renal failure in the elderly. Lancet 1973; 1: 90-91.