GRAM-NEGATIVE SEPTICEMIA

THESIS

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BY

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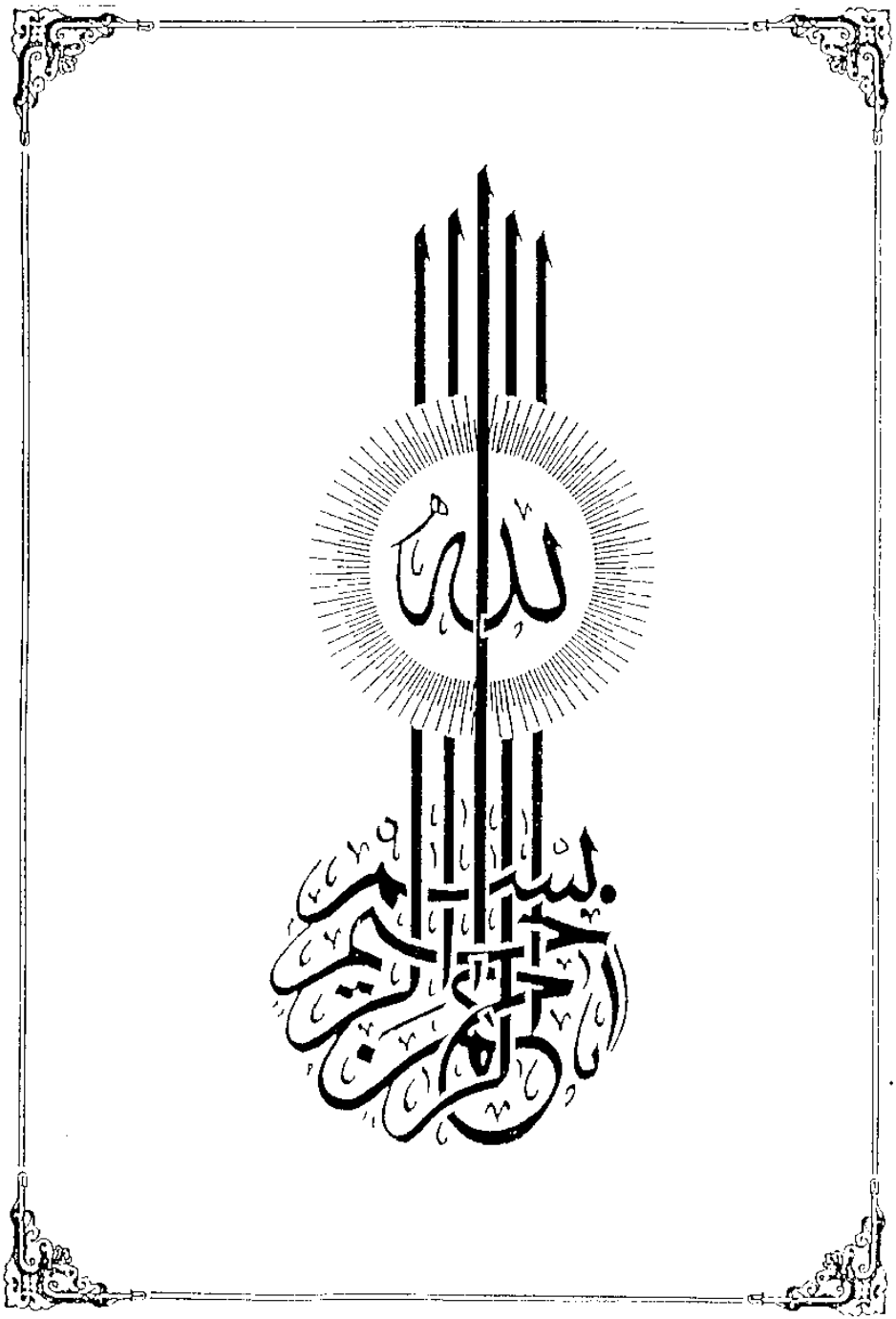

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INTRODUCTION

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Septicemia is a silent killer. In Europe, the term bacteremia indicates the temporary asymptomatic presence of bacteria in the blood, and septicemia is the disease caused by established bacteremia. In the United States, the word bacteremia is used for both. (Smith, 1982).

According to Charlton (1982), bacteremia means the presence of bacteria in the blood, and if accompanied by systemic illness it is called septicemia. Factors which convert a bacteremia to septicemia are the condition of the patient's defence mechanisms and the size and virulence of the infecting inoculum.

Prior to 1909, Jacob was able to collect only 39 cases of E. coli bacteremia from the world's literature. Only occasional case reports appeared subsequently, and bacteremia caused by gram-negative bacilli was considered an unusual clinical entity until Waisbren's report of 29 cases observed at The University of Minnesota

Hospital in 1951. Mc Cabe and Jackson, 1962 demonstrated a sixfold increase in the frequency of gram-negative bacteremia between 1951-1958.

Subsequent observations have indicated a continuing increase in frequency, with a tenfold increase during the 20 years 1951-1971.

Myerowitz, 1971 reported that, gram-negative bacteremia occurs in 1 of 100 hospital admissions. An even greater frequency, 1 per 56 hospital admissions, had been reported by Finland, 1970.

In recent years there appears to have been a steady increase in the incidence of gram-negative septicemia in the hospital population (Mc Cabe et al., 1972). This is due to the ubiquity of gram-negative bacilli in the hospital environment, the universal presence of gram-negative bacilli in the intestine and the frequency of antibiotic resistant strains. (Charlton, 1982).

The fatality of the condition is high, since most infections are occurring in debilitated patients

or under circumstances in which bacteria gain direct access to the bloodstream from sites of infection. The fatality rates from gram-negative bacteremia ranged from 30% to 50% in most series. (Mc Cabe, 1973). In a study undertaken by Weil et al., 1964, at the Los Angeles County Hospital they reported 692 patients with gram-negative septicemia: about a quarter went on to develop a shock-like state, and of these the mortality was 82% compared with 20% for the remainder. The fatality rate of gram-negative septicemia has continued to rise inspite of the introduction of new antimicrobial agents. In the field of surgery this may reflect our unwise enthusiasm for undertaking procedures in relatively unfit and aged patients, being blinkered by the benefits of surgery and forgetting that the host and his defences may be so deficient as to be unable to combat the insult inflicted. (Charlton, 1982).

Shock is a syndrome of generalized motabolic failure resulting from prolonged inadequacy of tissue perfusion. Its early clinical manifestations reflect malfunction of those organs most dependent on uninterrupted blood flow, particularly the brain, as well as compensatory adjustments designed to maintain adequate arterial pressure.

When shock occurs as a specific complication of infection, it is referred to as infectious shock, septic shock, bacteremic shock, and even endotoxin shock. (Heineman, 1981).

The condition that was formerly known by the popular name of blood poisoning is now called septic shock by most clinicians. This simply means widely disseminated infection in many areas of the body, with the infection being born trough the blood from one tissue to another and causing extensive damage.

Septic shock is extremely important to the clinician because it is this type of shock that, more frequently than any other kind of shock besides cardiogenic shock, causes patient death in the modern hospital. (Guyton, 1981).

Table 1. Mortality in 692 Patients with Gram-negative Bacteremia.

	Patients	Deaths	Died
	Bacteremia Alone		
	No.	No.	%
Male	185	51	28
Female	338	54	16
(obestetrical)	(155	(0)	(0)
Total	523	105	20
	Bacterial Shock		
Male	90	79	88
Female	79	59	75
(obestetrical)	(33)	(13)	(39)
Total	169	138	82

AETIOLOGY

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Although almost all gram-negative bacteria may produce bacteremia, the term gram-negative bacteremia is usually reserved for bacteremias produced by members of the families Enterobacteriaceae and Pseudomonadaceae. Bacteremias caused by other gram-negative bacteria (such as meningococci, gonococci, Brucella, Salmonella typhosa, and Haemophilus influenzae) may be associated with similar clinical manifestations but are usually considered as discrete clinical entities rather than under the general term of gram-negative bacteremia. (Mc Cabe, 1981).

The most frequent causative agents of gram-negative bacteremia observed in 612 patients in a Boston Hospital are shown in Table 2, with Escherichia coli accounting for slightly more than one third of cases and Klebsiella pneumoniae, Pseudomonas aeruginosa, and species of Proteus and Bacteroides following in this order. A variety of other genera of gram-negative bacilli, such as Serratia, Acinetobacter, Providencia, and Flavobacter, also are responsible for occasional instances of bacteremia, but the total number of cases caused by these less frequent

species constitutes only about 10 per cent of cases of bacteremia. Mixed or polymicrobic bacteremias in which more than one species of gram-negative bacilli or cocci and gram-negative bacilli are isolated, occur in approximately 15 per cent of cases.

Table 2. Etiologic Agents in Gram-Negative Bacteremia.

Etiologic Agent	Relative frequency (per cent)
E. coli	35
Klebsiella - Enterobacter - Serratia sp. (Klebsiella, 16%, Enterobacter, 9%; Serratia, 2%).	27
P. aeruginosa	12
Proteus sp.	11
Bacteroides sp.	8
Other gram-negative bacilli (Acinetobacter, Alcaligenes, Hafnia, Providencia, Achromobacter, Flavobacter, etc.)	7

Some variations in the relative frequency of etiologic agents may occur in individual hospitals. A higher incidence of bacteremia with Bacteroides and other anaerobic gram-negative bacilli would be anticipated

in hospitals with a large volume of abdominal and gynecologic surgery of large numbers of patients with abdominal trauma. Similarly, a higher proportion of bacteremias from P. aeruginosa occurs in hospitals with large numbers of patients with burns or hematologic malignancies. Bacteremias caused by gentamycin-resistant K-pneumoniae, P. aeruginosa, P. rettgerii and Serratia marcescens have also been reported in a number of hospitals (Freid and Vosti, 1968).

Table 3, lists the most frequent sites of origin of gram-negative bacteremia, factors predisposing to bacteremia, and the species most often causing bacteremia originating from these sites.

Factors involved in the increasing incidience of gram-negative bacteremia are more a reflection of the population affected and changing medical practices than of the virulence of gram-negative bacilli. Several factors appear to be implicated in the continuing increase in frequency of bacteremia.

Bacterial Characteristics

Despite the relatively limited capacity to produce invasive infection, other properties of gram-negative bacilli make them ideal for the production of opportunistic infections. Gram-negative bacilli are ubiquitous in their distribution. Some are major components of the fecal flora, others occur as normal inhabitants of the skin, and gram-negative bacilli are also found in large numbers within the hospital environment. In addition, gram-negative bacilli are relatively resistant to moisture, drying, and some disinfectants, and some are able to persist and multiply in water. Equally important is the proclivity among gram-negative bacilli for the development of antibiotic resistance, which is much greater than that observed with gram-positive bacteria. Resistance is mediated by self replicating, extrachromosomal genetic material termed plasmids. These plasmids are composed of two components: the resistance transfer factor (RTF), which is responsible for the transfer of resistance from one bacterium to another; is linked to resistance determinants (RD), which provide the genetic information required to enable recipient bacteria to perform biochemical changes responsible for antibiotic resistance.