

Septic shock*

Bacteraemic and endotoxic shock

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In 1924 Sanarelli recorded that endotoxins of Gram-negative organisms would damage capillary and postcapillary venular endothelium. By 1935 it was known that two spaced doses of endotoxin given to rabbits would cause renal cortical necrosis and foci of damage in many organs, the Shwartzman reaction. This is due to a combination of vasospasm and intravascular coagulation. Human equivalents of the generalised Shwartzman reaction (GSR) are being recognised with increasing frequency¹ because of the use of accurate coagulation indices² and the sensitive radiofibrinogen catabolism study.³ Disseminated intravascular coagulation (DIC) has been shown to occur at the onset of many types of acute renal failure, and, by concurrent use of the Limulus assay, endotoxaemia has been found to be a frequent cause of renal failure in man.^{3,4} Whether DIC is damaging depends on (a) the fibrinolytic potential of normal renal vascular endothelium, (b) the fibrinolytic activity of the blood, reduced in post-operative and post-traumatic states, and (c) the capacity of the Kupffer cells to clear endotoxin, reduced by alcohol, anaesthetics, and shunting in liver disease. The lipid-A of endotoxin causes vasospasm and intravascular coagulation and in fact all those several factors that are known to contribute to renal shut-down.^{4,5} Lipid A is a concealed antigen on the bacterial surface but when released can insert into cell membranes so as to trigger the various pathophysiological mechanisms that together explain the GSR.⁶ Anti-lipid-A antitoxin antibodies are low in normal people,⁷ and this fact, coupled with relative inadequacy of the Kupffer cell defences in man, explains the susceptibility to the GSR. Genetic influences have not been explored. Even newer antibiotics have not reduced the mortality of Gram-negative bacteraemia much below 50%. One has to consider whether loading doses of antibiotics liberate endotoxin. Clearly, protective antibody, such as antiserum to lipid A-KDO, should be useful in many situations. The efficacy has yet to be demonstrated.⁸

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Aetiological agents and laboratory diagnosis of bacteraemic shock

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During the last 30 years in Britain, the incidence of bacteraemias due to Gram-negative organisms has greatly increased. This increase is associated with more frequent instrumentation and surgery on patients with gastrointestinal, urological, and respiratory disease; increased numbers of patients with impaired host defences against infection; the widespread use of broadspectrum antibiotics; and more frequent opportunities for the spread of Gram-negative bacteria in hospital.

The causes of bacteraemia in one year in a district hospital in London are shown in the Table together with some of the underlying conditions. Although numbers are small, the pattern of main aetiological agents is typical of that seen in many hospitals. *Escherichia coli* is by far the most frequent Gram-negative cause of bacteraemia. *Staphylococcus aureus* and *Streptococcus pneumoniae* are the most frequent Gram-positive causes. These three bacterial species were responsible for the great majority of cases of bacteraemic shock in an American study of