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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References

- ¹ Hjort PF, Rapaport SI. The Shwartzman reaction: pathogenetic mechanisms and clinical manifestations. *Ann Rev Med* 1965;16:135-68.
- ² Colman RW, Robboy SJ, Minna JD. Disseminated intravascular coagulation: an approach. *Amer J Med* 1972;52:679-89.
- ³ Wardle EN. Fibrinogen catabolism studies in patients with renal disease. *Quart J Med* 1973;42:205-19.
- ⁴ Wardle EN. Endotoxin and acute renal failure. *Nephron* 1975;14:321-32.
- ⁵ Wardle EN. Bacteraemic and endotoxic shock. *Brit J Hosp Med* 1979;21:223-31.
- ⁶ Morrison DC, Ulevitch RJ. The effects of bacterial endotoxins on host mediation systems. *Amer J Pathol* 1978;93:526-617.
- ⁷ Blake D, Hamlyn AN, Proctor S, Wardle EN. Anti-lipid A antibodies. *Experientia* 1980;36:254-5.
- ⁸ McCutchan JA, Ziegler EJ, Braude AI. Treatment of gram-negative bacteraemia with anti-serum to core glycolipid. *Europ J Cancer* 1979;15:77-80.

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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

50 cases of this condition.¹ Anaerobes, particularly bacteroides, are responsible for about 10% of bacteraemias.

Shock develops in approximately one-third of patients with Gram-negative bacteraemia, and there is a slightly lower incidence in Gram-positive bacteraemia. Clinically, it is often impossible to distinguish between Gram-negative and Gram-positive shock. About 6% of patients have polymicrobial bacteraemia. Shock is more likely to develop in these patients than in those with bacteraemia due to a single organism.

Microbial investigations

Blood cultures are the most important investigation. One blood culture set should be collected immediately from a patient with bacteraemic shock, and, if possible, a second set should be collected 30 minutes later, just before the start of antibiotic therapy. Anaerobic as well as aerobic media are included routinely in each set. A Gram stain of a turbid broth often gives rapid valuable information about the likely microbial diagnosis. As most bacteria can be isolated from the blood culture broth after only one day's incubation, a routine 24-hour subculture is recommended. Gas liquid chromatography may help the more rapid detection of anaerobes in blood cultures. References about blood culture techniques are given below.^{2 3}

Clinical findings often indicate the source of infection, and all relevant cultures should be taken. The detection of circulating antigen can be attempted

by countercurrent immunoelectrophoresis (CIE), but this is applicable to only relatively few bacterial species, such as *Strep. pneumoniae*.⁴ In a recent outbreak of infection due to gentamicin-resistant *Klebsiella aerogenes* serotype K2, the CIE method proved useful for the rapid detection of the klebsiella capsular antigen in the blood of bacteraemic patients.⁵ Conflicting results have been obtained with the Limulus lysate test for detecting endotoxin in the blood, and this test is not recommended for routine use.⁶

References

- Winslow EJ, Loeb HS, Rahimtoola SH, Kamath S, Gunnar RM. Haemodynamic studies and results of therapy in 50 patients with bacteraemic shock. *Amer J Med* 1973;**54**:421-32.
- Stokes EJ. *Blood Culture Technique*. ACP Broadsheet no. 81. 1974.
- Shanson DC. Blood culture techniques. In: Williams JD, ed. *Modern Topics of Infection*. Heineman; 1978.
- Spencer RC, Savage MA. Use of counter and rocket immunoelectrophoresis in acute respiratory infections due to *Streptococcus pneumoniae*. *J Clin Pathol* 1976;**29**:187.
- Simpson RA, Speller DCE. Detection of bacteraemia by countercurrent immunoelectrophoresis. *Lancet* 1977;**1**: 206.
- Stumacher RJ, Kovnat MJ, McCabe WR. Limitations of the usefulness of the Limulus assay for endotoxin. *New Eng J Med* 1973;**288**:1261-4.

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Bacteraemic cases at St Stephen's Hospital, 1977

Blood culture isolates	No. of cases	Underlying conditions included
Gram negative		
<i>Escherichia coli</i>	12	} Abdominal sepsis + surgery Urinary tract infection + instrumentation Leukaemia; pelvic abscess Cirrhosis of liver Gastroenteritis in elderly; typhoid
<i>Bacteroides fragilis</i>	5	
<i>Klebsiella aerogenes</i>	3	
<i>Proteus mirabilis</i>	3	
<i>Salmonella</i> species	3	
<i>Enterobacter</i>	1	} Respiratory infection and reticulosis
<i>Pseudomonas aeruginosa</i>	1	
<i>Haemophilus influenzae</i>	1	
<i>Neisseria meningitidis</i>	2	
<i>Neisseria gonorrhoea</i>	1	
Total	32	
Gram positive		
<i>Streptococcus pneumoniae</i>	10	} Pneumonia; meningitis Skin, bone, and joint infection. Wound and lung infections. Endocarditis and infected pacemaker
<i>Staphylococcus aureus</i>	8	
<i>Streptococcus pyogenes</i>	2	} Cellulitis Prematurity Abdominal sepsis Endocarditis Female genital tract sepsis
Group B streptococcus	1	
<i>Streptococcus milleri</i>	2	
<i>Streptococcus mutans</i>	1	
Anaerobic streptococcus	1	
<i>Clostridium welchii</i>	1	
Total	26	