Changes in the Microcirculation in Sepsis and Septic Shock

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Introduction

Sepsis and septic shock are characterized by a “mismatch” of oxygen supply and oxygen demand [7]. While in the initial state cardiac output is normal or above normal, and systemic vascular resistance is reduced, the difference between arterial and mixed venous oxygen content is low, indicating the inability of tissues to extract oxygen from arterial blood. This hyperdynamic circulatory state, first described by Waisbren [39], turns into hypodynamic septic shock in the later phases of the disease. It is generally assumed that inadequate oxygen extraction and the transition from the hyperdynamic to the hypodynamic state are due to microcirculatory failure [38]. Since the prognosis of hypodynamic septic shock remains poor, despite all efforts to treat these patients in intensive care units, it is essential to diagnose septic shock at its very onset, while still in the hyperdynamic state.

Recently developed experimental models of septicemia and septic shock have allowed the simulation of such a hyperdynamic circulatory profile by induction of systemic endotoxemia [8, 27, 28, 40]. These models are now being used to elucidate the effects of bacteria and bacterial endotoxins (lipopolysaccharides) on the humoral and cellular systems to identify early changes of microvascular blood flow, for example, its maldistribution within the microvascular bed. Our own recent results suggest that microvascular failure is present already during the initial hyperdynamic phase of endotoxemia, and that it may lead to the development of the multiple organ failure syndrome.

Systemic Endotoxemia

Diagnosis of incipient septic shock should no longer rely on the results of bacterial cultures but on the presence of bacterial endotoxins in the systemic circulation. Today, assays for quantitative determination of bacterial endotoxin in blood and body fluids are available [12, 18, 19]. Endotoxin can usually be demonstrated in peripheral blood before blood cultures give positive results. The presence of measurable amounts of endotoxin in the systemic circulation indicates that the clearance capacity of the reticuloendothelial system for endotoxin has been exhausted, resulting in a “spill-over” of endotoxin into the systemic circulation.

At this point, the bacterial endotoxin has begun all the reactions delineated schematically in Fig. 1: (a) the pyrogen reaction, resulting in fever; (b) stimulation of
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Fig. 1. Release of endotoxin and development of endotoxemia and its influence on cellular and humoral systems. The activation of the coagulation and complement system and, in particular, the tissue release reactions result in an impairment of microcirculatory perfusion, the severity of which varies in the different organs. RES, Reticuloendothelial system; DIC, disseminated intravascular coagulation; IL-1, interleukin 1. (From Messmer et al. [33])

the humoral immune response: (c) activation of the coagulation and complement systems; and (d) tissue release reactions, including activation of monocytes and macrophages, with release of interleukin 1 (IL-1) and subsequent stimulation of the arachidonic cascade [16, 17, 35].