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Comment on “Sublingual capnometry tracks microcirculatory changes in septic patients” by Creteur et al.

Accepted: 21 July 2006
Published online: 29 August 2006
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This comment refers to the article available at: <http://dx.doi.org/10.1007/s00134-006-0343-y>

Sir: We read with great interest the study by Creteur et al. [1]. In resuscitated septic shock patients they demonstrated that increasing systemic blood flow using the β -adrenoreceptor agonist dobutamine at 5 $\mu\text{g}/\text{kg}$ per minute augments capillary surface area in the tongue by increasing the number of perfused capillaries. Simultaneously observed were

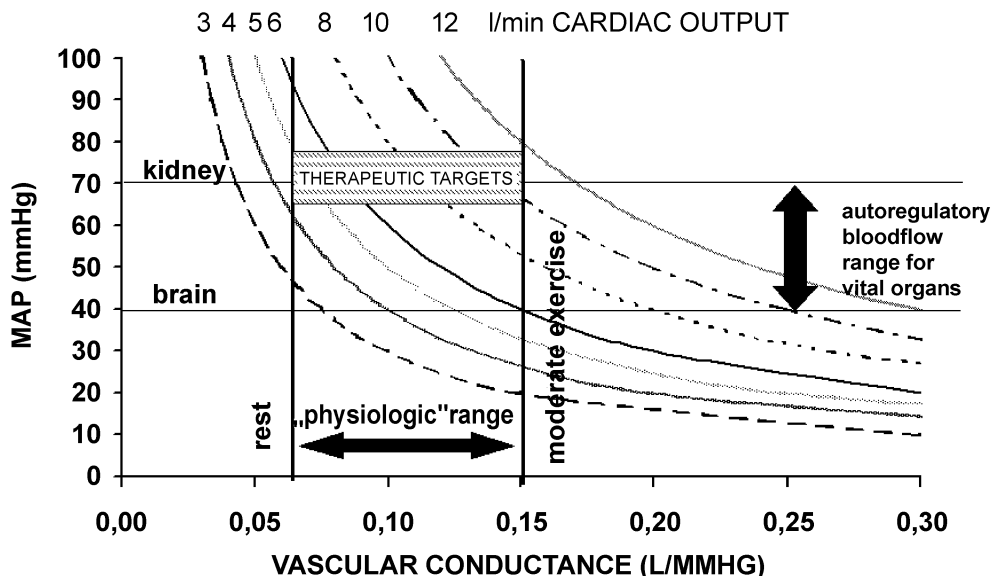
a significant decrease in sublingual carbon dioxide pressure (PslCO_2) and gastric mucosal to the arterial PCO_2 gradient (PgCO_2 gap), an increase in mixed venous oxygen saturation, and a small but significant decrease in blood lactate concentration. The latter findings were related to an existing tissue oxygen supply deficit before dobutamine infusion. The authors concluded that microcirculatory blood flow alterations are present in their patients despite systemic hemodynamic stabilization, and that infusion of dobutamine beneficially improves the microcirculation. The accompanying editorial by Dr. Ince greatly supported the conclusions made by the authors [2].

Although the data are fascinating, we feel that the conclusions drawn are probably premature because important questions remain unanswered. The tongue is a skeletal muscle. Skeletal muscle has an enormous capillary surface area, estimated at 7 m^2/kg , or 210 m^2 in a 75-kg human with 30 kg skeletal muscle [3]. Under resting conditions oxygen consumption is very small, and oxygen extraction is only about 30%. In addition, at rest the neural control

of blood flow predominates while metabolic regulation supervenes during contractions, a finding which is in striking contrast to other organs, for example, the kidney, heart, and brain [4, 5, 6]. Therefore the number of perfused capillaries (capillary surface area) is directly related to skeletal muscle metabolism. This leads to the important but unresolved question of how many well perfused capillaries are necessary for adequate oxygen supply.

Unfortunately the fasted gut including the stomach behaves very similarly to skeletal muscle. Under resting conditions oxygen consumption and oxygen extraction are low. In addition, similar to skeletal muscle, autoregulation of blood flow is strongly associated with organ specific workload [7]. Concerning oxygen, diffusion limitation may well become a major problem for maintaining tissue metabolism if available capillary surface area is critically reduced, for example, in disseminated intravascular coagulation where capillaries are blocked by clots. However, because of the high solubility of carbon dioxide its elimination may remain a purely blood flow limited

Fig. 1 Relationship between vascular conductance (= the reciprocal value of systemic vascular resistance) and mean arterial pressure for different values of cardiac output. Hemodynamic therapeutic targets are aimed at achieving a sustained systemic blood flow presumably consistent with a mean arterial pressure (MAP) that ensures autoregulation of blood flow to vital organs and a vascular conductance within “physiological” limits, thus avoiding myocardial complications and excessive vasoconstriction in tissues rich of smooth muscle α -adrenoreceptors such as skin, skeletal muscle, and gut



process. Thus an increase in tissue blood flow even without increasing capillary surface area still effectively decreases tissue $p\text{CO}_2$ under these conditions.

Since carbon dioxide diffuses approx. 20 times more rapidly through tissues than does oxygen, PslCO_2 is considered to represent true tissue or cellular $p\text{CO}_2$. If tissue $p\text{CO}_2$ is artificially reduced by one-half from normal values of 40–46 mmHg to approx. 20 mmHg, as in the study by Creteur et al., profound effects on cellular acid base balance and consequently tissue metabolism can be expected. Under conditions of diffusion-limited oxygen supply the development of tissue alkalosis may have detrimental effects on tissue survival. Unfortunately, even the observed small decrease in arterial lactate concentration by 0.5 mEq/l during infusion of dobutamine cannot be taken as evidence for improved tissue oxygen supply, because of the complexity of lactate metabolism.

The major problem of hemodynamic management in septic shock patients is the mismatch between cardiac output, which is often severely compromised by acute cardiac dysfunction and vascular conductance, which is abnormally increased due to progressive arterial vasodilatation (Fig. 1). Our therapeutic targets are certainly aimed at achieving a systemic blood flow and vascular conductance presumably consistent with the autoregulation of blood flow to vital organs. Unfortunately, we are often faced with extreme limitations in cardiac function in particular in patients with preexistent cardiac disease. Still, adequate blood flow to vital organs can be maintained

within a relatively broad range of different cardiac outputs by manipulation vascular conductance within physiological limits.

Finally, in the presented study infusion of dobutamine was associated with a significant increase in cardiac index at the expense of an elevation in heart rate by approx. 11 beats/min without changes in stroke volume. Even moderate elevations in heart rate have the potential to be detrimental in intensive care patients if they persist for several hours in particular in patients with preexistent cardiac disease [8].

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