Re. "Changes in lipid metabolism in pediatric patients with severe sepsis and septic shock"

To the Editor:

We would like to congratulate the authors [1] for their careful and interesting article, and offer some considerations and questions regarding their work on pediatric sepsis. We became interested in the association between severe hypocholesterolemia and poor outcome in septic adults by serendipity, as cholesterol has long been part of the standard biochemistry profile of our surgical patients. After a few decades, doubts and uncertainty still remain and any study yielding valuable information on pediatric septic patients [1] is welcome and precious. Our partly unpublished observations suggest that poor outcome is not simply associated with single and isolated measurements of severe hypocholesterolemia, but that death in general follows the persistence of very low cholesterol for several days [2,3], which perhaps explains the lack of correlation of initial cholesterol measurements with outcome in the authors' study [1]. In adults, a cholesterol level even lower than 0.50 mmol/L (≈19 mg/dL) could be followed by survival if reversal of hypocholesterolemia and clinical improvement subsequently ensued [3]. The inexpensive monitoring of cholesterol may enrich the usual clinical and laboratory criteria in individual patients; furthermore unexplained hypocholesterolemia may raise the suspicion of occult sepsis, and reversal of hypocholesterolemia may support the clinical judgment of progressive recovery. The problem is the interpatient variability of cholesterol, which does not allow precise cutoffs and landmarks of risk that are valid for all patients (as it occurs for instance with creatinine). This limitation may sometimes be overcome in routine surgical patients by somehow "normalizing" cholesterol and using the ratio with the baseline preoperative value, but this is not always enough [2,unpublished observations].

We would like to ask the authors [1] whether someone among their patients had cholestasis, and they found some effect of cholestasis in moderating degree of hypocholesterolemia, as observed in adults [3]. This should not be with regard only to obstructive cholestasis, but also "biochemical" cholestasis (increased alkaline phosphatase and γ-glutamyltranspeptidase—although in early age the activity of these enzymes is also influenced by different factors, compared to adult age). The practical implication would be that, in the presence of cholestasis, moderation of the degree of hypocholesterolemia might lead to underestimation of severity of illness.

The authors [1] commented on the effect of endotoxin and cytokines on lipoproteins, immune function, and hypocholesterolemia. Another side of the issue could be the inability to produce sufficient amounts of cholesterol for stress hormone synthesis and for the production and function of new cells taking part in host defense and tissue repair [3–5]. Indeed, cholesterol synthesis is a very demanding process and cholesterol is a main component of cell membranes, simply by weight alone. However, immune and pathophysiologic implications of hypocholesterolemia are still poorly known; for instance, among the unpublished results from our databases, there is a direct correlation between cholesterol and absolute lymphocyte count (and not other white blood cell types) and platelet count in several categories of patients, as shown, for example, for partial hepatectomy patients in the following regression:

$$\text{Cholesterol} = 1.6137 + 0.8502(\text{lymphocytes}) + 0.0037(\text{platelets}) - 0.8885_{[\text{sepsis}]} (r = 0.63, n = 245, P < 0.001 \text{ for each coefficient and whole regression; cholesterol mmol/L; lymphocyte and platelet count} \times 10^9/\text{L}; \text{last coefficient: mean decrease in cholesterol associated with sepsis})$$

whose interpretation, despite significance and repeatability of the results, would be too speculative without more specific assessment.

The other question that we would like to ask is whether the authors [1] (perhaps by evaluating complementary measurements not reported in their study) found some direct correlation between degree of hypertriacylglycerolemia and severity of illness. Their pediatric patients had a median central tendency for hypertriacylglycerolemia, and hypertriacylglycerolemia is often reported as a general feature of sepsis. However, we have long had a different experience, as most of our septic patients had normal or low triacylglycerols, except that triacylglycerols often (not always) increased with the worsening of septic illness. This apparent incongruence might be partly explained by considering that we mostly observed patients in surgical wards (in general with early, less severe septic states) before the worsening of their illness mandated transfer to the intensive care unit; or the issue should also include differences in host response, perhaps due to specific microorganisms or to other causes.

We congratulate once more the authors for their work, and remain grateful for their kind attention.

References

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