

## What tests can help diagnose and estimate the severity of sepsis?

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All critically ill patients with a systemic inflammatory response syndrome or a multiple organ dysfunction syndrome look septic; in spite of this, only half of them are infected.<sup>1</sup> Giving antibiotics to all these patients may seem a good thing to do, at least at first glance. There are indeed data suggesting that the outcome of septic critically ill patients who received antibiotics sooner is better. On the other hand, giving too many antibiotics increases the “antibiotic pressure” in a given intensive care unit, which could result in the development of multiresistant bacteria. There are data suggesting that the administration of more antibiotics increases the risk of contracting a nosocomial infection caused by a multiresistant bacterium<sup>2</sup> and doubles the risk of death.<sup>3,4</sup> Therefore, there is a trade-off here: it is possible that giving antibiotics sooner improves the outcome of infected patients, but it can also increase their risk of contracting an infection caused by a multiresistant bacterium. The best strategy could be to prescribe antibiotics as soon as possible, but only if there is a great *a priori* chance that a critically ill patient who looks septic will really become infected, and to postpone such prescription if the *a priori* chance is small. Therefore, a test able to rapidly differentiate infected from non-infected patients could be of great interest. Bacterial culture remains the gold standard to do so, but the results are available only 1 or 2 days after the question about a possible infection is raised at the bedside. In practice, the physician estimates the chance that a patient will become infected on clinical grounds and on rapid tests, such as white blood cell count, C-reactive protein, and procalcitonin.

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C-reactive protein and procalcitonin are two acute-phase reaction proteins of the inflammatory process. Their blood concentrations increase rapidly after the onset of an inflammation; this increase is usually much more important if the inflammation is caused by an infection and/or if the pathology is severe. Procalcitonin seems to be a more reliable diagnostic marker of inflammation caused by a bacterial infection than C-reactive protein.<sup>5</sup> The normal procalcitonin blood level is lower than 0.1 ng/mL. With a cut-off point of 1 or 2 ng/mL, its sensitivity in diagnosing a bacterial infection ranges between 65% and 100%, and its specificity is between 61% and 100%. The overall sensitivity and specificity, as measured in a systematic review, are 88% (95%CI 80-93) and 81% (95%CI 67-90), respectively.<sup>5</sup> A blood level higher than 10 ng/mL is almost always associated with severe sepsis (a systemic inflammatory response syndrome caused by an infection and associated with at least one organ dysfunction).<sup>6</sup>

Most available data on procalcitonin come from adults, but there are some pediatric studies.<sup>7-12</sup> These data may look better than they are. In many studies, procalcitonin was not measured when practitioners needed to know whether the patient was infected or not: it was sometimes measured days after the infection was suspected, and such time lag may have allowed its further increase in blood, which could increase its apparent diagnostic validity. Actually, the picture could be different if only measurements on blood drawn immediately when the infection was suspected are analyzed. There are very few data addressing this specific question: is procalcitonin a good diagnostic marker of bacterial infection in critically ill children when sepsis is suspected for the first time? Only one study of 61 children provided data on this: St-Louis et al.<sup>13</sup> reported that the positive predictive value of a blood level over 1.8 ng/mL was 67% (it was only 50% for the C-reactive protein).

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Another clinically significant question would be: is there a relationship between the severity of infection and serum procalcitonin level? The study conducted by Fioretto et al.<sup>14</sup> and published in this issue of the *Jornal de Pediatria* was designed to answer this question. They enrolled 90 children with a clinical picture of severe sepsis or septic shock. In all instances, procalcitonin was measured soon after the patients were seen for the first time for their possible infection, i.e. right at their admission to the pediatric intensive care unit and 12 hours later. They found that the blood concentration of procalcitonin was significantly higher in cases of septic shock in both instances. Actually, with a cutoff of 2 ng/mL, the positive diagnostic value to detect cases of septic shock was 60%, and the negative predictive value to exclude septic shock was 81%; with a cutoff of 10 ng/mL, they were respectively 68 and 72%.

The available data suggest that procalcitonin has some diagnostic value in detecting cases of sepsis among critically ill children. Two questions remain: what is the added value of this information over clinical data, and can it change the outcome of patients? Stated differently, the question could be: is procalcitonin useful, given the clinical information already available at the bedside? The results of one study suggest that using procalcitonin to guide the prescription of antibiotics in children with lower respiratory tract infection can decrease antibiotic pressure without influencing the outcome of patients.<sup>15</sup> Nonetheless, more data are required, and a randomized clinical trial should be undertaken to assess test effectiveness before strongly recommending the use of procalcitonin. Meanwhile, we agree with Dr. Fioretto and colleagues that procalcitonin can be used to estimate the severity of illness in septic critically ill children, but only if the clinical data are taken into account.

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