

Procalcitonin: handle with care

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The article by Pieralli and coll. brings to our attention the fact that the use of procalcitonin (PCT) improves the management of respiratory symptoms, which are caused only in part by bacterial infections. In this paper they provide interesting data derived from real-world practice and combine appropriateness with attention to risks and costs of currently used therapies.¹ Although based on a smaller number of patients, their results confirm what larger experimental studies showed about the utility of PCT for diagnosis and management of respiratory tract infections.²⁻⁴ Several papers published in recent years have shown that, in the presence of an opacity on chest X-ray, the negativity of PCT can reasonably exclude an underlying infectious bacterial cause. One of the most significant conclusions of the paper of Pieralli *et al.* is that the duration of antibiotic therapy in respiratory tract infections can be significantly shortened by using PCT, with clinical outcomes comparable to *standard* duration regimens, as previously reported by many other studies and by a Cochrane meta-analysis.⁵ As for all tests, both biochemical and instrumental, it should be always remembered that their value and their significance must be interpreted within the clinical context of the patient that is being evaluated. In fact, currently available data in the literature are almost exclusively focused on respiratory infections, especially those of the lower respiratory tract, and therefore they cannot

be properly downloadable in other clinical settings. In addition, the value of serum PCT could not be appropriately interpreted if performed too early with respect to the onset of symptoms or during antibiotic treatment.⁶ Several conditions which may sometimes present with persistent fever, such as cancer,⁷ endocrine disorders,⁸ and trauma,⁹ are also associated with falsely positive PCT measurements. In these cases, a negative value of C-reactive protein could be useful, if correctly used, to rule out an underlying infectious bacterial cause and to move the attention towards alternative diagnoses.¹⁰ Unlike the respiratory setting, in these different conditions, a positive PCT value must be weighted within the specific clinical context and should not be viewed as directly pointed toward a diagnosis of bacterial infection with consequent automatic prescription of antibiotic therapy. Conversely, for other situations of infectious diseases in other organs, the physicians should know in advance the value of PCT determination. In fact, in presence of closed collections such as abscesses of deep organs or slightly bacteremic diseases such as osteomyelitis or cellulitis, the PCT is usually negative.¹¹ In other settings, such as infective endocarditis, the PCT is not useful for the diagnosis, but may rather guide towards the possible microbiological etiology.¹² In this condition, the diagnostic suspicion should be independent from PCT determination, whereas PCT values may be useful for discriminating between staphylococcal *versus* streptococcal etiology.¹³ Likewise, in front of a frankly septic patient, a particularly high value of PCT should orient to a greater likelihood of sepsis by Gram negative germs.¹⁴ To make this question even more problematic, the key to symbols reported by certain laboratories at the bottom of the report sometimes shows values and cut-off for suspected or confirmed bacterial infections that, if evaluated outside of the clinical context, may induce the clinicians to commit errors of assessment and to embrace uncritically a provisional diagnosis of bacterial infection, resulting in inappropriate empirical antibiotic treatment. In conclusion, as for any other biohumoral or instrumental examination, the use of PCT in the clinical practice should be extremely targeted and appropriate. In the respiratory system diseases, PCT can be a valuable aid to improve the evaluation of fever when there are

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doubtful findings on chest X-ray and, with even more solid data, to optimize the duration of antibiotic therapy. In the presence of fever of undetermined origin, a persistent negative PCT value can be of particular value to direct towards diagnoses different from a bacterial infection.¹⁵ In all other situations, this test should be ordered only if it is well known in advance what could derive from its determination. Instead, we must avoid ordering it uncritically because a possible positive result may determine improper diagnostic and therapeutic consequences, especially if incorrectly framed into the appropriate clinical setting.

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