



# Enfermedades Infecciosas y Microbiología Clínica

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## Editorial

### The challenge of infectious diseases in the emergency department: Presentation of 3 cases<sup>☆</sup>



### El reto de la enfermedad infecciosa en los servicios de urgencias: a propósito de 3 estudios

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Infectious diseases are one of the most prevalent conditions treated in hospital emergency departments (EDs). However, they are also one of the most difficult to diagnose, as shown by the fact that more diagnostic errors occur with infectious diseases than with other conditions, and that 1 in 6 patients with fever discharged from EDs will be readmitted within 7 days of discharge.<sup>1,2</sup> Three research articles that underline the persistence of these diagnostic, treatment and prognostic challenges faced by ED physicians are presented in this issue of *Enfermedades Infecciosas y Microbiología Clínica*. While each article deals with a completely different condition, they are all studies conducted in hospital EDs by emergency department staff, hereinafter referred to as *emergency physicians*. This means that the questions that they pose and the solutions they recommend all fall under this particular remit.

In terms of diagnostic challenges, Morales-Casado et al. investigate the capacity of different biomarkers to establish a differential diagnosis between acute bacterial and viral meningitis.<sup>3</sup> This is without a doubt one of the key unresolved problems of the 21st century, at least in terms of establishing a differential diagnosis during the patient's first consultation. In a retrospective series of 154 patients, the authors conclude that the biomarkers independently associated with acute bacterial meningitis diagnosis, in order of level of association, are: cerebrospinal fluid (CSF) lactate  $\geq 33$  mg/dl (odds ratio [OR]: 51), serum procalcitonin  $\geq 0.8$  ng/ml (OR: 46), glycorrachia  $< 60\%$  blood glucose (OR: 21) and proportion of CSF polymorphonucleocytes  $> 50\%$  (OR: 20). Three aspects really stand out from the study's results. Firstly, according to the results of this and other studies,<sup>4,5</sup> the classic glycorrachia and leukocyte differential count parameters seem to have been superseded

by CSF lactate and plasma procalcitonin. As other authors have also suggested,<sup>6</sup> we are probably on the verge of a new paradigm in the differential diagnosis of meningitis in the ED. Before this can happen, however, certain deficiencies in hospital EDs will have to be addressed. While lactic acid availability is practically universal across EDs, the same cannot be said for procalcitonin. For example, only 20 of the 79 hospital EDs in Catalonia (25%) had the facility to measure procalcitonin 24 h a day in 2012, and in 58% this test was not available at any time of day.<sup>7</sup> Secondly, and following on from the point above, procalcitonin may be the first accurate non-CSF biomarker that can support the decision-making process. In fact, a concentration  $\geq 0.8$  ng/ml yields a positive predictive value of 98.5%, according to the results presented in the study. This means that antibiotic treatment should be initiated immediately if a patient presents with clinical symptoms of acute meningitis plus a procalcitonin value  $\geq 0.8$  ng/ml, even if symptoms are suggestive of viral meningitis. Finally, the results generated by the study by Morales-Casado et al. do not solve the problem posed by partially-treated meningitis; that is, those patients in whom a fall in CSF glycorrachia and an increase in CSF polymorphonucleocytes cannot be determined as a result of prior antibiotic use. As such, when the authors analyzed patients with possible partially-treated meningitis, the expected increases in plasma procalcitonin and CSF lactate observed in confirmed cases were not seen in this patient population.

The study by González del Castillo et al., on the other hand, dealt with the complex topic of appropriate antibiotic prescribing in hospital EDs.<sup>8</sup> As in many other areas of clinical practice, this decision must initially be taken empirically. The authors report that antibiotics are inappropriately prescribed in approximately 1 out of every 10 patients, and that inappropriate prescribing is correlated to an increased length of hospital stay. It is important to point out that empirical antibiotic prescribing in EDs can improve. This takes on particular relevance if we assume the authors' premise that such an improvement would lead to more optimal outcomes. In this

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regard, Monclús Cols et al. studied antibiotics prescribed by EDs to both admitted and discharged patients and found that, while the antibiotic administered in the ED was adequately adjusted to renal function in 95% of patients and dosing intervals were correct in 94% of cases, 37% of patients with positive cultures had to switch antibiotic in accordance with the microbiological isolates.<sup>9</sup> As such, the implementation of clinical guidelines, establishment of consensus statements and founding of infection control committees should be the best tools for ensuring increasingly appropriate antibiotic prescribing in hospital EDs.<sup>10,11</sup> The advantage of the series by González del Castillo et al. is that it is quite a representative sample, the patients having been consecutively recruited when the authors were on duty. However, this is somewhat offset by the fact that the study was conducted in a single hospital ED and only included hospitalised patients. It should be noted that it is vitally important for *emergency physicians* to identify those patients discharged who are at the greatest risk of bacteraemia, as the possibility of correcting antibiotic therapy is smaller and would probably happen later.<sup>12</sup> Until recently, blood cultures have been taken systematically in patients diagnosed in the ED with major infections, such as pneumonia, urinary tract infection, cellulitis and gastroenteritis. However, numerous studies have questioned this practice in recent years and the debate continues to rage.

Finally, Julián-Jiménez et al. tackle the crucial subject of establishing a prognosis in patients who attend hospital EDs due to infection.<sup>13</sup> As important as choosing the appropriate treatment, the *emergency physician* must decide whether to admit or discharge the patient. Knowing the short-term prognosis of the patient plays a crucial role in this decision. This is never an easy decision, and is even more complicated in elderly patients in whom identifying warning signs can often be more difficult.<sup>14</sup> In this scenario, the study by Julián-Jiménez et al. has special merit. The authors propose a scale, known as LIBPAS, comprising serum lactate concentration, the Barthel index and systolic blood pressure, which offers extremely high diagnostic performance to predict 30-day mortality, with an area under the ROC curve of 0.971. On this basis, the authors propose certain cut-off points to separate groups with vastly differing mortality: from 4.5% in the low-risk group (0 points on the LIBPAS scale) to 95.5% in the high-risk group (5 points on the LIBPAS scale). These spectacular results require deeper analysis, both in terms of internal validation (not presented by the authors) as well as external validation in general clinical practice in hospital EDs. The LIBPAS scale was conceived from an observational study in 8 Spanish EDs for patients aged 75 years and above. One aspect that the study fails to clarify is the percentage of patients for whom treatment was withheld or limited, as it would appear that this option was chosen for a significant number of patients with a low Barthel index and low systolic blood pressure. If this were the case, the high mortality associated with a high LIBPAS score would be a reflection of the medical practice (palliative) rather than the severity of the condition, at least exclusively. Equally, the recommendation to admit patients with a high LIBPAS score to the intensive care unit, as proposed by the authors, could have limited scope in the specific target population. In any event, the study by Julián-Jiménez et al. underlines the importance of agreeing an approach to treating infectious disease in hospital EDs. In this light, the recent publication of the PIPA project (infection in elderly patients project) could represent the first step on this journey.<sup>15</sup>

I could not let this unique occasion pass, upon which 3 ED-based infection studies conducted by *emergency physicians* have been published in *Enfermedades Infecciosas y Microbiología Clínica*, without acknowledging the combined research efforts of both *infectologists* and *emergency physicians*; 2 medical specialties with no tradition thus far of contributing to medical research in Spain.

Hospital emergency departments are a unique setting that play host to the first hours of acute conditions, including infections and, in exceptional cases, sepsis.<sup>14,16,17</sup> As such, there are certain aspects that can only be approached in this setting and the collaboration of both specialties is vital. This has been going on for some time in the field of cardiovascular disease, with promising results.<sup>18–20</sup> Multidisciplinary research is undoubtedly the key to advancing our knowledge of infectious diseases in the future, and this collaboration between the different specialties can only benefit the patient.

## Conflicts of interest

The author has no conflicts of interest with regards to this article.

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