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# 'Plus ça change' for the future of sepsis?

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Question: How do you eat an elephant? Answer: One bite at a time.

The articles in the recent special collection of the British Journal of Anaesthesia (https://bjanaesthesia.org/world-sepsisday-2019) to mark World Sepsis Day (September 13, 2019) illustrate some of the complexities in understanding and addressing sepsis, one of the most challenging diseases to treat and a major killer. Although many of these articles increase our knowledge of the biology of sepsis, sepsis is not a single condition and the potential impact of infection on an individual can be unpredictable and significant. Changes in the epidemiology of sepsis as a result of modified diagnostic criteria add another dimension: the more we increase our overall knowledge, the more it requires re-examination and reconsideration of what we understand as sepsis.<sup>1</sup> One useful approach then is to acknowledge this complexity and utilise a multifaceted approach to improving recognition, diagnosis, and treatment as discussed by Nunnally.<sup>2</sup>

Early recognition of patients with, or at risk of developing, sepsis is key to timely and effective management. Campaigns to increase public awareness of sepsis have gone hand in hand with publications such as National Institute for Health and Care Excellence (NICE) guidance NG51, which have identified recommendations for managing suspected sepsis in the community and acute hospital settings.<sup>3</sup> Adoption of the UK National Early Warning Score (NEWS 2) facilitates earlier recognition of the deteriorating patient in hospital.<sup>4</sup> Running alongside a drive to recognise deterioration has been the implementation of response services such as Critical Care

Outreach teams and prompt ward level management strategies that may have an impact on the morbidity and mortality associated with sepsis in hospital.<sup>5</sup> There is also a <u>need to</u> cohort people who need more than simple ward level care but <u>do not require admission to critical care units</u>. The ability to monitor the 'at risk' patient with an increased frequency of observations and more complex interventions should be delivered in an <u>enhanced care area</u> in a hospital. Development of these enhanced care services is one of the <u>recommenda-</u> tions of the Faculty of Intensive Care Medicine's 'Critical Futures' Initiative in the UK and is a current Faculty work stream to develop guidance for UK hospitals.<sup>6</sup>

Not all deteriorating patients have sepsis, and not all patients with sepsis are the same. Determining the true incidence of sepsis and septic shock has definitional difficulties, but may also in part be attributable to better recognition in an ageing hospital population with increasing co-morbidities.<sup>7</sup> Sepsis is a syndrome in which the clinical presentation depends on the type of infection, patient comorbidities, patient immune response, and degree of organ dysfunction. This spectrum of physiological response and unpredictable outcome can, in extreme cases, lead to ICU admission, multiple morbidities, or even death. Approximately 30% of admissions to intensive care in England are attributable to sepsis with the most common site of infection being in the respiratory system.<sup>8</sup> ICU mortality caused by sepsis in some parts of the world has decreased, most likely because of early recognition and timely intervention. In a 12 yr review of survival from sepsis in the Australian and New Zealand intensive care database, mortality decreased from 35% to 18%, suggesting that improved overall quality of care can have an impact on mortality.  $^{\rm 9}$ 

Over the years, intensivists have embraced multiple approaches to sepsis treatment, all of them aimed to improve survival after diagnosis with targeted therapies, and all of them failed to deliver on the promise that there was a unifying form of treatment for a condition that is characterised by multiple heterogeneous pathological triggers and host responses. Goal-directed therapies aimed at increasing tissue oxygen delivery and consumption, coinciding with the rise of the pulmonary artery catheter, gave way to the prospect of immunotherapies, the most well-known of which (Centoxin) was a monoclonal antibody targeting gram-negative sepsis. Centoxin was withdrawn after an excess of deaths in patients with gram-positive sepsis who received the drug at a time when laboratory diagnostic services were unable to differentiate between gram-negative and gram-positive sepsis in the necessary timescale to make Centoxin a realistic therapy.<sup>10</sup> The new millennium dawned with the prospect that drotrecogin alpha (Xigris) could improve the end-organ damage and failure associated with severe sepsis. A brief period of anticipatory hope ensued with the manufacturer-funded Protein C Worldwide Evaluation in Severe Sepsis (PROWESS) study,<sup>11</sup> but the subsequent PROWESS-SHOCK study failed to show a statistically significant reduction in all-cause mortality from sepsis, which led to the manufacturer withdrawing the drug from the market in 2011.<sup>12</sup>

The formation of the Faculty of Intensive Care Medicine in 2010 has helped create a significant change in perceptions of intensive care medicine (ICM) as a standalone medical specialty in the UK. Historically, clinicians who trained as anaesthetists led ICM practice in the UK. ICM clinicians now come from increasingly diverse training backgrounds, and a significant proportion (10%) have chosen to practice or choose to train exclusively within ICM whereas many more devote the bulk of their working week to ICM or identify themselves professionally as 'an intensivist'. Having recognised that intensivist-led care improves patient outcomes, it has been adopted as a quality indicator and is a standard in 'Guidance on Provision of Intensive Care Services', which is published jointly by the Faculty of Intensive Care Medicine and the Intensive Care Society.<sup>13</sup>

The creation by the Faculty of UK ICM training curricula for medical staff and advanced critical care practitioners, means that those delivering medical care in UK ICUs are trained in all aspects of the care and management of a person with sepsis. The focus of the medical team therefore moves away from single targeted treatments to a more holistic approach that tracks knowledge and involvement in the entire patient journey from recognition of need for admission to recovery, rehabilitation and follow up.

Some deaths from sepsis may not be preventable nor may it be desirable to attempt aggressive treatment in some cases. A recent cohort study of 568 sepsis deaths in six <u>US</u> hospitals identified that <u>40.4%</u> of patients <u>dying</u> from <u>sepsis</u> had a <u>hospice-qualifying condition</u> on admission to hospital, indicative of the impact that chronic diseases such as cancer and dementia and the syndromes of frailty in an increasingly ageing population have on risk factors for sepsis.<sup>14</sup>

Osler's description of pneumonia as the 'friend of the aged' recognised what can sometimes be forgotten in high-intensity hospital medicine, that pain and suffering have a part to play in the manner and timing of a person's death. Intensivists are trained to recognise that and frequently adopt an inclusive view that considers not only what is possible, but also what is appropriate for a person and consistent with their wishes. A 30% risk of mortality from pneumonia for those admitted to ICU masks the fact that for many older people ICU survival may mean a shift from previous independent living to permanent institutional care, an outcome that would be undesirable or unacceptable for some. Knowing 'what matters to me' for each person is a considerable piece of ongoing work as we learn more about the impact of survival after critical care admission. Recent guidance highlights that this holistic approach begins in the community and should include discussions on advance planning and end-of-life care.<sup>15</sup> This means that should a person with a life-limiting condition be admitted to hospital, and perhaps referred for intensive care treatment, clinicians can tailor treatment plans to actual patient wishes rather than assumptions. It could also result in a patient deciding not to have antibiotics or be admitted to hospital at all.

ICM is a medical specialty that is uniquely placed to recognise sepsis from all causes, able to help educate and support other specialties in managing sick patients. Moreover, it is uniquely placed to encourage and inform others to have conversations with individuals who are frail or elderly about the implications for them of aggressive treatment for sepsis before they become unwell. The Faculty of Intensive Care Medicine in the UK is leading the way in improving care for the sickest patients in the hospital and promoting the importance of advance care planning. No one single intervention or treatment can ensure that outcomes from sepsis are improved, but we are working to ensure that care of patients with or at risk of sepsis is improved. As the articles in the 2019 BJA World Sepsis Day Special Collection illustrate, improving the total body of knowledge can effect change, one step at a time.

#### Authors' contributions

Both authors contributed to the design, drafting, and final version of this editorial.

#### **Declarations of interest**

DCB is Vice Dean Elect of the Faculty of Intensive Care Medicine. AJP is Dean Elect and present Vice Dean of the Faculty of Intensive Care Medicine.

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# Emergency front-of-neck airway: strategies for addressing its urgency

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The performance of an emergency front-of-neck airway (eFONA) is a time-critical task that is often associated with poor patient outcomes and significant long-term psychological impact on healthcare personnel. In this issue of the British Journal of Anaesthesia, Groom and colleagues<sup>1</sup> show that anaesthetists who have trained in eFONA could perform as skilfully as head and neck surgeons when presented with a simulated 'can't intubate, can't oxygenate' (CICO) scenario. Their work supports the need for multidisciplinary CICO training as part of a complex management strategy. eFONA is not a common procedure, and yet, it has high-stakes outcomes for patients.

The study by Groom and colleagues<sup>1</sup> showed that there were no significant differences in deliberation time between anaesthetists, head and neck surgeons, and general surgeons (median times: 30, 31, and 23 s, respectively). However, the procedural time was significantly different amongst the three groups, with anaesthetists taking a median time of 50 s, head and neck surgeons 74 s, and general surgeons 86 s. In contrast,

findings from the 4th National Audit Project<sup>2</sup> showed that nine patients had a surgical airway completed in under 5 min, whilst 11 patients took more than 1 h to secure the airway. Are these differences in deliberation and procedural times clinically important?

It should be recognised that, in a crisis, time is critical. Currently, no evidence exists to recommend a minimum duration from start of CICO to completion of eFONA. Groom and colleagues<sup>1</sup> divided the time for eFONA into (i) deliberation time (from onset of CICO to starting eFONA) and (ii) procedural time (from starting to finishing eFONA). The former would normally include any time delay by the anaesthetist to declare that eFONA is required and the time to bring eFONA equipment to the point of care.

Using their terminology, we can postulate what the reasonable times are for both deliberation and procedural eFONA. Obviously, ethical constraints do not allow prospective research in this area. However, modelling studies to predict the time for significant oxyhaemoglobin desaturation and possible hypoxic brain damage with loss of airway provide a surrogate for calculation of an appropriate target time for eFONA management.<sup>3,4</sup>

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