

# Sepsis Care Pathway 2019

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## EDITORIAL

Background: Sepsis, a medical emergency and life-threatening disorder, results from abnormal host response to infection that leads to acute organ dysfunction<sup>1</sup>. Sepsis is a major killer across all ages and countries and remains the most common cause of admission and death in the Intensive Care Unit (ICU)<sup>2</sup>. The true incidence remains elusive and estimates of the global burden of sepsis remain a wild guess. One study suggested over 19 million cases and 5 million sepsis-related deaths annually<sup>3</sup>. Addressing the challenge, the World Health Assembly of the World Health Organisation (WHO) passed a resolution on better prevention, diagnosis, and management of sepsis<sup>4</sup>.

Current state of sepsis guidelines: Despite thousands of articles and hundreds of trials, sepsis remains a major killer. The cornerstones of sepsis care remain early recognition, adoption of a systematic evidence-based bundle of care, and timely escalation to higher level of care. The bundle approach has been advocated since 2004 but underwent major modifications in subsequent years with more emphasis on the time-critical nature of sepsis and need to restore physiological variables within one hour of recognition. A shift from a three and six-hour bundle to one-hour bundle has been recommended<sup>5</sup>. This single hour approach has been faced with an outcry and been challenged<sup>6-8</sup>.

One size never fits all: Over several decades, the individual components of the sepsis bundle have not changed. Encountering a patient with suspected sepsis, one should measure lactate, obtain blood cultures, swiftly administer broad spectrum antimicrobials and fluids, and infuse vaso-pressors. A critical question arises: should we do this for all patients? Sepsis is not septic shock and guidelines did not make distinctive recommendations for each. Septic patients will present differently with some having more subtle signs and symptoms. Phenotypically, we do not know which patient with infection will develop a dysregulated host response and will succumb to sepsis and/or shock<sup>6-8</sup>. The existing bundle lacks high quality evidence to support its recommendations and a blanket implementation for all patients with 'suspected' sepsis could be harmful<sup>7</sup>. Indeed, a significant reduction of sepsis and septic shock in Australia and New Zealand was observed in a bundle-free region<sup>8</sup>.

Emergency Department (ED) challenges: Upon arrival in the ED, patients will be triaged. This is 'time zero'<sup>5</sup>. Those with hypotension and hypoperfusion will be easily recognised and at most need to receive emergent care. Sepsis, per se, may not manifest clear cut signs and expertise to identify it is required. Those with non-specific symptoms may trigger an early warning scoring system and receive unnecessary antimicrobials and a large volume of intravenous (IV) fluids. Both therapies are not without significant side effects. Putting pressure on ED physicians to implement the 60-minute bundle without individualisation of care puts our patients at risk<sup>6-8</sup>.

Diagnostic challenges: Given the heterogenous nature and diverse pathobiological pathways, sepsis diagnosis can be challenging and both over and under-treatment can result. Established biomarkers such as procalcitonin and

C-reactive protein lack specificity to rule out infection as the cause of inflammation. Currently, no laboratory test or biomarker helps predict which patients with infection or inflammation will develop organ dysfunction. A dire need for a specific sepsis biomarker exists<sup>10</sup>.

Modern molecular-based technologies are evolving and utilise polymerase chain reaction (PCR), nanotechnology, and microfluidics for point-of-care testing. Some devices identify causative microorganisms and their sensitivity in less than an hour<sup>10</sup>. The bundle components: Catecholamines along with IV fluids are indicated to restore perfusion. However, inadvertent side effects may arise, especially at higher doses. Anti-adrenergic  $\beta$ -blockers improve cardiac performance, enhance receptor responsiveness, and possess anti-inflammatory action. All are desirable in patients with septic shock<sup>11</sup>.

One randomised trial showed beneficial and protective effects of  $\beta$ -blockers in septic shock. Rapidly acting titratable agents should be used in conjunction with appropriate hemodynamic monitoring and after adequate volume resuscitation. There is no consensus on target heart rate but an arbitrary cut off of 80–95 beats per minute is reasonable<sup>11</sup>.

Fluid resuscitation is the cornerstone of sepsis management. There is also compelling evidence that too much fluid is bad. Starch-based colloids should not be used in septic shock. Albumin is an alternative when large volumes are required but is not appropriate in traumatic brain injury. Balanced, less chloride and less acidic crystalloids are safer for the kidneys and are preferred over normal saline. Doses of IV fluids should be tailored to the patient's condition and a 30 ml/kg recommendation should be reviewed.<sup>12</sup>

Effective sepsis management requires adequate dosing of antimicrobials. Significant alteration of pharmacokinetics and

pharmacodynamics is characteristic of septic shock<sup>13</sup>. Accurate and effective dosing is challenging particularly in patients with multiple comorbidities and those receiving extracorporeal organ support. Underdosing results in treatment failure, whilst overdosing leads to toxicity and the risk of developing multi-drug resistant organisms<sup>13</sup>.

An individualised approach supported by therapeutic drug monitoring is suggested to ensure clinical efficacy<sup>13</sup>.

Sepsis research: The search for a cure for sepsis is ongoing. A large prospective, randomised two-arm, parallel group study aims to recruit over 200 patients with septic shock across critical care units in Qatar. Evaluation of Hydrocortisone, Vitamin C, and Thiamine (HYVITS) examines the safety and efficacy of this triple therapy<sup>14</sup>.

Sepsis in the young patient: Children are particularly vulnerable to sepsis. 1 in 6 children admitted with septic shock to ICU will die. As the majority of paediatric sepsis cases are community acquired, there is a strong need to raise awareness both for families and primary healthcare providers. Akin to adults, a bundle-approach to paediatric sepsis is strongly encouraged. National programs for paediatric sepsis have been established<sup>15</sup>. The Qatar paediatric multidisciplinary sepsis program was established under the umbrella of the adult programme in 2017. A structured and standardised approach to sepsis across all neonate and paediatric facilities has been developed and implemented. Improvement in timely sepsis recognition and administration of antimicrobials within the golden hour has been observed. The program aims to achieve a 95% compliance to the paediatric sepsis bundle by the end of 2019. A screening tool and order set have been put in place and are presented in this special issue of Qatar Medical Journal<sup>16,17</sup>.

Obstetric sepsis: Pregnancy and childbirth are risk factors for sepsis. Multi-organ failure and

death can result from puerperal sepsis<sup>18</sup>. Sepsis is the direct and leading cause of maternal mortality in the UK<sup>19</sup>. Attention to maternal sepsis with a tailored approach is encouraged. The Qatar National Sepsis Program developed a sepsis care pathway for pregnant women and during their early post-partum period.

Challenges in low socioeconomic societies: A broader, national – or better yet – a global approach to further sepsis management and outcome should be considered. There are a number of significant challenges to address. One such challenge is the inconsistency of the operational definition and diagnostic approaches for sepsis including coding and documentation<sup>1,3</sup>.

Significant deficiencies in healthcare systems have been highlighted by sepsis. This is most obvious in medium- and low-income countries. A major limitation to effective sepsis management is inadequate medical staffing and poor knowledge and awareness of sepsis. Both have a negative impact on sepsis outcome<sup>3</sup>.

Poor medical facilities in many countries pose significant challenges to sepsis care. Lack of critical care capacity – a global phenomenon – has been linked to poor outcome of sepsis cases and septic shock. This could be attributed to provision of suboptimal critical care, monitoring and critical interventions outside of the ICU. ICU availability is subject to inconsistency and inequity.<sup>2,3</sup>

Lack of adequate surgical capacity to accomplish timely source control adversely affects sepsis management. This, unfortunately, in medium- and low-income countries, is accompanied by inadequate medical supplies, diagnostic capacity, and manpower which increases sepsis mortality and morbidity<sup>3</sup>.

Global concerns: Antimicrobials are critical for sepsis care. A global concern is the development of multi-drug resistant

organisms and the lack of novel antimicrobials and this adds pressure on those caring for septic patients. Effective antimicrobials should be utilised to eradicate infections. Misuse, inadequacy, inferior agents, and lack of timely access to effective and affordable agents significantly hinders patient's recovery from sepsis<sup>2,3</sup>.

Optimum sepsis outcome mandates attention to acute sepsis complications (e.g. acute renal or respiratory failure) as well as addressing post-discharge complications and disability. These challenging issues remain poorly studied or addressed<sup>3</sup>.

Conclusion: Sepsis and septic shock are major global health concerns. Progress has been

achieved in understanding this life-threatening syndrome at a biological, metabolic, and cellular level. Efforts should be coordinated to improve sepsis care. Better and more accurate diagnostics are needed and governments are encouraged to invest in sepsis research and care. More integrated, inclusive, and focused research is desperately needed. Public education and increased awareness among primary healthcare providers are also critical to improve sepsis outcome.

Keywords: sepsis pathway, bundle, guidelines

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