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# Management of the Urologic Sepsis Syndrome

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**Abstract**

In approximately one-third of patients with sepsis, the source of infection is the urinary tract. The management of sepsis has rapidly changed over the past two decades, and a review of urosepsis management is paramount. It is estimated that in 30% of patients with severe sepsis and septic shock, the underlying reason is a urinary tract infection (UTI). The prevalence of microbiologically proven urosepsis in urology departments has been reported as 1.5% (quarter of health care–associated UTIs). On a global level, it has been postulated that 5.4 million deaths occur due to sepsis. The main causes of urosepsis are indwelling urinary catheters and urologic interventions (stone treatment, prostate biopsies, and endoscopic urethral stricture treatment). Urosepsis-causative pathogens are primarily gram-negative bacteria; this is different from sepsis overall, which is dominated by gram-positive bacteria. Its been reported that the resistance rates of pathogens in urosepsis are >10% for almost all antibiotics. The main principles of management of urosepsis and sepsis are the same, including early goal-directed treatment and antibiotic administration within the first 45 min. Early goal-directed therapy was recently shown not to be superior to standard care; however, these results may not be applicable to settings in which standard care needs improvement. Selection of an appropriate antibiotic for the initial empirical treatment in urosepsis requires knowledge of previous interventions, antibiotic usage, and local resistance rates. Future research on the management of urosepsis should be directed toward identification of groups at risk of developing urosepsis, antibiotic selection, and value of biomarkers in treatment response (eg, lactate, procalcitonin).

***Patient summary:*** In approximately one-third of patients with sepsis, the source of infection is the urinary tract. This review assessed causes and management of urosepsis and directions for future research.



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## 1. Introduction

Sepsis is a systemic deleterious host response to infection that is associated with high rates of unfavorable outcomes. Mortality rates for severe sepsis and septic shock have been reported to be as high as 28–41% [1,2]. In a significant proportion of these cases, the source of infection is the urinary tract (severe sepsis: 9%; septic shock: 31%) [3].

Similar to other sepsis syndromes, urosepsis that develops due to urinary tract infections (UTIs) is also

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associated with significant mortality and morbidity. Most commonly, it develops in the context of health care–associated UTIs. Common underlying risk factors for urosepsis are obstruction of the urinary tract for reasons such as stones, urethral stricture, or congenital anomalies. Urinary tract interventions and prostate biopsies can also lead to urosepsis.

Antibiotics that are used for both treatment and prevention of infections are currently subject to high resistance rates. This increases the risk of insufficiency in prophylaxis and treatments, with an associated increased risk of postintervention urosepsis or insufficient treatment of urosepsis. Clinicians should be well aware of the local surveillance results and general practice guidelines.

Rapid and appropriate management of sepsis, including the administration of an initially adequate intravenous antibacterial, is essential for optimal outcomes [4]. Inadequate coverage of initially administered antibiotics in urosepsis hampering treatment success is more common compared with other causes of sepsis [5]. Urosepsis has other unique characteristics compared with other causes of sepsis. In this review, management of urosepsis will be summarized.

## 2. Definitions

*Urosepsis* is defined as sepsis due to a UTI. The following terms will be used within this manuscript:

- *Bacteremia:* Bacteria is present in blood, as confirmed by culture, and may be transient.
- *Systemic inflammatory response syndrome* (SIRS): Response to a wide variety of clinical insults that can be infectious, as in sepsis, but also that may be noninfectious (eg, burns, pancreatitis). This systemic response is manifested by two or more of the following conditions:
  - Temperature >38 °C or <36 °C
  - Heart rate >90 beats/min
  - Respiratory rate >20 breaths/min or $PaCO_2$ <32 mm Hg (<4.3 kPa)
  - White blood cell count >12 000 cells/$mm^3$ or <4000 cells/$mm^3$ or ≥10% immature (band) forms
- *Sepsis:* Activation of the inflammatory response syndrome due to infection.
- *Hypotension:* A systolic blood pressure of <90 mm Hg or a reduction of >40 mm Hg from baseline in the absence of other causes of hypotension.

Clinical diagnostic criteria of sepsis are summarized in Table 1 [6,7]. By using these criteria, sepsis can be classified into three categories:

- Simple sepsis: criterion 1 plus two or more criterion 2
- Severe sepsis: criterion 1 plus two or more criteria 2 and one or more criterion 3, per affected organ (kidney, lung, liver)
- Septic shock: criterion 1 plus two or more criteria 2 and therapy-refractory arterial hypotension ≤90 mm Hg

## 3. Epidemiology of urosepsis

In a study conducted in the United States looking at the time period 1979–2001, investigators identified an increase in the incidence of sepsis from 82.7 to 240.4 per 100 000 population [1]. It is estimated that in 30% of patients with severe sepsis and septic shock, the underlying cause is a UTI [8]. A multinational surveillance study in urology departments reported the prevalence of microbiologically proven urosepsis as 1.5% (quarter of health care–associated UTIs) [9]. Sepsis incidence in hospitals of high-income countries was identified as 288 cases per 100 000 person-years (95% confidence interval [CI], 215–386), and incidence of severe sepsis treated in hospitals was 148 cases per 100 000 person-years (95% CI, 98–226)[10]. In this study, simulations estimated the annual mortality rates of all causes of sepsis to be 5.4 million deaths per year globally [10]; however, this estimation includes very broad assumptions made from low-income countries from which there is a lack of robust

**Table 1 – Criteria used in diagnosing and classifying sepsis**

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| Criterion 1 | Presence of bacteremia (positive blood culture) or clinical suspicion of sepsis. Bacteremia can be of low inoculum (<10 bacteria per milliliter) or of short duration. Multiple blood cultures are recommended. |
| Criterion 2 | Systemic inflammatory response syndrome<br>Body temperature: ≥38 °C or ≤36 °C<br>Tachycardia: ≥90 beats/min<br>Tachypnea: ≥20 breaths/min<br>Respiratory alkalosis: $PaCO_2$ ≤32 mm Hg<br>Leukocytes: ≥12 000/μl or ≤4000/μl<br>Segmented neutrophils: >10% |
| Criterion 3 | • Multiple organ dysfunction syndrome<br>• Circulation: Arterial systolic blood pressure ≤90 mm Hg or mean arterial blood pressure ≤70 mm Hg during ≥1 h despite adequate fluid resuscitation and adequate intravascular volume or use of vasopressors to maintain systolic blood pressure ≥90 mm Hg<br>• Kidney: Urine production <0.5 ml/kg body weight per hour during 1 h despite adequate fluid resuscitation<br>• Lung: $PaO_2$ ≤75 mm Hg (at ambient air) or $PaO_2/FiO_2$ ≤300 (acute lung injury), or $PaO_2/FiO_2$ ≤200 (acute respiratory distress syndrome) at assisted ventilation<br>• Thrombocytopenia: Platelets <80 000/μl or decrease of platelets ≥50% within 3 d<br>• Metabolic acidosis: Blood pH ≤7.30 or base excess ≥5 mmol/l; plasma lactate ≥1.5-fold of normal.<br>• Encephalopathy: Somnolence, agitation, coma, confusion |

$FiO_2$, inspiratory oxygen concentration; $PaO_2$, partial pressure of arterial oxygen.