Regence

Medical Policy Manual Medicine, Policy No. 172

Treatment of Adult Sepsis

Effective: October 1, 2023

Next Review: June 2024
Last Review: August 2023

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Sepsis is a life-threatening condition that requires rapid identification and action to prevent mortality or other devastating consequences.

MEDICAL POLICY CRITERIA

Notes:

- Services described in this medical policy are not routinely reviewed; however, claims may be subject to audit including but not limited to review of member benefit application, medical appropriateness, frequency utilization, documentation requirements, accurate code selection, and reimbursement. Some devices or services may be subject to the health plan's reimbursement policy manual or may not be covered based on benefit contracts. Claim adjudication is also subject to claim processing guidelines and provider contracts.
- This policy only addresses adults age 18 and over.

I. Clinical documentation supports the diagnosis of adult sepsis (and sepsis-related care in other diagnosis related groups) and septic shock when all of the following are met (A. – C.):

A. Sepsis, the systemic response to infection, is manifested by *two or more* of the

following conditions as a result of suspected infection:

1. Temperature: fever (> 38.0°C) or hypothermia (< 36.0°C)
2. Tachycardia (pulse > 90)
3. Tachypnea (respiratory rate > 20 bpm)
4. Leukocytosis or leukopenia (white blood cell count outside of the normal range, as specified by the performing laboratory) or Bands > 10%
5. Lactate > 1.0 mmol/L (> 4.0 is equivalent to septic shock)
6. Procalcitonin elevated >2 SD above the normal value
7. C-reactive protein elevated >2 SD above the normal value
8. Altered mental status
9. Mottling of the skin or prolonged capillary refill
10. Non-diabetic hyperglycemia (blood sugar > 110mg/dl)
11. Other evidence of acute organ failure (e.g. persisting hypotension, sequential organ failure assessment score [SOFA] ≥2); and

B. The physiologic changes in sepsis represent an acute alteration from baseline in the absence of other known causes for such abnormalities, including but not limited to chemotherapy-induced neutropenia and leukopenia; and

C. When sepsis is identified, a response is initiated including rapid treatment and frequent reassessment of the patient (see Policy Guidelines). There must be clear and consistent provider documentation of sepsis and response to sepsis that aligns with the documented clinical findings (e.g., labs, treatments, vital signs, etc.), including all of the following:

1. Sepsis is clearly documented on the clinical record on each day it is suspected or present until either documentation states that sepsis is resolved or includes clinical evidence of resolution of sepsis (e.g. stable and normal vital signs and de-escalation of sepsis-related care, including fluids, antimicrobials, and cardiovascular support, as relevant); and
2. Sepsis is clearly documented in the discharge summary; and
3. Documentation that all of the following have been completed, as applicable (a. – c.):
    a. Blood cultures have been obtained; and
    b. Parenteral antimicrobials (antibiotics, antivirals or other treatment specific to the underlying infectious cause of sepsis) have been administered; and
    c. Resuscitative fluids (i.e. bolused aliquots of crystalloid or colloid, not maintenance hydration) have been administered when clinically appropriate.

II. Clinical documentation does not support the diagnosis of sepsis (and sepsis-related care in other diagnosis related groups) and septic shock when Criterion I. is not met.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

RAPID TREATMENT

Rapid treatment of sepsis typically should occur within three hours of time of identification of sepsis.

DEFINITIONS

This policy addresses adults, defined as age 18 and older.

Sepsis-3 provides the following definitions:[1]

- Sepsis: “life-threatening organ dysfunction caused by a dysregulated host response to infection.”
- Septic shock: “a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.”

LIST OF INFORMATION NEEDED FOR REVIEW

REQUIRED DOCUMENTATION:

The information below **must** be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and physical/chart notes
- Indication for the requested service
- Documentation of symptoms, associated diagnoses, and treatments

CROSS REFERENCES

1. Extracorporeal Membrane Oxygenation (ECMO) for the Treatment of Cardiac and Respiratory Failure in Adult, Medicine, Policy No. 152

BACKGROUND

Sepsis is a life-threatening condition that requires rapid identification and action to prevent mortality or other devastating consequences. Professional and research organizations, including the 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference[2] and the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference[3], have published documents addressing sepsis definitions, clinical tools, and treatment protocols for sepsis.

EVIDENCE SUMMARY

There are many studies evaluating the diagnosis and treatment of sepsis, and the definition and recommended courses of action are constantly evolving. The professional organization guidelines and recommendations described below have systematically reviewed the available literature and present recommendations based on the evidence in combination with expert consensus. Of the systematic reviews supporting the guidelines, the most recent as of this update are a systematic review published by Shankar-Hari (2016) supporting the Sepsis-3 definitions and the systematic review conducted by the National Institute for Health and Care Excellence (NICE), updated in 2017.[4, 5]

In the Shankar-Hari systematic review, a total of 44 studies representing 116,479 patients met inclusion criteria.[4] Significant heterogeneity was identified in septic shock mortality and septic shock case definition. Septic shock case definitions and corresponding variables reported in the identified studies, including infection status, number of systemic inflammatory response syndrome (SIRS) criteria met, and systolic blood pressure, as well as mortality by septic shock definitions, were used to inform the Delphi survey questions, from which the Sepsis-3 definitions were developed.

The NICE systematic review included 47 studies that evaluated scoring systems and 43 that addressed individual physiological signs and symptoms to identify whether sepsis is present.[5] Most were retrospective single center studies and they were generally rated very low quality of evidence. Significant variability was identified for the included population, patient outcomes, and the statistical measures that were reported and analyzed. No meta-analysis was conducted of the use of scoring systems because studies with comparable populations reported different patient outcomes or used different statistical analyses, nor was a meta-analysis conducted of the diagnostic accuracy data or the odds ratios because of heterogeneity in the study settings and cut-off values of signs and symptoms and lack of a reference standard. Both sensitivity and specificity were considered to be of equal importance because the focus was equally on not missing cases and not ruling in non-affected individuals.

PRACTICE GUIDELINE SUMMARY

Many aspects of care are supported by strong agreement within and across guidelines, including rapid treatment and frequent reassessment of patients after sepsis is identified. In addition, while there are a variety of definitions of sepsis, this medical policy aligns with the 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference and the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference, which are the most firmly established and well-supported definitions.

AMERICAN COLLEGE OF CHEST PHYSICIANS/SOCIETY OF CRITICAL CARE MEDICINE

In 1992, an American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference was held to define sepsis, and the results were published in “Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis”.[3] The report proposed the phrase systemic inflammatory response syndrome (SIRS) to describe the inflammatory process observed during sepsis. Sepsis, severe sepsis, and septic shock are defined as follows:

- Sepsis as the systemic response to infection, manifested by two or more of the following conditions as a result of infection: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or PaCO2 <32 mm Hg; and white blood cell count > 12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms;
- Severe sepsis as sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status; and
- Septic shock as sepsis-induced hypotension, persisting despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients receiving inotropic or vasopressor agents may no longer be hypotensive by the

time they manifest hypoperfusion abnormalities or organ dysfunction, yet they would still be considered to have septic shock.

These definitions are widely used, although alternative definitions have been proposed, as described below.

2001 SCCM/ESICM/ACCP/ATS/SIS INTERNATIONAL SEPSIS DEFINITIONS CONFERENCE

In 2001, several North American and European intensive care societies convened a conference to reevaluate the definition of sepsis proposed at the 1992 conference. The conclusions from this conference, sponsored by the Society of Critical Care Medicine (SCCM), The European Society of Intensive Care Medicine (ESICM), The American College of Chest Physicians (ACCP), the American Thoracic Society (ATS), and The Surgical Infection Society (SIS) were reported in two publications by Levy (2003).[2, 6] The group concluded that although the current definition of sepsis did not allow precise staging and the diagnostic criteria are overly sensitive and nonspecific, SIRS remains a useful concept. They proposed an expanded list of signs and symptoms of sepsis to better reflect the clinical response to infection. This expanded list is referred to as Sepsis 2.

EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE/SOCIETY OF CRITICAL CARE MEDICINE

In 2014, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine convened a task force of specialists to create an updated definition of sepsis supported by the current evidence. The group published recommendations in 2016 with new definition for sepsis, which was labeled as Sepsis 3. The Sepsis 3 definition is “life-threatening organ dysfunction caused by a dysregulated host response to infection.”[1] Functionally, sepsis is defined as a suspected infection and an acute change in total Sequential Organ Failure Assessment (SOFA) score of two or more points, with SOFA measures including respiration, platelets, bilirubin, MAP, Glasgow Coma scale, creatinine, and urine output.

Septic shock is defined as “a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.” Functionally, “patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation.”

The task force also proposed quick SOFA (qSOFA), a clinical tool that can be used to rapidly score patients at the bedside. It is stated to be less robust, but a rapid measure that can indicate the need for further investigation and increased monitoring.

THE NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

The National Institute for Health and Care Excellence (NICE) published a guideline addressing diagnosis and early management of sepsis in 2016 that was updated in 2017.[5] The guideline stratifies patients by risk for sepsis, using the presence of a number of signs and symptoms, including altered mental state, elevated heart or respiratory rate, low blood pressure, low urine output, mottled or ashen appearance, cyanosis of skin, lips, or tongue, or non-blanching rash. For those at high risk of sepsis, it recommends monitoring continuously, or at a minimum of every 30 minutes, conducting blood tests, delivering IV antibiotics, fluid administration. In addition, for those with suspected sepsis and any high-risk criteria, it recommends immediate

review by a senior clinical decision maker.

SURVIVING SEPSIS CAMPAIGN

The Surviving Sepsis Campaign, initiated in 2002, is a collaboration between the Society of Critical Care Medicine and the European Society of Intensive Care Medicine, with the goal of reducing mortality from severe sepsis and septic shock. In 2012, the campaign gathered an international consensus committee consisting of 68 international experts representing 30 organizations. The results of this discussion were published in International Guidelines for management of Sepsis and Septic Shock (2012).[7] The guideline lists many recommendations, including blood cultures prior to the delivery of antibiotics, confirmation of the source of infection, and fluid resuscitation with a crystalloid.

In 2016, the campaign gathered another consensus committee, this time including 55 international experts representing 25 international organizations. This panel published International Guidelines for Management of Sepsis and Septic Shock (2016).[8] Regarding the definition of sepsis, the publication states “As these guidelines were being developed, new definitions for sepsis and septic shock (Sepsis-3) were published. Sepsis is now defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Septic shock is a subset of sepsis with circulatory and cellular/metabolic dysfunction associated with a higher risk of mortality. The Sepsis-3 definition also proposed clinical criteria to operationalize the new definitions; however, in the studies used to establish the evidence for these guidelines, patient populations were primarily characterized by the previous definition of sepsis, severe sepsis, and septic shock stated in the 1991 and 2001 consensus documents.”

The guidelines were updated again in 2021. Both the 2016 and the 2021 guidelines include 93 recommendation statements on early management and resuscitation of patients with sepsis or septic shock. The guidelines do not include specific criteria for determining the presence of sepsis. Regarding evaluation of patients, the guideline states the following:

> One of the most important principles of managing complex septic patients is the need for a detailed initial assessment and ongoing re-evaluation of the response to treatment.

The 2021 guidelines also include the new recommendation:

> We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single-screening tool for sepsis or septic shock. (Strong recommendation, moderate-quality evidence)

ROYAL COLLEGE OF PHYSICIANS

The Royal College of Physicians published the National Early Warning Score (NEWS) in 2012 and published an updated version, NEWS2, in 2017.[9] NEWS is an aggregate scoring system for the assessment of acute-illness severity based on physiological measurements used within the National Health System in the United Kingdom. Physiological measurements include respiration rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness or new confusion, and temperature.

SUMMARY

Sepsis is a life-threatening condition that requires rapid identification and action to prevent

mortality or other devastating consequences. Professional organization guidelines and recommendations support rapid treatment and frequent reassessment of patients after sepsis, identified according to a set of signs and symptoms. Therefore, clinical documentation supports the diagnosis of adult sepsis (and sepsis-related care in other diagnosis related groups) and septic shock when criteria are met.

When the defining signs and symptoms of sepsis are not present, professional organization guidelines and recommendations do not support the same treatment and testing as when sepsis is present. Therefore, when criteria are not met, clinical documentation does not support the diagnosis of adult sepsis (and sepsis-related care in other diagnosis related groups) and septic shock.

REFERENCES

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CODES

Codes	Number	Description
CPT	None	
HCPCS	None	

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