Sepsis and Septic Shock Part III:

Identification and Control of the Source of Infection

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Intended Learning Outcomes

Sepsis and Septic Shock Part III: Identification and Control of the Source of Infection

1. Describe a systematic approach to identifying the source of infection in a septic patient.
2. Identify potential types of infection based upon the anatomic location.
3. Describe the pros and cons of different methods (clinical, laboratory, imaging) to identify the source(s) of infection.
4. Understand the importance of sepsis phenotyping in the diagnosis and control of sepsis.
5. Discuss the importance of timely source control on morbidity and mortality in sepsis.
6. Identify the array of source control options available based upon the site of infection.

eModule Information

Relevant Competencies from CoBaTrICE

Sepsis and Septic Shock Part III: Identification and Control of the Source of Infection

- **1.1** Adopts a structured and timely approach to the recognition, assessment and stabilisation of the acutely ill patient with disordered physiology.
- **2.2** Undertakes timely and appropriate investigations.
- **2.5** Obtains appropriate microbiological samples and interprets results.
- **2.10** Integrates clinical findings with laboratory investigations to form a differential diagnosis.
- **4.1** Prescribes drugs and therapies safely.

1. Identification and Control of the Source of Infection

Sepsis is a life-threatening medical emergency, characterized by an organ dysfunction secondary to a deregulated inflammatory response caused by infection, as defined by Sepsis-3 criteria (Singer et al. 2016). Its precise and timely diagnosis permits early initiation of therapy and is crucial for patients' survival and outcomes (Tang et al. 2024). Identification and proper control of the underlying source of infection is essential and can be challenging as clinical signs are often non-specific, and may, therefore, mimic other inflammatory, but non-infectious, conditions (Singer et al. 2026). An accurate patient assessment (e.g., a focused history, examination and targeted investigations) should be carried out in order to properly address the potentially vast differential diagnosis in this setting and identify the syndrome in special populations, such as geriatric or immunocompromised patients, in which it may present in a more subtle scenario (Goodacre et al. 2023; Deinhardt-Emmer et al. 2025).

> ★ **Important**
>
> Sepsis is a medical emergency. Consider it present in every critically ill patient until proven otherwise. Timing of antibiotics initiation is of extreme importance. Administer antibiotics immediately (ideally within 1 hour) in patients with shock or when sepsis is definite or highly probable. In stable patients with moderate to low suspicion of sepsis, rapid diagnostic assessment should be performed and antimicrobials should be initiated within 3 hours if infection remains a likely cause (Figure 1). If the scenario is complex and infection cannot be ruled out, have a low threshold for commencing empiric therapy. A posteriori, antibiotic prescription and de-escalation can be evaluated, based on patient clinical and laboratory evolution, together with microbiologic results.

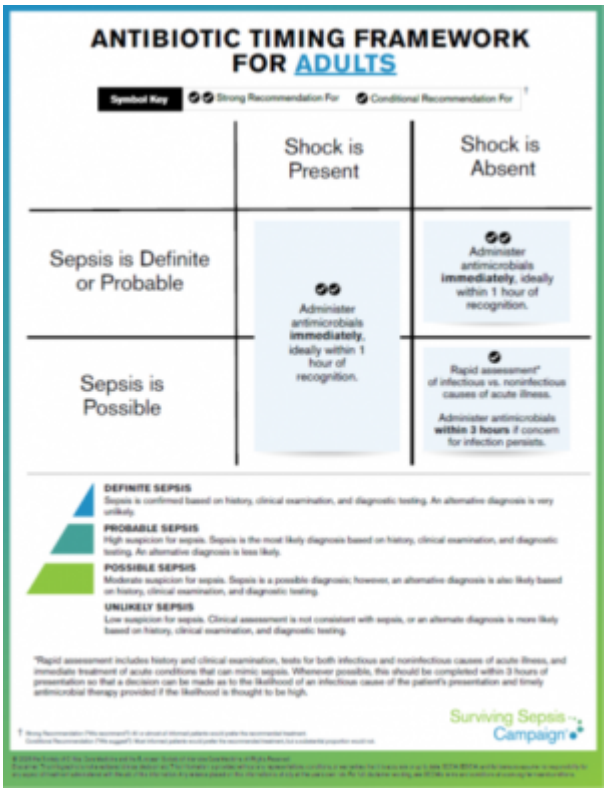

Figure 1: Schematic antibiotic timing overview.

Important

Source control is one of the cornerstones in the propaedeutics of septic patients. This encompasses a broad range of interventions (for example, percutaneous CT-guided abscess drainage), which aim to optimize antibiotics tissue and biofilm penetration, with the ultimate goal of eradicating a focus of infection. A meta-analysis of observational studies suggests that septic patients who undergo timely source control interventions are more likely to survive when compared to matched patients who do not (Prescott et al. 2026).

Important

Special populations, such as geriatric and oncologic patients, may have life-threatening infections with very subtle clinical presentations. A high level of suspicion is required in this setting.

References

- Kim H, Chung SP, Choi SH, Kang GH, Shin TG, Kim K, Park YS, Han KS, Choi HS, Suh GJ, Kim WY, Lim TH, Ko BS, Impact of timing to source control in patients with septic shock: A prospective multi-center observational study., 2019, PMID:31247517
- Im Y, Kang D, Ko RE, Lee YJ, Lim SY, Park S, Na SJ, Chung CR, Park MH, Oh DK, Lim CM, Suh GY, Time-to-antibiotics and clinical outcomes in patients with sepsis and septic shock: a prospective nationwide multicenter cohort study., 2022, PMID:35027073
- De Waele JJ, Girardis M, Martin-Loeches I., Source control in the management of sepsis and septic shock., 2022, PMID:36102944
- Goodacre S, Fuller G, Conroy S, Hendrikse C., Diagnosis and management of sepsis in the older adult., 2023, PMID:37451817

- Tang F, Yuan H, Li X, Qiao L., Effect of delayed antibiotic use on mortality outcomes in patients with sepsis or septic shock: A systematic review and meta-analysis., 2024, PMID:38310764
- Singer M, Angus DC, Annane D, Bauer M, Kalil AC, Klompas M, Machado FR, Martin GS, Randolph AG, Shankar-Hari M, Shapiro NI, Van den Berghe G., Sepsis., 2026, PMID:41765030
- Goodacre S, Fuller G, Conroy S, Hendrikse C., Diagnosis and management of sepsis in the older adult. , 2023, PMID:37451817
- Deinhardt-Emmer S, Chousterman BG, Schefold JC, Flohé SB, Skirecki T, Kox M, Winkler MS, Cossarizza A, Wiersinga WJ, van der Poll T, Weigand MA, Cajander S, Giamarellos-Bourboulis EJ, Lachmann G, Girardis M, Scicluna BP, Ferrer R, Payen D, Sepsis in patients who are immunocompromised: diagnostic challenges and future therapies., 2025, PMID:40409328
- Prescott HC, Antonelli M, Alhazzani W, Møller MH, Alshamsi F, Azevedo LCP, Belley-Cote E, De Waele J, Derde L, Dionne JC, Evans L, Gershengorn HB, Hodgson CL, Honarmand K, Kesecioglu J, Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026., 2026, PMID:41869847
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC, The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)., 2016, PMID:26903338

1. 1. Clinical Recognition of Infection

Suspected infection merits prompt and comprehensive evaluation, as the clinical picture is diverse and can be misleading, especially in the elderly or immunocompromised patients. Non-specific symptoms (such as fluctuations in mental state) and signs (as newly-onset hyperglycemia) may be observed. To address these and other challenges, clinicians should use a low threshold for diagnosis suspicion in critically ill patients who are at risk for sepsis (Prescott et al. 2026). See Sepsis and Septic Shock Part 1.

Important

Awareness, active investigation and further diagnostics are essential for the recognition of infection and sepsis

1. 1. 1. Key principles

1. A focused history and physical examination provides valuable information to establish the presence of infection and its systemic repercussions. Among others, consider the following data collection:
    1. Age
    2. Comorbidities and medication history (for example, an immunosuppression state secondary to drugs like corticosteroids or chemotherapy)
    3. Presence of non-organic or nonhuman material prosthetics or devices, (e.g.: biologic heart valves, indwelling vascular catheters, etc.)
    4. Social and work history, (e.g.: intravenous drug use, occupational exposition, etc.)
    5. Location where the infection was acquired, (e.g.: community, hospital, institution, abroad, etc.)
    6. Previous hospital admissions and/or operations
    7. Previous infections/known colonization with pathogenic organisms
    8. Previous antibiotics use
2. Treat a patient with suspected infection the same as you would treat a patient with a proven diagnosis, especially if there is evidence of organ dysfunction, until infection has been ruled out.
3. Whenever possible, obtain blood (at least two pairs) and suspected infection site cultures prior to initiating treatment. This aims to optimize microbiological exam sensitivity and pathogen identification probability. DO NOT delay therapy if unable to obtain adequate samples in a timely manner.
4. Start treatment with antimicrobials targeted against the presumed pathogen without delay. Broad-spectrum drugs may be initiated in situations without an obvious site of infection and later de-escalated, if feasible.
5. Search for the source of infection. Use clinical examination, laboratory, imaging, microbiological and molecular data, (e.g.: blood, urine, bronchial secretions, pleural aspiration, cerebrospinal fluid, swabs, tissue samples, if collection available in your institution).
6. Evaluate the potential role for source control as early as possible – think multidisciplinary!
7. Whenever possible, biomarkers should be integrated into clinical evaluation to support the diagnosis of sepsis or to guide decision-making in antibiotic stewardship.
8. Reassess the patient frequently. Once the source is identified, target (escalate or deescalate) therapy in accordance with microbiological findings and susceptibility results. This should preferentially occur within 72 hours. Do not continue antimicrobial therapy without justification or for unnecessarily long periods.

References

- Prescott HC, Antonelli M, Alhazzani W, Møller MH, Alshamsi F, Azevedo LCP, Belley-Cote E, De Waele J, Derde L, Dionne JC, Evans L, Gershengorn HB, Hodgson CL, Honarmand K, Kesecioglu J, Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026., 2026, PMID:41869847

1. 2. Sources of Infection

Table 1 represents an overview of potential foci and sources of infection.

Table 1: Sources of infection

Bone and Joint Infection	Osteomyelitis, Septic Arthritis, Disc space infection, Joint or bursa infection, Prosthetic joint infection, Spondylodiscitis
Central Nervous System Infection	Intracranial infection and abscesses, Encephalitis, Meningitis or ventriculitis, Spinal abscess
Cardiovascular System Infection	Pericarditis, Endocarditis, Mediastinitis, Mycotic Aneurysm, Arterial or venous infection
Head and Neck Infections	Orbital cellulites, Odontogenic/tooth infection, Mastoiditis, Oral infections and abscesses, Sinusitis, Otitis, Pharyngitis, Laryngitis, Epiglottitis
Gastrointestinal System Infection	Gastroenteritis, Colitis, Intraabdominal abscess, Bowel perforation and Peritonitis, Clostridioides difficile infection, Diverticulitis, Cholecystitis, Cholangitis, Hepatic abscess, Appendicitis, Necrotizing Pancreatitis, Splenic abscess
Lower Respiratory System Infection	Tracheobronchitis, Pneumonia, Pleural empyema
Reproductive Tract Infection	Pelvic Inflammatory Disease, Post-partum Endometritis, Episiotomy infection, Amnionitis/septic abortion, Prostatitis

Skin and Soft Tissue Infection	Lymphadenitis, Abscesses, Mastitis, Erysipelas, Cellulitis, Necrotizing Fasciitis, Infected Burn wound, Decubitus ulcer infection
Renal and Urinary System Infection	Cystitis, Pyelonephritis, Perinephric abscess
Sepsis of the newborn	Early onset neonatal sepsis, Late onset neonatal sepsis
Heath care associated infections	Catheter-related bloodstream infection (CRBI), Catheter-associated urinary tract infections (CAUTI), Surgical site infection (SSI), Ventilator-associated pneumonia (VAP), Prosthetic joint and heart valves infections, Pacemaker/defibrillator infections

1. 3. Clinical Examination, Laboratory Investigations, Microbiological Testing and Imaging

Finding the source of infection may require, besides a proper history and physical examination, extensive diagnostic investigation. Such propaedeutic includes biochemical and microbiological exams, together with complementary radiological and molecular tests, as suited for each scenario.

Laboratory investigation should include, based on clinical necessity, a full blood count, tests of organ function (cardiovascular, respiratory, hepatic and kidney functions, etc.) and, if feasible, infection-associated biomarkers. Table 2 describes laboratory values useful for the diagnosis of infection. Of note, SOFA score data should be assessed in this setting as it objectively quantifies organ dysfunction needed to define Sepsis *per se* (Singer et al. 2016). Several biomarkers are now routinely available and may serve different purposes including support the diagnosis, aiding monitoring response to therapy or even with prognostic value.

Among the available biomarkers, procalcitonin (PCT) has been widely used and studied in this scenario.

Procalcitonin has moderate diagnostic accuracy for sepsis (AUC 0.79 (95 % CI 0.73-0.86) but can, however, be falsely elevated in cases of chronic kidney disease, trauma, surgery, hyperthermia, thyroid medullary carcinoma or malignancies and cannot reliably discriminate between bacterial, fungal, and viral infections in critically ill patients, particularly in severe viral illness such as influenza or COVID-19 where PCT

may be elevated in proportion to disease severity rather than bacterial coinfection (Falcão Gonçalves, Menezes Falcão and Duque Pinheiro. 2017; Ghatak et al. 2026; Gautam et al. 2020). For this reason, despite its usefulness, current guidelines do not recommend routine use of biomarkers for sepsis diagnosis and recommend against using PCT to guide antibiotic initiation in critically ill patients (O'Grady et al. 2023; Prescott et al. 2026).

Procalcitonin titers also rapidly decline along with infection resolution, making it a useful adjunct to clinical evaluation for the guidance of antimicrobial therapy discontinuation in patients with an initial diagnosis of sepsis or septic shock and adequate source control, particularly when optimal duration of therapy is unclear (Dark et al. 2025; Prescott et al. 2026).

In addition to its diagnostic value, it can also have a part in stratifying patients' outcomes – as those in whom PCT levels remain elevated for longer duration, despite treatment, tend to have a worse prognosis (Schuetz et al. 2017).

C-reactive protein (CRP) is also a widely used biomarker; however, despite its well-established use in clinical practice, its diagnostic accuracy and specificity are lower than those of PCT, and it has no proven role in guiding antimicrobial therapy (Dark et al. 2025).

Together with CRP and PCT, other molecules have been studied, such as cytokines (e.g.: IL-6, IL-8 and IL-10), anaphylatoxins (such as complement 5a), among others. Although several of these markers are already routinely measured in selected hospitals, most still require further evidence of clinical utility, which limits their broad implementation in daily practice, especially in resource limited settings.

> ★ **Important**
>
> Many types of infection presentation are possible and often not readily diagnosed. Finding the source of infection can be challenging. Extensive investigation, including laboratory testing and imaging are often necessary.

> ★ **Important**
>
> Caution should be exercised in the interpretation of biomarkers for infection, as with any test. Adequate correlation with the clinical presentation should always be made.

Table 2: Examples of laboratory values for the detection of infection

Exams*	Threshold value	Sensitivity	Specificity	AUC
White blood cell count	>12 or <4 10^6 cells/mm^3	16-40%	50-94%	0.52-0.55

Immature (band) forms	>10% of total cell count	84%	71%	
C-reactive protein (CRP)	>10 mg/L	80-83%	56-61%	0.73
Procalcitonin (PCT)	>0.5ng/mL	68-82%	69-79%	0.79-0.87
Interleukin-6	variable 18-423 pg/mL	72%	70%	0.77

*Table 3: Specific Pathogen Tests/Assays**

Test	Pathogen	Threshold value	Sensitivity	Specificity
Legionella antibodies	Legionella spp	Positive		
Beta-D-Glucan (BDG)	Pneumocystis jirovecii, Aspergillus spp., Candida spp	> 80 pg/mL	50-70%	80-90%
Galactomannan	Aspergillus spp.	>1 ng/mL	50-100%	80-100%
Quantiferon	Mycobacterium tuberculosis	Positive		
Influenza Antigen	Influenza A, Influenza B	Positive	80%	85%
Enzyme imunoessays for toxins detection	Clostridioides difficile	Positive	29-86%	

(*) Many other tests are commercially available. These should be tailored to each clinical scenario (not only based on local epidemio and microbiologic data, but also financial limitations).

1. 3. 1. Microbiological Testing

Appropriate microbiological specimens for cultures should be obtained, preferentially, before antimicrobial therapy in patients with suspected/diagnosed sepsis or septic shock but this recommendation must not delay the start of treatment.

Positive blood cultures provide objective evidence of the systemic dissemination of a microorganism. However, blood culture sensitivity may vary, depending on the source and severity of infection. Sampling techniques and microbiology laboratory expertise

may also contribute to test results. Fever alone has poor predictive value for bacteremia detection, with only 45% of bacteremic patients having fever > 38°C (Speaker et al. 2023). Procalcitonin may be useful, when combined with clinical characteristics, to help exclude bacteremia when values are low (Kaal et al. 2026).

Following adequate skin preparation, at least two blood culture pairs (aerobic and anaerobic bottles) should be obtained from different peripheral sites or intravascular catheters (depending on the clinical setting), inoculating at least 10 mL of blood into each specimen bottle (Miller et al. 2024). The collection of a third aerobic bottle has been shown to improve yield (O'Grady et al. 2023). Positive cultures of other locations as, for example, normally sterile fluids (e.g.: pleural or peritoneal fluid), obtained using adequate technique, could also provide strong evidence of infection.
Specimens obtained from skin surfaces or pressure ulcers, are less reliable, as the differentiation between colonization and infection is difficult and the threshold for interpretation remains controversial. Positive sputum or urine cultures in intubated or catheterized patients may also reflect colonization of the tracheobronchial tree or lower urinary tract, respectively, rather than active infection of the site. The use of quantitative culture techniques and more invasive interventions (such as bronchoscopy with bronchoalveolar lavage) to obtain specimens can improve the data reliability.

> ★ **Important**
>
> Microbiological sampling, especially blood cultures, is essential for pathogen identification and enables targeted therapy and possibly drug de-escalation, contributing to antimicrobial stewardship.

Table 4: The most common types of microbiological samples that can be collected.

- Blood cultures (at least 2 pairs of an anaerobic and anaerobic cultures; fungus specific cultures when indicated)
- Urinalysis and culture
- Tracheal aspirates
- Bronchoalveolar lavage fluid
- Cerebrospinal fluid
- Tissue swabs
- Fluid/aspirates from abscesses and body cavities (pleural effusions, articular effusions and others)
- Surgical material specimens (bone fragments, heart valves samples, biopsy material, foreign body implants or prosthetics, etc.)

The interval between specimen collection and definitive microbiological identification

represents a critical window during which patients may receive suboptimal empirical antimicrobial therapy.

Definitive isolation of an implicated pathogen species – and posterior evaluation of its drug sensitivity profile – are not typically available for at least two to three days after specimen collection, depending on the microbiology infrastructure apparatus. Early presumptive microbial diagnosis can be made using direct visualization methods such as Gram or Chinese ink stains (particularly of blood, cerebrospinal fluid or urine samples). These are complementary to an adequate patient history and aid in timely initiation of proper antimicrobial therapy, leading to better outcomes.

By significantly reducing the time to pathogen identification compared with conventional culture methods, these techniques enable earlier initiation of targeted antimicrobial therapy (Zhou et al. 2026; Liborio et al. 2024). Methods such as PCR-based assays, multiplex syndromic panels, MALDI-TOF mass spectrometry and point-of-care diagnostics can identify pathogens and key resistance markers within hours (Dunbar, Benavides and Gardner. 2025; Candel et al. 2024). This rapid turnaround improves diagnostic accuracy, facilitates timely optimization and de-escalation of antimicrobial therapy and supports antimicrobial stewardship programs (Peri et al. 2024). In addition, early pathogen identification and resistance profiling have been associated with improved clinical outcomes, including reduced mortality, shorter hospital stays, and lower healthcare costs (Zhou et al. 2026) . Rapid tests are particularly valuable in syndromic approaches, such as bloodstream infections, respiratory infections, and central nervous system infections (Candel et al. 2024). However, results must always be interpreted in the clinical context, as molecular assays may detect colonization or non-viable organisms rather than true infection (Liborio et al. 2024). Limitations include cost, availability, and variability in diagnostic performance depending on the pathogen and sample type (Alatawi et al. 2025). Overall, rapid microbiological diagnostics represent a major advancement in infectious disease management, complementing rather than replacing conventional culture-based methods.

1. 3. 2. Imaging

Imaging is often necessary to broaden and refine history and clinical examination data. It may help determine whether source control measures are indicated and can stratify disease macroscopic severity (e.g.: computed tomography for evaluation of lung compromise in pneumonia).

> ★ **Important**
>
> Imaging may contribute to differential diagnosis rationale.

1. 3. 2. 1. Modalities:

- **X-ray** may support the diagnosis of respiratory tract infections, as well as intrabdominal or other foci (for example, enteric or colonic distension, semi-occlusion, air between soft tissue surrounding a prosthetic joint, etc.)

- **Ultrasonography** is widely available, feasible to be performed routinely at bedside, inexpensive and reproductible with a good agreement between experienced observers – and even among those less experienced, depending on exam type and protocol. Its utility lies in detecting infections arising from abdominal hollow viscus (for example, gallbladder and biliary tree leading to acute cholecystitis or cholangitis), free-fluid detection in the abdomen – corroborating organ perforation, intestinal loop ischaemia or other inflammatory syndromes, etc. Also, it may be useful in detecting pneumonia, pleural effusion, soft tissue purulent collections, among other uses.
- **Echocardiography, transthoracic or transoesophageal modalities,** is essential for diagnosing endocarditis or peri/intracardiac abscesses and hemodynamic evaluation in states of shock.
- **Computed tomography (CT)** scanning is one of the most useful diagnostic modalities for evaluating patients with suspected infections, regardless of body compartment involvement. It is also useful in evaluating the extent of complex soft tissue infections. Oral or rectal contrast aids in CT interpretation by delineating gastrointestinal tract and identifying perforations, when these are present. Intravenous contrast permits the identification of vascular structures and can demonstrate areas of inadequate tissue perfusion, which may be suggestive of ischaemia or infarction. It can also help diagnose abscesses or other lesions of different infectious aetiologies.
- **Magnetic resonance imaging** can be helpful in the diagnosis of soft tissue infections or spondylodiscitis. However, it is a time consuming and not readily available exam and, therefore, should only be elicited outside of an urgency scenario.
- **Positron emission tomography scan** may be a useful exam to identify areas of inflammation and delineate suspected chronic infection of bone or adjacent structures, as well as central nervous system foci, when investigations listed above have failed to yield a diagnosis. It is, although, still an expensive exam, limited to restricted centres and not routinely used.

References

- Schuetz P, Birkhahn R, Sherwin R, Jones AE, Singer A, Kline JA, Runyon MS, Self WH, Courtney DM, Nowak RM, Gaieski DF, Ebmeyer S, Johannes S, Wiemer JC, Schwabe A, Shapiro NI., Serial Procalcitonin Predicts Mortality in Severe Sepsis Patients: Results From the Multicenter Procalcitonin MOnitoring SEpsis (MOSES) Study, 2017, PMID:28257335
- Prescott HC, Antonelli M, Alhazzani W, Møller MH, Alshamsi F, Azevedo LCP, Belley-Cote E, De Waele J, Derde L, Dionne JC, Evans L, Gershengorn HB, Hodgson CL, Honarmand K, Kesecioglu J, McIntyre L, Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2026., 2026, PMID:41870560

- Prescott HC, Antonelli M, Alhazzani W, Møller MH, Alshamsi F, Azevedo LCP, Belley-Cote E, De Waele J, Derde L, Dionne JC, Evans L, Gershengorn HB, Hodgson CL, Honarmand K, Kesecioglu J, Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026., 2026, PMID:41869847
- Falcão Gonçalves P, Menezes Falcão L, Duque Pinheiro I., Procalcitonin as Biomarker of Infection: Implications for Evaluation and Treatment., 2017, PMID:25803230
- Ghatak T, Pal A, Rochwerg B, Samanta S, Kumar A, Sajjad SA, Das A, Singh RK. , he diagnostic accuracy of serum procalcitonin for sepsis in critically ill adults. A systematic review and diagnostic meta-analysis., 2026, PMID:41421176
- Gautam S, Cohen AJ, Stahl Y, Valda Toro P, Young GM, Datta R, Yan X, Ristic NT, Bermejo SD, Sharma L, Restrepo MI, Dela Cruz CS., Severe respiratory viral infection induces procalcitonin in the absence of bacterial pneumonia., 2020, PMID:32826284
- O'Grady NP, Alexander E, Alhazzani W, Alshamsi F, Cuellar-Rodriguez J, Jefferson BK, Kalil AC, Pastores SM, Patel R, van Duin D, Weber DJ, Deresinski S., Society of Critical Care Medicine and the Infectious Diseases Society of America Guidelines for Evaluating New Fever in Adult Patients in the ICU., 2023, PMID:37902340
- Dark P, Hossain A, McAuley DF, Brealey D, Carlson G, Clayton JC, Felton TW, Ghuman BK, Gordon AC, Hellyer TP, Lone NI, Manazar U, Richards G, Biomarker-Guided Antibiotic Duration for Hospitalized Patients With Suspected Sepsis: The ADAPT-Sepsis Randomized Clinical Trial. , 2025, PMID:39652885
- Speaker SL, Pfoh ER, Pappas MA, Schulte R, Hu B, Gautier TN, Rothberg MB., Relationship Between Oral Temperature and Bacteremia in Hospitalized Patients., 2023, PMID:36997793
- Kaal AG, Nieberg M, Stegmeijer K, Steyerberg EW, van Nieuwkoop C., The diagnostic accuracy of procalcitonin for community-acquired bacteraemia: an updated systematic review and meta-analysis., 2026, PMID:41519266
- Miller JM, Binnicker MJ, Campbell S, Carroll KC, Chapin KC, Gonzalez MD, Harrington A, Jerris RC, Kehl SC, Leal SM Jr, Patel R, Pritt BS, Richter SS, Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2024 Update by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM)., 2024, PMID:38442248
- Zhou B, Chen Z, Zhu H, Chen B, Fang J, Jin X., Impact of molecular rapid diagnostic testing on clinical outcomes in bloodstream infections: a meta-analysis., 2026, PMID:41877090
- Liborio MP, Harris PNA, Ravi C, Irwin AD., Getting Up to Speed: Rapid Pathogen and Antimicrobial Resistance Diagnostics in Sepsis. , 2024, PMID:39338498

- Dunbar SA, Benavides M, Gardner C., Advances in diagnostic methods for detection of bloodstream pathogens and antibiotic resistance determinants., 2025, PMID:41446279
- Candel FJ, Salavert M, Cantón R, Del Pozo JL, Galán-Sánchez F, Navarro D, Rodríguez A, Rodríguez JC, Rodríguez-Aguirregabiria M, Suberviola B, Zaragoza R., The role of rapid multiplex molecular syndromic panels in the clinical management of infections in critically ill patients: an experts-opinion document., 2024, PMID:39736683
- Peri AM, Chatfield MD, Ling W, Furuya-Kanamori L, Harris PNA, Paterson DL., Rapid Diagnostic Tests and Antimicrobial Stewardship Programs for the Management of Bloodstream Infection: What Is Their Relative Contribution to Improving Clinical Outcomes? A Systematic Review and Network Meta-analysis., 2024, PMID:38676943
- Alatawi AD, Hetta HF, Ali MAS, Ramadan YN, Alaqyli AB, Alansari WK, Aldhaheri NH, Bin Selim TA, Merdad SA, Alharbi MO, Alatawi WAH, Algammal AM., Diagnostic Innovations to Combat Antibiotic Resistance in Critical Care: Tools for Targeted Therapy and Stewardship. , 2025, PMID: 40941733
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC, The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)., 2016, PMID:26903338

1. 4. Sepsis phenotypes

A recent field of research in many areas is a more personalized approach to patient care and, regarding Critical Care, it is no different. Although sepsis is seen as a syndrome of inflammatory dysregulation leading to organ dysfunction, its heterogeneity of presentation is no surprise for the bedside clinician.

The idea of stratifying Sepsis in phenotypes and trying to correlate these with prognosis and even therapeutic targets is valid, may impact outcomes and optimize resource allocation. Therefore, multiple classification systems have been proposed (Figure 2), with potential to improve outcomes and optimize resource allocation through precision medicine approaches.
Major phenotype classifications include:

- Clinical phenotypes derived from routinely available data at hospital presentation or trajectories of bedside vital signs, with different mortalities (Seymour et al. 2019; Bhavani et al. 2022);

- Molecular phenotypes (hyperinflammatory vs. hypoinflammatory) identified using biomarkers and clinical data, showing differential treatment responses to activated protein C (Sinha et al. 2023);
- Transcriptomic endotypes including Sepsis Response Signatures (SRS1-2) and MARS clusters (Reddy et al. 2020; Scicluna et al. 2017).

An adequate profiling in sepsis can contribute to different clinical applications:

- Predicting the risk of sepsis development before organ dysfunction
- Optimize clinical recognition of stablished sepsis
- Improve differential diagnosis between bacterial and non-bacterial sepsis
- Stratify potential disease severity and outcomes

Predict response to patient support and treatment as simulation models demonstrate treatment benefit or harm conclusions are sensitive to phenotype distributions.

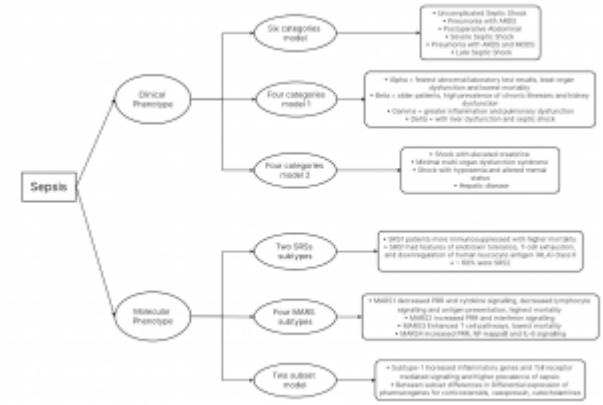

Figure 2: Clinical and molecular examples of Sepsis phenotyping. Adapted from Shankar-Hari et al 2019.

Abbreviations:

- ARDS: Acute respiratory distress syndrome;
- MODS: Multiple organ dysfunction syndrome;
- SRS: sepsis response signatures;
- MARS: Molecular Diagnosis and Risk Stratification of Sepsis project;
- PRR: Pattern recognition receptors

Despite being based on a strong and physiologically coherent rationale, the clinical and therapeutic impact of phenotyping sepsis and critically ill patients remain to be validated.

References

- Seymour CW, Kennedy JN, Wang S, Chang CH, Elliott CF, Xu Z, Berry S, Clermont G, Cooper G, Gomez H, Huang DT, Kellum JA, Mi Q, Opal SM, Talisa V, van der Poll T, Visweswaran S, Vodovotz Y, Weiss JC, Yealy DM,

Yende S, Angus DC., Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis., 2019, PMID:31104070

- Gårdlund B, Dmitrieva NO, Pieper CF, Finfer S, Marshall JC, Taylor Thompson B., Six subphenotypes in septic shock: Latent class analysis of the PROWESS Shock study., 2018, PMID:29933169
- Bhavani SV, Semler M, Qian ET, Verhoef PA, Robichaux C, Churpek MM, Coopersmith CM., Development and validation of novel sepsis subphenotypes using trajectories of vital signs., 2022, PMID:36152041
- Sinha P, Kerchberger VE, Willmore A, Chambers J, Zhuo H, Abbott J, Jones C, Wickersham N, Wu N, Neyton L, Langelier CR, Mick E, He J, Jauregui A, Churpek MM, Gomez AD, Hendrickson CM, Identifying molecular phenotypes in sepsis: an analysis of two prospective observational cohorts and secondary analysis of two randomised controlled trials., 2023, PMID:37633303
- Reddy K, Sinha P, O'Kane CM, Gordon AC, Calfee CS, McAuley DF., Subphenotypes in critical care: translation into clinical practice., 2020, PMID:32526190
- Scicluna BP, van Vught LA, Zwinderman AH, Wiewel MA, Davenport EE, Burnham KL, Nürnberg P, Schultz MJ, Horn J, Cremer OL, Bonten MJ, Hinds CJ, Wong HR, Knight JC, van der Poll T, Classification of patients with sepsis according to blood genomic endotype: a prospective cohort study., 2017, PMID:28864056

1. 5. Source Control

Source control management should be taken with the same importance as proper and timely antibiotics initiation. It is well known that antibiotics do not have a good penetration in acid environment or bacterial biofilms. Thus, addressing localized collections or infected devices enables best antimicrobial effect and assures optimized therapy.

It is well established that early source control interventions reduce mortality (Prescott et al. 2026). However, the optimal timing of these interventions remains controversial, largely due to heterogeneous definitions of “early” across studies. Early source control was most commonly defined by a 6-hour cut-off from either diagnosis or sepsis, diagnosis of septic shock, or identification of the need for source control. Therefore, patients with sepsis or septic shock should always be promptly evaluated for possible sources of infection requiring source control procedures and interventions should be achieved as soon as possible following initial resuscitation. However, the selection of optimal timing and source control methods should be individualized for each patient

and must weigh the benefits and risks of the specific intervention, consider hemodynamics, ventilatory and other organ function status, clinician expertise, availability, potential delays, and probability of success, as all procedures carry risks.

Table 4: Source of infection vs Interventions

SOURCE	INTERVENTIONS
Bone and Joint Infection	Surgical drainage and/or lavage, prosthetics removal
Neurosurgical drainage, lavage, intrathecal antibiotics	
Cardiovascular System Infection	Abscess drainage, valve replacement
Head and Neck Infections	Oral and/or maxillofacial or neck drainage
Gastrointestinal System Infection	Surgical, percutaneous or endoscopic drainage of collections or ductal obstructions; surgical removal of infected or necrotic tissue
Lower Respiratory System Infection	Drainage of empyema or abscesses
Reproductive Tract Infection	Surgical drainage and/or lavage of collections or infected tissue, uterine curettage
Skin and Soft Tissue Infection	Surgical drainage and/or lavage of collections or infected tissue, Estomatherapy for infected pressure ulcers and chemical or mechanical debridement(*)
Renal and Urinary System Infection	Hydronephrosis and/or abscess drainage
Heath care associated infections	Intravascular or urinary catheter, pacemaker/defibrillator removal

(*) It is reasonable to assume that topical treatment with special dressings also stand as first-line of treatment.

References

- Prescott HC, Antonelli M, Alhazzani W, Møller MH, Alshamsi F, Azevedo LCP, Belley-Cote E, De Waele J, Derde L, Dionne JC, Evans L, Gershengorn HB, Hodgson CL, Honarmand K, Kesecioglu J, Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026., 2026, PMID:41869847

- Martínez ML, Ferrer R, Torrents E, Guillamat-Prats R, Gomà G, Suárez D, Álvarez-Rocha L, Pozo Laderas JC, Martín-Loeches I, Levy MM, Artigas A; Edusepsis Study Group., Impact of Source Control in Patients With Severe Sepsis and Septic Shock., 2017, PMID:27611975

1. 6. Conclusion

Sepsis recognition and adequate management optimizes patient outcomes. Therefore, all efforts should be made to address this enormous challenge. It all starts with healthcare team education and continues through daily clinical multidisciplinary experience. Knowledge and use of all available tools may help overcome local environment limitations, with the ultimate goal of improving patient care.

1. 6. 1. Take home Points:

1. In sepsis, TIMING is everything! A low threshold for suspicion and an accurate diagnosis of Sepsis or Septic Shock are of utmost importance for better patient outcomes!
2. A focused analysis of history, physical examination and complementary laboratory and imaging data ensures an adequate clinical rationale. This, by itself, promotes a better care for our critically ill patients. Use every available tool!
3. Source control together with an adequate initial choice of antimicrobials saves lives. Always weight risk vs benefits in every decision. CHECK for cultures results and hidden foci!
4. Treat right, treat fast!