# Initial management of critically-ill patients with community-acquired sepsis and septic shock when the source is not yet identified

**Sepsis:** Life-threatening organ dysfunction due to a dysregulated host response to infection

**Septic shock:** Subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Identified by the need for vasopressors to maintain a MAP ≥ 65 mm Hg and serum lactate level ≥ 2 mmol/L in the absence of hypovolaemia.

Identification of the source of infection requires careful history and targeted investigations.

History should include

1. recent travel
2. infectious contacts
3. past medical history, particularly details of recent infections, diabetes and organ transplantation
4. drug misuse behaviour (including intravenous drug use or subcutaneous drug use such as skin popping)
5. drug history including recent antimicrobials, cancer chemotherapy and other immunosuppressants
6. occupational history and details of unusual hobbies or pastimes
7. sexual history

**Investigations for all septic patients in whom the source of infection is unclear**

1. Blood samples
    a. Minimum 2 sets of peripheral blood cultures (i.e. two anaerobic AND two aerobic bottles), ideally prior to antimicrobial therapy. If infective endocarditis is suspected, 3 sets of peripheral blood cultures should be sent. See 'Blood Cultures in Critical Care' guidance for appropriate sampling technique.
    b. HIV test
    c. Early EDTA sample for MBAC PCR (S. pneumoniae, H. influenzae, N. meningitidis)
2. Urine culture. If catheterised, CSU should be taken using an aseptic, non-touch technique only from the sampling port on the drainage bag
3. Respiratory samples.
    a. Sputum culture if not intubated
    b. If intubated, consider BAL or mini-BAL. If this is contraindicated, send endotracheal aspirate (4 samples). See CAP/VAP guidelines for more details and Trak orders.
    c. If atypical respiratory infection is suspected and unable to send BAL or mini-BAL, urinary Legionella antigen should be sent.
    d. COVID PCR
4. CXR
5. MRSA screen

**Targeted investigations to consider depending on presentation**

1. Cross-sectional imaging – consider CT chest, abdomen, pelvis, head, extremities (e.g. if concern for severe soft tissue infection)
2. Additional microbiological sampling

    a. CSF via lumbar puncture if suspected CNS infection and no contraindications to this. If ventriculitis is suspected in a neurosurgical patient, particularly in the presence of an indwelling device, then see ventriculitis guideline for further management.
    b. Skin swabs if broken skin/rashes
    c. If loose stools, send stool for C. diff toxin testing and Norovirus PCT. If initial sample is negative for bacterial enteric pathogens, up to two further samples should be sent on separate days. If immunocompromised, consider other infective causes e.g. CMV.
    d. Pleural fluid via ultrasound-guided thoracocentesis to assess for empyema
    e. Paracentesis in patients with chronic liver disease and ascites to rule out spontaneous bacterial peritonitis.
    f. If immunosuppressed then consider induced sputum or BAL to investigate for PJP, CMV, fungi including Aspergillus, and Mycobacteria (4 separate requests on Trak). Where a BAL is being done for mycology culture, galactomannan should also be requested on the BAL fluid.
    g. If catheter related bloodstream infection is suspected, peripheral cultures, line cultures and line tip should be sent following removal where appropriate.
3. Echocardiogram
    a. Comprehensive transthoracic echocardiogram by BSE-accredited sonographer is first line investigation to assess for endocarditis. Focused echo is not appropriate for this indication.
    b. Liaise with cardiology registrar if suspicion of endocarditis and negative initial transthoracic echocardiogram, particularly if patient has a prosthetic valve. Trans-oesophageal echocardiogram may be required.
4. Investigation of malaria +/- other tropical diseases if recent travel history to endemic area
5. CPE screen if high risk for colonisation. Refer to NHS Lothian CPE guidance.

**Non-infectious sepsis mimics**

1. Cardiogenic shock
2. Pancreatitis
3. Occult haemorrhage
4. Addisonian crisis
5. Malignancy
6. Hemophagocytic lymphohistiocytosis (HLH). Consider if ferritin > 5000mcg/l

**Initial management**

1. Consider need for isolation and PPE
2. Prompt antimicrobial therapy as per Antimicrobial Companion App
3. Early source control. Liaise with surgeons if suspected intra-abdominal or soft-tissue source. Consider removal of indwelling lines.
4. IV fluid therapy +/- noradrenaline. Target MAP 60-65 mmHg is appropriate in most patients.
5. Early discussion with microbiology if recent antimicrobial use
6. If escalating noradrenaline requirements, consider adding vasopressin and shock dose steroids (see Steroids in Septic Shock guideline) plus focused echocardiogram to guide haemodynamic management and assess for cardiac pathology contributing to shock (e.g. LV or RV systolic dysfunction).
7. Consider dobutamine in patients who show evidence of LV dysfunction and persistent hypotension despite adequate fluid loading and vasopressor therapy.
8. Consider IVIG in patients with severe soft tissue infection. See NHS Lothian guidance on Antimicrobial Companion app.

If significant travel history or diagnosis remains elusive then consider seeking an Infectious Diseases consultation.

**If deteriorating over 48-72 hours despite initial therapy, consider:**

7. Source control – is the imaging adequate and does it need to be repeated?
8. Progression of systemic inflammatory response despite appropriate antimicrobial therapy (e.g. development of ARDS)
9. Antibiotic regimen:
    a. Ineffective antibiotic regimen due to opportunistic or atypical bacterial organisms. Consider molecular testing on samples already acquired (pleural, joint, CSF etc)
    b. Resistant organisms that have not yet been cultured - particularly VRE, MRSA, penicillin resistant pneumoococcus or CPE.
    c. Not appropriate for site of infection
    d. Dosed incorrectly for site of infection or patient, particularly if patient receiving renal replacement therapy. Consider therapeutic drug monitoring
    e. Drug interaction
    f. Fungal infection
10. If patient has risk factors for candidaemia (immunosuppressed, recurrent candida growth in respiratory or urine samples, TPN use, unresolved abdominal sepsis, central venous lines, neutropaenia, haematological malignancy, renal replacement therapy or burns) and has persistent fever despite antibacterial therapy, measure beta glucan and consider empirical anti-candida therapy while the results are awaited
11. Review for possible inflammatory conditions that could mimic sepsis including vasculitis etc. Review the history of possible immunocompromising conditions.

If no source of infection identified and culture sterile – reconsider whether this is a bacterial infection and consider stopping antibiotics. Many acute infections are adequately treated after 5 days of broad-spectrum parenteral antibiotics.


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