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UNDERSTANDING THE DISEASE

Source control in the management of sepsis and septic shock

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Source control is an important element of the treatment of sepsis and septic shock [1]. Lack or delay of source control has been associated with worse outcomes for patients with peritonitis [2], and also in other types of infections, the role of source control cannot be underestimated [3, 4]. The 2021 Surviving Sepsis Campaign guidelines recommend identifying the anatomical source of infection that may require source control and implementing this as soon as logistically and medically possible [1]. Although the evidence base for source control mainly consists of retrospective studies with sometimes methodological issues, adequate source control is difficult to define, and often a post hoc finding [5]; the optimal timing of source control is difficult to study and methods for source control not standardized. While uniformity in reporting source control characteristics would help us to better understand its role, these problems should not be used to ignore the role of source control in patients with sepsis and septic shock.

The goal of source control is to eliminate the source of infection, control ongoing contamination, and restore premorbid anatomy and function [6]. Strategies used to achieve source control include drainage of purulent collections, open or percutaneously, removal of the infected and/or necrotic tissue (debridement), creation of diverting 'ostomies', and removing obstruction, among others. Not all goals may be required for every infection, and strategies can be applied selectively, based on the type of infection.

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In this article, we aim—for patients with a source of infection amenable to source control—to highlight the broader relevance of source control in different infections, to emphasize the importance of a multidisciplinary approach and choosing the appropriate methodology, as well as to discuss the complex issue of failed source control.

Identifying the need for source control is closely linked to the diagnostic process itself when investigating a patient with sepsis or septic shock. Once a source of infection has been identified, further examinations may be necessary to evaluate the need for source control, although the extensive use of computed tomography (CT) scan and ultrasound in the diagnostic process may already point this out at this stage. It may be necessary to modify or extend a diagnostic approach to screen for sources of infection that require source control, e.g., by adding oral or intravenous contrast in a patient requiring CT scanning.

Think outside the (abdominal) box

While source control is considered as particularly important in patients with abdominal infection, we advocate that source control should be considered in every patient presenting with sepsis or septic shock, albeit that it may not be necessary to control a source of infection in many. Figure 1 provides an overview of different infections that may require source control.

For many infections listed in Fig. 1, the need to control the source of infection may not reach the same level of urgency as in patients with four-quadrant peritonitis. It should be clear that also in these infections, the role of source control is evident. A patient with cholangitis caused by an obstruction of the biliary tract should be treated as stringently as patients with postoperative fecal peritonitis.

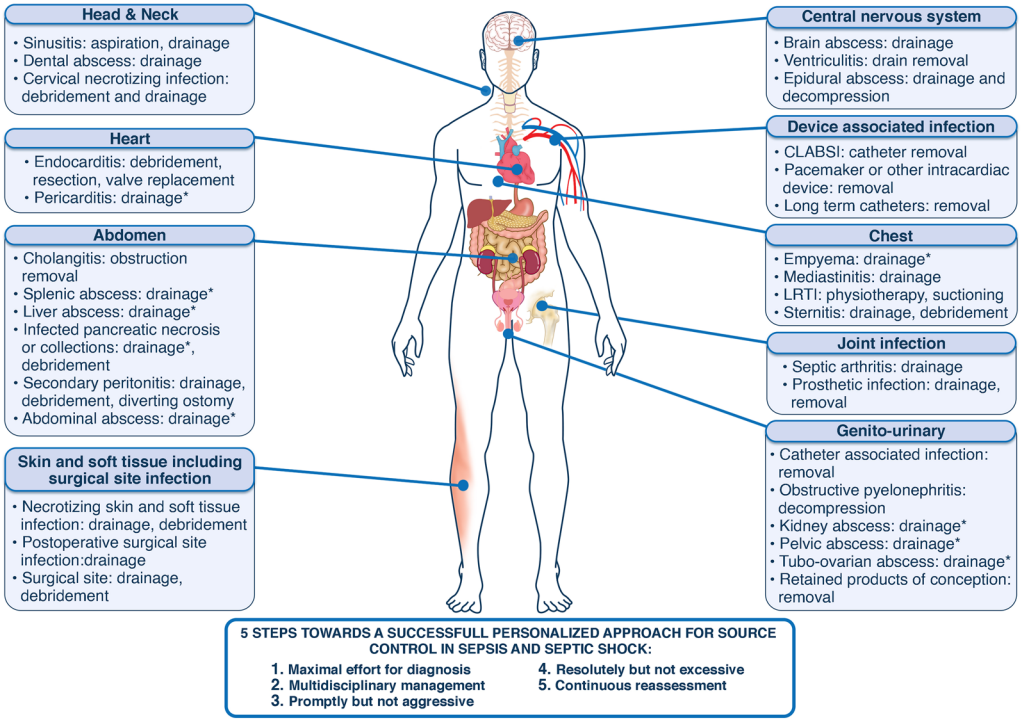

Fig. 1 When to think of source control in patients with sepsis or septic shock. Overview of the different types of infections where source control should be considered, including possible approaches to achieve source control. *Minimally invasive approach preferred

Blood stream infections (BSI) pose a specific challenge in identifying the focus of infection and appropriate source control strategy. While a clear source of infection may not be identifiable in patients with bacteraemia, in some situations, e.g., BSI caused by specific pathogens such as *Staphylococcus aureus*, or *Candida* spp., disseminated infection may be present and a diligent search for infectious foci should be started.

One particularly challenging problem in daily care is the management of central venous catheters in catheter-related bloodstream infection (CRBSI). While in most patients, it is clearly necessary and straightforward to remove the catheter, in some situations such as neutropenic patients, a more conservative approach has been suggested—often triggered by the fear of complications caused by inserting a new catheter. However, the use of ultrasound during catheter insertion has significantly reduced this risk of mechanical complications, and in neutropenic patients with sepsis or septic shock caused by a catheter-related infection, the catheter should be removed [7]. Also, in sepsis or septic shock patients with tunneled catheters, catheter removal is recommended (particularly in case of non-fermenting Gram-negative bacilli, *Candida* spp. or *Staphylococcus aureus*) and a temporary non-tunneled catheter should be inserted [8]. Only in rare cases where there is no alternative, the use of systemic antibiotics and an antibiotic lock can be considered as an attempt to salvage the catheter.

The need for a multidisciplinary approach

Procedures for source control should be tailored to the infection site and extent, and the degree of derangement of patient physiology [9]. The range of infections that may require source control implies that different strategies can be applied to reach the goals of source control. With often different options available to control the source of an infection on the one hand, and variable patient physiology on the other, a well-balanced decision as to the timing and methodology for source control is mandatory.

Clearly, many factors may play a role. Patient factors such as severity of illness (including hemodynamics, respiratory, and metabolic status) and coagulation are important variables to consider when selecting the best strategy—but also location and extent of infection, presence of ongoing contamination and risk of collateral damage associated with source control interventions, need to be considered. Additional factors include surgeon and interventional radiologist availability and experience, as well as logistical considerations.

Therefore, we advocate for a multidisciplinary approach involving surgeons, infectious disease physicians, interventional radiologists, interventional endoscopists,

anaesthesiologists, and intensivists to ensure selecting the best source control strategy for the individual patient.

First do no (additional) harm

These decisions should be governed by generic principles such as choosing the least invasive procedure in that guarantees maximal source control, while avoiding additional damage or creating long-term disability. Patients with sepsis or septic shock may be more prone to complications of surgical procedures due to poor tissue perfusion, disturbed physiology, impaired wound healing, or deranged coagulation.

In some situations, a temporizing strategy may be preferred. Often this is dictated by patient physiology and a patient is considered too sick to undergo major surgery, e.g., acute cholecystitis where percutaneous drainage can be used as a first step. While it is often possible to provisionally control a source of infection in this manner, definitive intervention should not be delayed when patient physiology has improved. Persistent infection resulting from incomplete source control can result in unresolving sepsis and septic shock. In such situation, a more aggressive approach may be necessary, and should not be delayed.

The complexity of failed source control

Failure of source control does occur regularly, and may be a sign of ongoing infection, incomplete source control, ongoing contamination, or combinations thereof [10]. This is often caused by a lack of success of the source control intervention, but lack of effective antimicrobial therapy may also contribute. Poor penetration at the infection site, or inappropriate antimicrobial selection may lead to ongoing bacterial growth, and recurrent infection. This again emphasizes the importance of both pillars of sepsis and septic shock management—antimicrobial therapy and source control. Still, this is a balancing act. In some situations, a more conservative approach should be balanced against the risk of causing more damage when trying to maximize source control.

Failed source control is often difficult to diagnose. While biomarkers may aid in the diagnosis, no definite diagnostic tool is available. Most often the diagnosis is made based on lack of clinical improvement, persistent signs and symptoms of inflammation, and targeted imaging [11]—often, a "smoking gun" is missing. Therefore, monitoring the success of source control, with a low index of suspicion if a patient does not improve, is of paramount importance.

Source control is a determinant of outcome in patients with sepsis and septic shock who require it. Although typically considered in patients with abdominal infections, its principles can be applied to many infections. Interventions should be tailored to the patient's clinical condition by a multidisciplinary team, as open surgery is no longer the only or primary option in many instances. Avoiding additional harm while maximalising efficacy of the intervention and continued monitoring thereof are the keys to success.

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Conflict of interest
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