Fever is a normal adaptive brain response to infectious and noninfectious causes involving a cytokine-mediated response, the generation of acute phase reactants, and the activation of numerous physiologic, endocrinologic and immunologic systems. Ninety percent of patients with severe sepsis in the intensive care unit (ICU) will experience fever during their hospitalization, while the half of the new detected febrile episodes are of noninfectious origin. In the ICU, fever should be treated in cardiorespiratory and neurosurgical patients and in those in whom temperature exceeds 40°C (104°F). Antipyretic therapy must be justified regardless of the metabolic cost (if fever exceeds its physiologic benefit), the result (if the symptomatic relief adversely affects the course of the febrile illness) and the side effects.

The diagnosis and management of severe sepsis and septic shock is a complex and dynamic process. Newer evidence-based interventions are constantly being developed and implemented with the purpose of improving morbidity and mortality. Current investigations are being performed in hospital environments to determine the change in behaviors and clinical impact with the most recent recommendations. The use of standardized treatment protocols in addition to newer diagnostic and treatment modalities in patients who have severe sepsis and septic shock can continue to improve patient-related outcomes and the damaging effect of these diseases on society.

Community-acquired pneumonia (CAP) is the leading cause of death from infectious diseases in the United States. It accounts for 500,000 hospitalizations and 45,000 deaths each year, and it represents one of the most common causes of ICU admission. The mortality rate due to severe CAP has shown little improvement over the past few years, with rates as high as 58% when patients were admitted to the ICU. Significant interest has focused on the sickest patients who have pneumonia treated in the ICU, regarding identification of need for ICU admission and therapies directed...
to improve outcomes in patients who have severe CAP. This article re-
views epidemiologic, microbiologic, therapeutic, preventive, and out-
comes data in patients who have CAP in the ICU.

Management of Ventilator-Associated Pneumonia 521

Emili Diaz, Marta Ulldemolins, Thiago Lisboa, and Jordi Rello

Ventilator-associated pneumonia (VAP) management depends on the in-
teraction between the infective agent, the host response, and the antimi-
crobial drug used. After the pathogen reaches the lungs, two outcomes
are possible: either the microorganisms are eliminated by the host immune
system, or they overcome the immune system and cause pulmonary infec-
tion. When a patient is thought to have VAP, two steps are strongly recom-
mended: etiologic diagnostic testing and the immediate initiation of
antibiotics. The daily management of VAP remains a challenge for physi-
cians in the ICU. In recent years, a more dynamic approach has evolved,
updating local epidemiology, evaluating VAP and diagnostic tools every
day, and assessing host response using clinical and biochemical
parameters.

Approach to the Immunocompromised Host with Infection in the Intensive
Care Unit 535

Peter K. Linden

Despite significant advances in the prevention, diagnosis, and treatment of
infection in the immunocompromised host, it remains a major cause of
morbidity, increased length of stay, total costs, and of course mortality. Int-
tensive care mortality rates are significantly higher among immunocom-
promised hosts in part due to the higher incidence of infection severity.
The superimposition of the compromised host defenses and critical illness
makes the detection and management of infections in such patients more
difficult, but crucial toward salvaging patient outcome. Moreover, although
there is a rapidly increasing evidence base in intensive care medicine,
many interventional trials for the management of severe sepsis (activated
protein C, adjunctive corticosteroids, goal-based resuscitation), acute
lung injury (low stretch ventilation), and other organ failures have excluded
immunocompromised hosts.

Bloodstream Infection in the ICU 557

Jordi Vallés amd Ricard Ferrer

Hospital-acquired infections (HAI) occur in 5%–10% of patients admitted
to hospitals in the United States, and HAIs remain a leading cause of mor-
bidity and mortality. Patients admitted to ICUs account for 45% of all hos-
pital-acquired pneumonias and bloodstream infections (BSIs), although
critical care units comprise only 5% to 10% of all hospital beds. The severity
of underlying disease, invasive diagnostic and therapeutic procedures
that breach normal host defenses, contaminated life-support equipment,
and the prevalence of resistant microorganisms are critical factors in the
Severe Soft Tissue Infections

Lena M. Napolitano

Severe skin and soft tissue infections (SSTIs) frequently require management in the ICU, in part related to associated septic shock or toxic shock syndrome or associated organ failure. Four fundamental management principles are key to a successful outcome in caring for patients who have severe SSTIs, including (1) early diagnosis and differentiation of necrotizing versus nonnecrotizing SSTI, (2) early initiation of appropriate empiric broad-spectrum antimicrobial therapy with consideration of risk factors for specific pathogens and mandatory coverage for methicillin-resistant Staphylococcus aureus (MRSA), (3) source control (ie, early aggressive surgical intervention for drainage of abscesses and debridement of necrotizing soft tissue infections), and (4) pathogen identification and appropriate de-escalation of antimicrobial therapy. MRSA has emerged as the most common identifiable cause of severe SSTIs; therefore, initiation of empiric anti-MRSA antimicrobials is warranted in all cases of severe SSTIs. In addition, appropriate critical care management—including fluid resuscitation, organ support and nutritional support—is a necessary component in treating severe SSTIs.

Intra-abdominal Sepsis: Newer Interventional and Antimicrobial Therapies

Joseph S. Solomkin and John Mazuski

Complicated intra-abdominal infections are the second most common cause of septic death in the intensive care unit. Although there have been improvements in the outcome of sepsis regardless of etiology, this is even more striking for intra-abdominal infections. From observation, recent advances in interventional techniques, including more aggressive use of percutaneous drainage of abscesses and use of “open abdomen” techniques for peritonitis, have significantly affected the morbidity and mortality of physiologically severe complicated intra-abdominal infection.

Central Nervous System Infections: Meningitis and Brain Abscess

Hitoshi Honda and David K. Warren

Despite advances in antimicrobial and antiviral therapy, meningitis and brain abscess are infections that result in significant morbidity and mortality. A multidisciplinary approach, including intensive care, is often required in the treatment of these infections. Meningitis is defined by the presence of the inflammation of the meninges, with characteristic changes in cerebrospinal fluid. Brain abscess is a focal infection of the brain parenchyma, commonly caused by bacterial, fungal, and parasitic pathogens. This article reviews the common infectious etiologies of central nervous system infections, especially bacterial meningitis and brain abscess, and their subsequent management in the intensive care unit.
Pulmonologists and intensivists often care for patients at risk for infections caused by both *Aspergillus* and *Candida*. Infection with either can lead to severe life-threatening disease, particularly in immunosuppressed patients, with mortality rates for invasive fungal disease often exceeding 30%. For both organisms, multiple diagnostic challenges remain while newer diagnostic modalities are being developed and tested. Fortunately, therapeutic paradigms are shifting, and clinicians have many new agents in their armamentarium for combating fungal infection. Given the rapidly changing literature in this broad area, it is imperative that physicians caring for immunosuppressed patients and for the critically ill remain abreast of this evolving field.

Acute infective endocarditis is a complex disease with changing epidemiology and a rapidly evolving knowledge base. To consistently achieve optimal outcomes in the management of infective endocarditis, the clinical team must have an understanding of the epidemiology, microbiology, and natural history of infective endocarditis, as well as a grasp of guiding principles of diagnosis and medical and surgical management. The focus of this review is acute infective endocarditis, though many studies of diagnosis and treatment do not differentiate between acute and subacute disease, and indeed many principles of diagnosis and management of infective endocarditis for acute and subacute disease are identical.

Timely provision of adequate antimicrobial coverage in an initial anti-infective treatment regimen results in optimal outcomes for bacterial and fungal infections. However, selection of appropriate antimicrobial regimens for treatment of infections in the intensive care unit (ICU) can be challenging due to expansion of resistance, which typically requires use of multidrug anti-infective regimens to provide adequate coverage of important pathogens commonly seen in the ICU setting. Indeed, a recent additional call to action by the Infectious Diseases Society of America (IDSA) has enforced the impact that antimicrobial-resistant pathogens can have on patient care. The term *ESKAPE* has been coined by this IDSA group to refer to *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species, the etiologic causes of the majority of hospital-acquired infections in the United States that are able to effectively “escape” our antibiotic arsenal and that also mandate discovery of new antimicrobial agents. This article reviews select antibacterial agents and an antifungal agent in late stages of clinical development that appear to have potential for treatment of infections in the ICU.
Critical-care units can be barometers for appropriate antimicrobial use. There, life and death hang on empirical antimicrobial therapy for treatment of infectious diseases. With increasing therapeutic empiricism, triple-drug, broad-spectrum regimens are often necessary, but cannot be continued without fear of the double-edged sword: a life-saving intervention or loss of life following *Clostridium difficile* infection, infection from a resistant organism, nephrotoxicity, cardiac toxicity, and so on. While broadened initial empirical therapy is considered a standard, it must be necessary, dosed according to pharmacokinetic-pharmacodynamic principles, and stopped when no longer needed. Antimicrobial stewardship interventions shepherd these considerations in antimicrobial therapy. With pharmacists and physicians trained in infectious disease and critical care, clear-cut interventions can be focused on beginning or growing a stewardship program, or proposing future studies.

Hospital-acquired infections have profound social, economic, and personal costs to patients in the intensive care unit (ICU). Numerous risk factors, such as poor nutrition and hyperglycemia, directly involve patients. Meanwhile, hand hygiene, environmental cleaning, and appropriate hospital staffing can impact ICU infection rates. A multidirectional approach—including continuing staff education, minimizing risk factors, and implementing guidelines established by national committees—is necessary to decrease infections such as catheter-related bloodstream infections, urinary tract infections, ventilator-associated pneumonia, and *Clostridium difficile*. Infection-control committees can assist in implementing policies. This is an active area of research and we anticipate continued advancements to improve patient care.

*Clostridium difficile* infection (CDI) is becoming more common worldwide. The morbidity and mortality associated with *C difficile* is also increasing at an alarming rate. Critically ill patients are at particularly high risk for CDI because of the prevalence of multiple risk factors in this patient population. Treatment of *C difficile* continues to be a difficult problem in patients with severe or recurrent disease. This article seeks to provide a broad understanding of CDI in the intensive care unit, with special emphasis on risk factor identification, treatment options, and disease prevention.