Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, which is clinical problem often faced by intensive care units (ICU) doctors. Without positive treatment, the incidence and mortality of sepsis are high. As hospital infection control plays an essential role in treating the nosocomial infections in the ICU, and according to the clinical presentation of critically ill patients, the biological characteristics of pathogenic microorganisms and the ICU environment, this article put forward a strategy for the nosocomial infections in the ICU.

From the definition of systemic inflammatory response syndrome categorized as Sepsis 1.0 to the life-threatening organ dysfunction caused by deregulation of infection in Sepsis 3.0, we have generated an improved understanding of serious infection, and greater attention is now devoted to organ dysfunction caused by sepsis. Sequential Organ Failure Assessment (SOFA) score has been emphasized in Sepsis 3.0 to determine organ damage caused by infection. A SOFA score or its acute change ≥2 points indicates that organ dysfunction or exacerbation occurs, and the more severe the infection is, the greater the damage is. As infection is the primary cause of organ damage in critically ill patients, finding and treating infectious lesions is critical for clinicians. The latest SCC guidelines in 2018 even stipulate that the use of antibiotics in the previously suggested 3-h bundles should be updated to 1 h, which emphasizes the importance of early detection and control of infectious lesions and the necessity of early anti-infection treatment. Therefore, we should assess the level of organ function in sepsis or septic shock patients and strive to control and remove the lesions and make early empirical use of targeted antibiotics. Tissue perfusion targeted hemodynamic therapy should be started simultaneously.

With the advancement of diagnostic techniques, studies have shown that ultrasound is better than bedside X-rays for diagnosis of pulmonary infection. A critical ultrasound can replace or support X-ray and CT images in screening or excluding infectious lesions. For example, critical ultrasound can quickly identify infections in the chest (pulmonary infection, infective endocarditis, and pleural effusion), abdominal and pelvic cavity (infection of the biliary tract, gastrointestinal effusion, abdominal effusion, parenchymal organ liquid lesions) and central nervous system (intracranial hypertension). For different characteristics of lung infection present on CT, ultrasound can also show different signs. For example, consolidation and focal exudate are typical pathological changes in lobar pneumonia and bronchopneumonia, while ultrasound shows the manifestation of debris signs and air bronchograms. Interstitial pneumonia, which is diagnosed based on diffuse exudative lesions in bilateral lungs shows B line signs in ultrasonograms. Pneumonia caused by different pathogens shows various image characteristics; therefore, we can easily determine the type of pathogen. For instance, *Pneumococcus, Staphylococcus aureus, Klebsiella pneumoniae*, and *Legionella* cause consolidation changes; mycoplasma, chlamydia, *Pneumocystis Carinii*, and *Cytomegalovirus* cause diffuse interstitial changes. However, it should be noted that hematogenous infections and urinary tract infections do not have definitive ultrasound manifestations. Therefore, we should consider hematogenous infection and urinary tract infections after excluding parenchyma or cavity infection. In addition, retroperito-
neal and sinus infections may be more cryptic and difficult to diagnose.

The essence of nosocomial infections is the opening of the approach and destruction of the barrier. It is common for large catheters (eg, endotracheal intubation, central venous catheters, urinary catheters, gastric tube, and various drainage tubes) to be inserted in critically ill patients due to serious illness and complex treatment. The insertion of a large number of catheters creates a new path for bacterial invasion, destroying the original mucosal and vascular barrier functions of the body, thereby increasing the possibility of nosocomial infection. At the same time, patient trauma, deterioration of the self-defense mechanism (eg, weakened coughing ability and catheter placement) and the impairment of barrier function caused by related treatments (eg, surgery and trauma) can increase the risk of infection. Once bacteria invade the body through any route, blood flow may become a channel for spread of infection, causing infections in multiple parts of the body, resulting in increased infection or delayed healing. Therefore, prevention and control of nosocomial infections are key to the treatment of infection of critically ill patients.

Differentiating between colonization and infection can reduce antibiotic use and drug resistance. The state of colonization is a precursor to infection, which does not require antibiotic intervention; thus, clinical attention must be paid to it. ICU is a complex environment that distributes various pathogens. It is common to detect pathogens in critically ill patients; however, this does not mean that the patients will be infected. If the relationship between colonization and infection cannot be clearly distinguished, it may lead to the abuse of antibiotics and induce resistance to the antibiotic. There are several factors to consider in distinguishing between colonization and infection: (1) qualified smears and culture results; (2) clinical signs and symptoms, such as whether the patient has fever, rapid heart rate, rapid breathing rate, low blood pressure, and high white blood cells; (3) host factors, including basic diseases, immune status, prior antibiotic treatment, and other risk factors related to morbidity, such as mechanical ventilation and time. There should be no preventive use of antibiotics among ICU patients, and reducing the use of antibiotics for colonizing bacteria can decrease the occurrence of bacterial drug resistance. In addition, it is important to pay attention to the cleanliness and care of drainage of infected lesions and the skin, oral cavity and perineum.

The pathogenic characteristics of different pathogens need to be understood. Gram-negative bacteria are widespread in ICUs and are classified as fermenting or non-fermenting according to their ability to use glucose. For light-to-moderate fermentation (non-ESBL Enterobacteriaceae) infections (mostly local infections, including urinary tract infections, liver abscesses, biliary tract infections, peritonitis, and nosocomial infections), a β-lactamase inhibitor may be selected in combination with drug sensitivity results. Intractable ICU fermenters mainly refer to ESBLs and AmpC-producing Enterobacteriaceae, including Escherichia coli, Klebsiella, Proteus mirabilis, and Enterobacter cloacae. Carbapenem antibiotics are the first choice for severe infection with ESBL-producing Enterobacteriaceae. Carbapenem resistant enterobacteriaceae (CRE) is currently the leading cause of high mortality in severe ICU infections. As the fermentation bacterium is primarily derived from the human body, drainage and isolation are important means to control progression and spread in CRE patients. Tigecycline or polymyxin base combined with carbapenem may be suitable for such patients, but more emphasis should be placed on prevention and control of nosocomial infections.[13] Non-fermentative bacteria refers to a group of aerobic or facultative anaerobic, non-sporulant gram-negative bacilli that cannot use glucose or can only use glucose in an oxidized form, primarily including Pseudomonas aeruginosa, Acinetobacter, Alcaligenes, Burkholderia, Flavobacterium, and Stenotrophomonas Malotphila. P. aeruginosa and Acinetobacter exist in the environment and are mostly conditional pathogens. However, in recent years, the proportion of non-fermenting bacteria in the infection of gram-negative bacilli has increased significantly. The reason for this increase is that iatrogenic factors may be the critical factor in infection. The key treatment for this problem involves improving awareness of prevention and control of nosocomial infections and fundamentally addressing the source of patients’ infections and eliminating the possibility of increased infection or progression.

Gram-positive bacteria primarily consist of S. aureus and enterococci. Among the positive bacterial infections, methicillin-resistant S. aureus (MRSA) and vancomycin-resistant enterococci (VRE) have become the main pathogens for intractable ICU infections that lead to poor prognosis. The main risk factors associated with MRSA infection are advanced age, admission to ICU and nursing facilities, mechanical ventilation, catheter placement, parenteral nutrition, renal replacement therapy, surgery, broad-spectrum antibiotics, hormonal applications, and drug injections. Also, a variety of iatrogenic operations and inappropriate use of antibiotics are the other primary reasons for MRSA infection. Therefore, controlling nosocomial infection is the constant principle. Vancomycin is the first choice for MRSA treatment. Enterococcus as one of the normal flora of humans is widely distributed in nature and often inhabits human and animal intestines and the female genital urinary system. In recent years, due to abuse of antibiotics, Enterococcus has gradually become multidrug-resistant, similar to resistance of cephalosporins, fluoroquinolones and aminoglycoside antibiotics. Common risk factors for VRE infection include severe illness; patients staying in ICU wards for a long time; severe immunosuppression, such as with cancer patients; patients undergoing major surgical procedures for chest or abdomen; invasive procedures such as central venous catheters; patients who have VRE colonization; patients who receive broad-spectrum antimicrobial therapy; and those who receive oral and intravenous vancomycin treatment. VRE can be transmitted between patients and can also be carried by clinical staff. In addition, contaminated environments, medical devices, and various appliances can also transmit VRE. As the incidence of VRE infection is increasing year by year, strict compliance within a nosocomial infection control strategy (such as drainage, isolation, and strict aseptic system) is the best treatment for patients.
There are 2 major classes of fungi that can be pathogenic in the clinic, yeasts and molds. The most important and largest species of yeast is *Candida*. *Candida* can be detected throughout the body, among which *Candida albicans* is the most common pathogen, but recent data also suggest that infectious rates of non-Albicans, such as *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida krusei*, are gradually increasing. The sources of *Candida* infection can be divided into endogenous factors (colonization of the gastrointestinal tract and mucous membranes) and exogenous factors (contact transmission and infusion contamination). The ability of *Candida* to colonize multiple sites throughout the body has become a risk factor for candidemia. According to epidemiological investigations, parapsilosis candidemia has ranked second among global non-albicans *Candida* bloodstream infections. The reason is that *C. parapsilosis* is easy to grow in gastrointestinal nutrient solution and can form a biofilm in catheters and other devices. This yeast is easy to spread in the hospital through unclean hands and can make newborns critically ill. Overall, we still emphasize that all objective features of *Candida* are not an excuse for infection; controlling and cutting off exogenous transmission is the fundamental strategy. Another risk factor for the development of candidemia is abdominal surgery. Doctors should consider if there is a *Candida* infection if patients who have received routine antibiotics treatment are becoming frail or their health deteriorates. When patients are suspected of having candidemia, we should also consider whether patients have Candida-like endophthalmitis. Triazoles are the first choice for treatment of *Candida*, and echinocandins are preferred for patients with renal insufficiency. In addition to *Candida* infection, mold infections (especially *Aspergillus*) have been found to be common. *Aspergillus* is spread throughout the environment and is a definitive conditional pathogen. *Aspergillus* can be spread through air, and whether patients have mold infections depends on the host’s immune status, such as persistent neutropenia, advanced HIV infection, primary immunodeficiency, and allogeneic hematopoietic stem cell transplantation and lung transplantation. Voriconazole is the first choice of anti-infection treatment for these patients. At the same time, prevention and control of the nosocomial infections, keeping air clean and proper environmental humidity can maximize the treatment effect.

The definition of immunocompromised patients is patients with definitive immune damage caused by specific hematosis or immune diseases. However, patients whose innate immunity and/or specific immune defense barriers can be destroyed by prolonged bed rest, limited nutritional intake, and traumatic stress infection in the ICU may all have immunodepression. These patients are susceptible to infection with *P. carinii* or *cytomegalovirus* (CMV). *P. carinii* pulmonary (PCP) is an interstitial plasma cell pneumonia caused by Pneumocystis. PCP is a conditional pulmonary infectious pathogen. Because of the use of immunosuppressive agents and cancer chemotherapy, this disease’s incidence has increased in recent years. The disease’s clinical manifestations include: dry cough, shortness of breath, difficulty breathing, high fever, and cyanosis. All of the symptoms are progressively worsened, but the signs are often less severe than the symptoms. CT imaging shows glassiness and a patchy, nodular, and reticulate appearance. Hexamin staining can indicate PCP infection, and positive detection of PCP-DNA is the gold standard for diagnosis. For the treatment of PCP, sulfonamides are the first-line drug, possibly in combination with caspofungin. Manifestations of CMV infection primarily include fever, cough, muscle aches, chest pain, neutropenia, and lymphopenia. Most pulmonary infections are bilateral, and the images show bilateral patches or frosted glass and solid changes. The etiology of the virus is difficult to diagnose. Viral antibodies and DNA should be tested in patients with suspected viral infection. Ganciclovir is an effective drug for viral infections. At present, whether the treatment of hormones and immunoglobulins is necessary requires more clinical and experimental evidence in immunocompromised patients. Non-immune patients are generally more susceptible to such infections as influenza virus and herpes virus, and the disease is more seasonal. In fact, whether the disease is in immunocompromised patients or non-immune patients, the change is our judgment of the cause and the choice of drugs. What remains unchanged is the status and significance of nosocomial infection control and respiratory support management.

A specific type of infection is defined as an atypical pathogen infection, including *mycoplasma, chlamydia*, and *Legionella*, all of which are conditional pathogens. These patients may come from many communities. Patients with *mycoplasma* and *chlamydia* infections are often younger than 60 years old, with minimal underlying disease, the main signs are persistent cough, no sputum, peripheral blood leukocytes of <10 × 10⁹/L. The lesion is most often focused in the upper lung fields and the typical lung imaging is central nodules of lobules, tree-bud signs, ground-glass opacities, thickening of the bronchial wall, and may show substantial changes in progressed disease. Legionnaires’ disease may occur in the elderly population, with extra-pulmonary symptoms. Imaging is glassy with a relatively clear-cut solid consolidation. Mycoplasma pneumoniae has a high resistance rate to macrolides in China, but it is still sensitive to doxycycline, minocycline or quinolones. For *chlamydia* and *Legionella*, quinolones and macrolides are the first choice. As most atypical pathogens are conditional pathogens, the emphasis is on prevention rather than treatment. “Conditional disease” refers to a disease that can happen in a certain situation. However, this situation is often caused by clinical staff who lack awareness of nosocomial infections. Therefore, we must strengthen the awareness of aseptic procedures.

To sum up, we put forward the ICU infection management strategy based on the prevention and control of nosocomial infections. According to the ICU environment, the characteristics of pathogenic bacteria, and the relationship between doctors and patients, we map the distribution pattern of common ICU bacteria. In view of the characteristics of these bacteria, we have proposed hospital management strategies for prevention and control of infections, which mainly include: (1) close the approach, reduce bacterial load; (2) enhance drainage, improve removal of infection foci, and avoid infection persistence;
(3) make isolation, clean environment, avoid cross-dissemination; (4) distinguish infection or colonization, avoid unnecessary use of antibiotics and reduce drug resistance. As for the clinical setting, it is still necessary to combine the biological characteristics of pathogenic bacteria, the ICU environment, and host factors of patients to propose concrete methods. For this reason, our team proposes the BEAT-Hands protocol [Figure 1] to clearly identify infections and colonization of common pathogens in the human body, the environment, the air, and the oropharynx colonization, and to clarify changes in the patient’s infection profile during medical procedures. Only focusing on the prevention and control of nosocomial infections can really reduce the incidence of nosocomial infections.

In brief, we must realize that infections in ICUs are different from traditional infections. The population of infected people, the environment of the ICU, and the biological characteristics of the microorganisms all suggest that treatment of ICU infection lies in a series of measures centered on the prevention and control of nosocomial infections, rather than the excessive use of antibiotics. We focus on environmental and air cleanliness, preventing colonization from turning to pathogenesis, and reducing pathogenic pathways to enhance pathogen clearance. We hope to protect every critically ill patient from the infestation of new pathogens or the exacerbation of existing infections. This is the real essence of ICU infection therapy, and it is the only way to solve future serious infections and drug resistance.

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**Conflicts of interest**

The authors declare that they have no conflicts of interest.

**Author contributions**

Su LX, Wang XT, and Chai WZ conceived, designed, and wrote the manuscript. Pan P participated in revising
the manuscript critically for important intellectual content. Chai WZ and Liu DW reviewed and gave the final approval of the version to be published. All of the authors read and approved the final manuscript.

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