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Mustafa D Younus
 Department of Therapeutic
 Nutrition Techniques, Nimrud
 Technical Institute, Northern
 Technical, University, Mosul,
 Iraq

Maad Abdullah Mansur
 Department of Community
 Health, Kirkuk Technical
 Medical Institute, Northern
 Technical University, Mosul,
 Iraq

Mohammed Hakeem Khalaf
 Department of Pharmacy
 Techniques, Kirkuk Technical
 Medical Institute, Northern
 Technical University, Mosul,
 Iraq

Corresponding Author:
Mustafa D Younus
 Department of Therapeutic
 Nutrition Techniques, Nimrud
 Technical Institute, Northern
 Technical, University, Mosul,
 Iraq

Wound Infections in Critically Burned Patients: Microbiology, Cytokine Response, and Clinical Outcomes

Mustafa D Younus, Maad Abdullah Mansur and Mohammed Hakeem Khalaf

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Abstract

Burn injuries continue to be one of the most serious form of trauma with infection being the most common cause of morbidity and mortality in patients with burns. The loss of the skin barrier, the body's main defence against microbial invasion, coupled with deep immunosuppressive therapy, the normal microbiome is disturbed and a wide range of invasive supportive therapies are used, all of which make the body very susceptible to microbial colonization and invasion. This review thoroughly discusses the microbiology of burn wound infections, the host's cytokine response to burn injury and secondary infection, and the effects of burn wound infections on outcomes. We examine the epidemiology and virulence of the most clinically important pathogens in burn units such as *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and fungal species, as well as the evolution of pro- and anti-inflammatory cytokines that characterise the post-burn immunological environment. The review also includes coverage of the growing problem of multidrug-resistant organisms (MDROs) in burn units, diagnostic studies, treatment options including both system and topical antimicrobials, and infection prevention and control. The cytokine profile is a particular focus both as a prognosis and as a therapeutic target, while clinical outcomes of specific infectious complications such as sepsis, bacteraemia, ventilator-associated pneumonia and fungal superinfection are considered.

Keywords: Burn Wound Infection; *Pseudomonas aeruginosa*; Sepsis; Infection Control; Burn Unit; Clinical Outcomes

1. Introduction

Burns are one of the most difficult clinical problems in current medical practice, both with regard to the degree of tissue damage and to the extensive systemic physiological upset resulting from such damage. Burns are estimated to account for 180,000 deaths globally a year, and most are in low and middle income countries where specialist advice on burn care is unavailable. Infection is the leading cause of death among burnt patients, and the leading cause of death in burn centres around the world in hospitalized cases, accounting for 50-75% of the mortality^[1, 2].

In addition to its mechanical barrier role, the skin is an active immune organ and tightly regulates innate and adaptive responses to microbial challenge. Additionally thermal injury destroys the barrier to colonization, washes away the resident microbiome that interferes with pathogen colonization, and reduces the ability of Langerhans cells and dermal dendritic cells to provide immune surveillance, as well as creating a warm, protein-rich, avascular eschar that serves as a growth matrix for bacterial and fungal colonization^[3, 4].

The post-burn immune response is paradoxical because of its destruction. The early pro-inflammatory phases (involving the secretion of high levels of TNF- α , IL-1 β , IL-6 and IL-8) result in systemic inflammatory response syndrome (SIRS), vascular leak and injury in other organs. This is followed by a prolonged compensatory anti-inflammatory response syndrome (CARS) involving IL-10, IL-4 and TGF- β that affects neutrophils and macrophages, reduces numbers of T lymphocytes and results in acquired immunodeficiency status for weeks to months^[5].

Disruption of barrier function, severe immunodeficiency, and the intensive care environment with its central venous lines, urinary lines, mechanical ventilation and long-term antibiotic use, facilitate the acquisition of infection with multidrug resistant organisms. In the past few decades, the epidemiology of burn wound infections has changed significantly, with gram-negative organisms and MDR pathogens increasing in prevalence in modern times compared to gram-positive organisms, which were more prevalent in the early post-burn era [6, 7].

It aims to condense existing research related to the microbiology, immunopathology, diagnosis, treatment, and prevention of burn wound infections by summarizing recent literature published in the last 5 years (2020-2025) that would have clinical relevance to those caring for critically burned patients [8].

2. Epidemiology and Microbiology of Burn Wound Infections

2.1 Incidence and Temporal Trajectory of Infection

Burn wounds are sterile at the time of injury, but they progress in predictable sequence of colonization over the following days. Surface colonization by gram-positive organisms (mainly *Staphylococcus aureus* and coagulase-negative staphylococci) of the wound eschar occurs within 24–48 hours, primarily from the patient's own skin flora and healthcare workers. Gram-negative organisms, such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli*, become present on days 3–5, usually via translocation from the gastrointestinal tract of the patient or from an environment source in the burn unit. When patients survive for more than 10–14 days, fungal colonization, mostly by *Candida* spp, is more common, especially when broad-spectrum antibiotic therapy is used [9, 10]. Histological criteria for invasive wound infection vs surface colonization

are: ≥ 105 cfus/g and invasion beyond viable tissue–eschar junction. This is the point at which failure of the skin graft occurs, and local signs of wound infection start to appear (Exudates increase, the wound turns red or blue, surrounding skin becomes red and there is oedema), as well as a risk of haematogenous dissemination leading to bacteraemia and sepsis [10].

2.2 The ESKAPE Pathogens in Burn Units

The ESKAPE pathogens (*Enterococcus faecium*, *S. aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter* spp.) are all associated with a high prevalence of nosocomial infections in the burn unit, and are known for their high virulence and multi-drug resistance. *P. aeruginosa* is the most common gram-negative pathogen in burn units around the world, with 25–40% of cultures from patients with a burn injury in an ICU setting being positive for this organism. It is a highly adaptable organism, a result of its ability to acquire resistance, its ability to form biofilms and its quorum sensing networks. [7, 11]

Most series report that *Staphylococcus aureus*/burn infection, including MRSA, accounts for 30–45% of gram-positive organisms isolated from burn wound infections. The prevalence of MRSA in burn units varies from 20–60% of all *S. aureus* isolates, according to geographic location and burn unit control measures. MRSA is a very virulent burn pathogen due to its combination of potent virulence factors (adhesins, toxins, biofilm) and broad beta-lactam resistance. With its capacity to survive for many weeks on environmental surfaces and its high rates of carbapenem resistance, *A. baumannii* has been responsible for epidemic outbreaks in burn units worldwide, especially in the context of conflicts and in ICUs with poor infection control [11, 12].

Table 1; Common microbial pathogens in burn wound infections: type, prevalence, key virulence factors, and resistance profile [10, 11, 13–17]

Pathogen	Type	Prevalence	Key Virulence Factors	Resistance Profile
Gram-Positive Bacteria				
<i>Staphylococcus aureus</i> (MRSA)	Gram+	30–45% burn units	PVL, TSST-1, MSCRAMMs, alpha-hemolysin, biofilm (icaA/icaD)	Methicillin, fluoroquinolones, macrolides
<i>Streptococcus pyogenes</i>	Gram+	5–12%	Streptolysin, hyaluronidase, M-protein, SpeA/SpeB toxins	Penicillin-susceptible; macrolide resistance rising
<i>Enterococcus faecalis</i> / <i>faecium</i> (VRE)	Gram+	4–9% late infections	Cytolysin, aggregation substance, surface adhesins	Vancomycin (vanA/vanB); ampicillin resistant (faecium)
Gram-Negative Bacteria				
<i>Pseudomonas aeruginosa</i>	Gram–	25–40% ICU burns	T3SS (ExoU/ExoS), QS biofilm, pyoverdine, elastase (lasB)	XDR common; MexAB-OprM efflux, NDM, VIM
<i>Klebsiella pneumoniae</i>	Gram–	10–20%	Hypermucoviscous capsule, siderophores (aerobactin), LPS	ESBL, KPC, NDM carbapenemases; colistin resistance
<i>Acinetobacter baumannii</i>	Gram–	8–18% ICU	OmpA, biofilm, outer membrane vesicles	CRAB; OXA-23/24/51; pan-resistant strains documented
<i>Escherichia coli</i>	Gram–	6–14%	Type III secretion, enterotoxins, iron acquisition	ESBL (CTX-M), fluoroquinolone resistance
Fungal Pathogens				
<i>Candida albicans</i> / <i>C. tropicalis</i>	Fungal	5–15% severe burns	Hyphae transition, Saps 1–10, biofilm, Als adhesins	Fluconazole resistance in <i>C. tropicalis</i> / <i>C. glabrata</i>
<i>Aspergillus fumigatus</i>	Fungal	2–8% ICU/steroid	Gliotoxin, conidial melanin, Siderophores, cell wall β -glucan	Azole resistance (cyp51A); voriconazole MIC creep

3. Virulence Mechanisms of Key Burn Pathogens

3.1 *Staphylococcus aureus*

S. aureus has an extraordinary armamentarium of virulence determinants, that collectively enable it to colonize, invade, evade immunity and resist antimicrobial therapy.

MSCRAMMs are surface-expressed proteins that include fibronectin-binding proteins (FnBPA, FnBPB), clumping factors A and B (ClfA, ClfB), and collagen-binding protein (CNA), which all contribute to the adhesion to exposed extracellular matrix components in the burn wound bed. The

ica gene locus that encodes PIA/PNAG is responsible for the formation of biofilms, 100–1000-fold more resistant to antibiotics than planktonic cells, that can be grown on wound surfaces, eschar and wound dressings by *S. aureus* [13, 14].

A set of toxins is of special importance in burn patients. Alpha-hemolysin (Hla) is an enzyme that forms heptameric pores in the hosts cell membranes, leading to the lysis of erythrocytes and leukocytes, and to direct tissue necrosis in the wound. PVL is a bicomponent leukocidin that is capable of lysing neutrophils and macrophages that are linked to more severe and rapidly progressive cellulitis and wound infections. In addition, cytokines are set free in response to massive non-specific activation of T-cells by superantigens, such as toxic shock syndrome toxin-1 (TSST-1) and staphylococcal enterotoxin A–E, which further contributes to the cytokine storm and the already dysregulated inflammatory state of the burned patient [13, 15].

3.2 *Pseudomonas aeruginosa*

Three integrated systems including the type III secretion system (T3SS), quorum sensing (QS) regulatory networks, and biofilm formation are responsible for orchestration of *P. aeruginosa* virulence in burn wound. The T3SS injects effector proteins directly into host cell cytoplasm: *ExoU*, a phospholipase A2, causes rapid membrane lysis; *ExoS* and *ExoT* disrupt actin cytoskeleton and phagocytic function; *ExoY* raises intracellular cAMP, disrupting endothelial barrier integrity. *ExoU*-producing strains are associated with particularly high mortality and should prompt consideration of aggressive combined antimicrobial therapy [16, 17].

The las/rhl/pqs quorum sensing circuits coordinately regulate production of elastase (*LasB*), alkaline protease (*AprA*), rhamnolipids, hydrogen cyanide, and pyocyanin—a redox-active phenazine that directly suppresses neutrophil oxidative killing. Iron acquisition through the pyoverdine siderophore, which also signals exotoxin A (*ExoA*) expression, provides the growth advantage in the iron-limited wound environment. Alginate overproduction creates a mucoid biofilm phenotype that is particularly resistant to both host immune clearance and antibiotic penetration, and is associated with transition from acute to chronic wound infection [18, 19].

3.3 Fungal Pathogens in Burn Wounds

Invasive fungal infections in burn patients are associated with mortality rates of 40–75% and represent an increasingly important clinical challenge as improved resuscitation and antibiotic therapy enable longer survival of severely burned patients. *Candida albicans* exploits the immunosuppressed burn patient through its capacity for yeast-to-hypha morphological switching, enabling active tissue penetration. Secreted aspartyl proteases (Saps 1–10) degrade structural proteins of the wound matrix; phospholipases disrupt cell membranes; and biofilm formation on central venous catheters and wound surfaces confers antifungal resistance [20, 21].

Aspergillus fumigatus wound infection, while less common than *Candida*, carries extreme mortality and occurs predominantly in patients receiving systemic corticosteroids, those with large total body surface area (TBSA) burns, and in the context of COVID-19-associated immunosuppression. Gliotoxin-mediated suppression of neutrophil oxidative burst and induction of macrophage apoptosis, combined

with the melanin-coated conidial surface that resists phagocytic killing, enables *A. fumigatus* to establish invasive wound infection despite apparently intact neutrophil counts [20].

4. Cytokine Response in Burned Patients

4.1 The Biphasic Inflammatory Response

The systemic inflammatory response to burn injury follows a characteristic biphasic pattern that profoundly shapes both the host's susceptibility to infection and the severity of infectious complications when they occur. Phase 1—the pro-inflammatory surge—begins immediately post-burn and is driven by release of damage-associated molecular patterns (DAMPs) including heat shock proteins, HMGB1, and DNA fragments from thermally destroyed cells. These DAMPs activate pattern recognition receptors on resident macrophages, triggering NF-κB-driven production of TNF-α, IL-1β, IL-6, and IL-8 within hours of injury [5, 22].

Burn size, expressed as percentage of total body surface area (%TBSA), is the primary determinant of cytokine response magnitude. Burns involving >20% TBSA reliably produce systemic pro-inflammatory cytokine elevations; burns above 40% TBSA trigger a cytokine storm of extraordinary magnitude, with IL-6 levels 100–1000-fold above normal, that drives the systemic inflammatory response syndrome, capillary leak, acute lung injury, and remote organ dysfunction. The liver responds to this cytokine signal with a massive acute-phase response—producing CRP, fibrinogen, complement components, and hepcidin—while simultaneously reducing production of protective proteins including albumin and transferrin [23, 24].

4.2 Individual Cytokines and Their Clinical Significance

IL-6 has emerged as the single most valuable cytokine biomarker in burn care. Its peak level within the first 24–48 hours post-burn correlates with burn size, predicts the subsequent development of sepsis, and identifies patients at highest risk of multi-organ failure and death. A meta-analysis of cytokine profiling in burn patients confirmed that IL-6 levels at hospital admission provide prognostic information superior to traditional scoring systems alone. Procalcitonin (PCT), while not a cytokine per se, is an acute-phase reactant whose burn-specific kinetics—elevation parallels inflammatory burden but more specifically indicates bacterial infection rather than burn-induced sterile inflammation—make it a valuable adjunctive sepsis biomarker when combined with clinical assessment and microbiological data [24, 25].

Compensatory upregulation of IL-10, IL-4, IL-13 and TGF-β leads to a transition to the anti-inflammatory stage, which begins 3–7 days after burns. This stage of immunity reduces inflammation to prevent it from running out of control, but it also makes the person most vulnerable to secondary infections. IL-10—produced by monocytes, regulatory T cells, and M2-polarised macrophages—suppresses TNF-α, IL-1β, and IL-12 production, impairs neutrophil oxidative burst, and reduces CD4+ and CD8+ T-cell function. The extent and duration of this IL-10-dominated immunosuppressive phase predict the risk of nosocomial infection, with studies demonstrating that persistently elevated IL-10 at day 7 post-burn independently predicts subsequent bacteraemia and pneumonia [26].

4.3 Cytokines as Therapeutic Targets

Recognition of the cytokine-mediated immunosuppressive phase as a modifiable target has driven investigation of immunostimulatory interventions in burn care. Granulocyte colony-stimulating factor (G-CSF) administration, by restoring neutrophil production and enhancing oxidative burst, has demonstrated benefit in reducing infectious complications in selected trials. Interferon-gamma (IFN- γ) supplementation, aimed at reversing M2 macrophage polarization and restoring TH1 immune function, has shown promise in small studies. Conversely, anti-TNF- α strategies, while effective in reducing SIRS manifestations, may paradoxically increase susceptibility to secondary infection and have not achieved clinical adoption in burn care [27, 28].

5. Clinical Outcomes: Sepsis, Bacteraemia, and Organ Failure

5.1 Defining Sepsis in Burns

The diagnosis of sepsis in burned patients is confounded by the fact that SIRS criteria—fever, tachycardia, tachypnoea, and leukocytosis—are virtually universal in the post-burn period as a consequence of the injury itself, irrespective of infection. The American Burn Association (ABA) has developed burn-specific sepsis criteria that incorporate TBSA-adjusted temperature thresholds, heart rate and respiratory rate parameters, and require documentation of a probable or confirmed infectious source, providing more clinically meaningful diagnostic criteria than generic Sepsis-3 definitions in this population [29, 30].

Bacteraemia—the haematogenous dissemination of wound pathogens into the bloodstream—occurs in 5–28% of hospitalized burn patients and is associated with a 2–5-fold increase in mortality compared to burn patients without bacteraemia. *S. aureus* bacteraemia from burn wounds may seed distant sites including heart valves (infective endocarditis), joints (septic arthritis), and vertebrae (osteomyelitis), creating a catalogue of metastatic infectious complications that further complicate clinical management. *P. aeruginosa* bacteraemia in burn patients is associated with particularly high mortality (30–70% in reported series), reflecting both the severity of underlying disease in affected patients and the inherent virulence of systemic pseudomonal infection [30, 31].

5.2 Respiratory Infections

About 30% of burns that require hospitalization are complicated by inhalation injury, which significantly increases the severity of the burn. In addition to the primary thermal and chemical damage to the tracheobronchial tree, inhalation injury can lead to a marked impairment of mucociliary clearance, disruption of airway epithelial barrier, and require mechanical ventilation in most patients with the injury. Ventilator-associated pneumonia (VAP) is common in burn patients who are mechanically ventilated, happening in 20–50% of them, a much higher prevalence than is seen in other patients in an intensive care unit (ICU), and the most common pathogens identified are *P. aeruginosa* and *S. aureus* [32, 33].

VAP is linked to an increment of 7–14 days of ICU stay, an increment of ventilator days, and 15–30% attributable mortality in burn patients. Early onset VAPs (those that occur within 5 days of intubation) are generally dominated by community-acquired organisms such as *S. aureus* and *S. pneumoniae*, whilst late onset VAPs are mainly comprised

of MDR gram-negative organisms such as *P. aeruginosa*, *A. baumannii* and ESBL-producing Enterobacterales, which are associated with HAP under antibiotic selective pressure [33].

5.3 Multi-Organ Dysfunction and Mortality

There is a bidirectional association between burn-induced dysfunction of various organs and infection, with severe infection leading to cytokine-mediated organ dysfunction and organ dysfunction making it harder to maintain immune function and deliver therapeutic agents, thereby allowing the infectious process to escalate. In severely burned patients, there is a risk of renal failure, which affects 15–40%, and may require dose adjustment of antibiotics, especially aminoglycosides and vancomycin. Loss of function of the liver leads to decreased production of complement and opsonin. Failure of the gastrointestinal mucosal barrier allows enteric flora, such as *Candida* species, to enter the portal and systemic circulation [34, 35].

Mortality prediction in burned patients has evolved from simple burn size and age calculations (Baux score) to integrated models incorporating infection burden, organ failure scores, inhalation injury, and inflammatory biomarkers. The Revised Baux Score, incorporating inhalation injury, and the revised Belgian Outcome in Burn Injury (BOBI) model remain widely used. Infection—particularly gram-negative bacteraemia, *P. aeruginosa* wound infection, and invasive fungal disease—consistently emerges as the most powerful modifiable predictor of mortality in contemporary burn outcome analyses, underscoring the centrality of infection prevention and management in burn care [36, 37].

6. Diagnosis of Burn Wound Infections

6.1 Clinical and Microbiological Criteria

The clinical diagnosis of burn wound infection requires the integration of local wound findings, systemic inflammatory markers, and microbiological data. Local signs suggestive of infection include conversion of partial-thickness to full-thickness injury (indicative of microbial proteolytic enzyme activity), change in wound colour (green discoloration suggesting *P. aeruginosa*; black discoloration suggesting fungal invasion), increased exudate, malodour, surrounding cellulitis, and oedema. However, these signs may be subtle or absent in immunocompromised patients, and systemic signs of infection—fever, tachycardia, rising inflammatory markers—must be actively sought [38].

Quantitative wound biopsy culture—the diagnostic gold standard—involves tissue sampling of 0.5–1.0 g from the wound bed and culture with colony count determination. The threshold of 10^5 CFU/g has been shown to be reasonably sensitive and specific for predicting graft failure and invasive infection. Surface swab culture is clinically more feasible and useful for detecting colonization rather than invasion, but should be interpreted with care, but can be used to monitor resistance trends and patterns in the unit and for empirical antibiotic selection [39, 40].

6.2 Molecular and Advanced Diagnostics

The rapid identification of bacterial and fungal pathogens and key resistance genes of these pathogens in 2–6 hours with multiplex PCR panels directly on wound swabs or tissue biopsies significantly improves the start of targeted therapy. MALDI-TOF mass spectrometry provides

definitive organism identification from positive culture plates within minutes, replacing biochemical identification methods. Next-generation sequencing (NGS)-based metagenomics, while not yet standard of care in most centres, can identify polymicrobial infections with unusual organisms that escape conventional culture detection, and is increasingly applied in outbreak investigations and cases of refractory infection^[33].

Inflammatory biomarkers guide antibiotic initiation and duration. Serum procalcitonin (PCT) has been validated in burn populations as a biomarker for discriminating infection from sterile SIRS, with PCT-guided antibiotic de-escalation protocols demonstrating reductions in antibiotic exposure without worsening clinical outcomes. C-reactive protein and ferritin kinetics, serial lactate measurement, and presepsin are additional biomarkers with supporting evidence in burn sepsis. For fungal infections, (1→3)- β -D-glucan and, in selected patients, serum galactomannan provide non-culture diagnostic support^[32, 34].

7. Treatment of Burn Wound Infections

7.1 Topical Antimicrobial Therapy

Topical antimicrobial agents are the cornerstone of local burn wound management, reducing bacterial and fungal burden, preventing wound desiccation, and facilitating wound bed preparation for grafting. Silver sulfadiazine (SSD, 1%), the historical gold standard, provides broad-spectrum activity against gram-positive and gram-negative organisms including *P. aeruginosa* and *Candida* species, though resistance to silver-based compounds is increasingly documented, particularly in *P. aeruginosa* and *A. baumannii* clinical isolates. Mafenide acetate has superior eschar penetration and retains activity in avascular devitalized tissue, making it particularly useful for deep full-thickness burns and electrical injuries, though its carbonic anhydrase inhibition may cause metabolic acidosis with prolonged use^[4].

The nanocrystalline silver dressings (Acticoat, Mepilex Ag) are being used extensively because of the continued release of silver ions, less frequent dressing changes and enhanced patient comfort over topical creams. Honey-impregnated dressings (Medihoney) have antimicrobial properties due to the generation of hydrogen peroxide, the osmotic effect of the honey and the low pH, which has been shown to have good antimicrobial activity in partial thickness burn care. NPWT has been used after surgical debridement and grafting to lower bacterial levels, enhance granulation tissue formation and provide mechanical support for grafts, and there is an increasing body of evidence to support its use in the management of complex burn wounds^[4].

7.2 Systemic Antimicrobial Therapy

Burn patients have special challenges with systemic antibiotic therapy. Major burns cause a hypermetabolic state, which enhances cardiac output, glomerular filtration rate and hepatic clearance, resulting in a large volume of distribution and clearance of hydrophilic antibiotics, such as beta-lactams, vancomycin and aminoglycosides. In major burn patients, standard dose and timing schedules based on non-burn populations consistently result in subtherapeutic levels of serum and tissue drug levels, relevant to efficacy and a risk of emergence of resistance. Extended infusion (e.g., time above the MIC) strategies are indicated for beta-

lactams and required for vancomycin, and therapeutic drug monitoring (TDM) is required for vancomycin and strongly recommended for aminoglycosides^[35].

Empirical antibiotic choice should be based on the local resistance profile of the burn unit, not an antibiogram from the hospital in general. For suspected MRSA wound infections, vancomycin with AUC/MIC-guided monitoring remains first-line; daptomycin and linezolid are alternatives. For MDR gram-negative infections, novel combinations including ceftolozane-tazobactam (XDR *P. aeruginosa*), ceftazidime-avibactam (KPC/OXA-48-producing organisms), and aztreonam-avibactam (NDM-producing strains) have transformed therapeutic options. Duration of antibiotic therapy should be guided by clinical response and PCT kinetics, with de-escalation to narrow-spectrum agents as soon as culture and sensitivity data permit^[36, 37].

8. Infection Prevention and Control in Burn Units

8.1 Standard and Transmission-Based Precautions

The prevention of healthcare-associated infections in burn units requires meticulous application of both standard precautions—applicable to all patient care interactions—and transmission-based precautions targeted at specific MDR organisms. Hand hygiene with alcohol-based hand rub or soap and water before and after every patient contact remains the single most effective infection control measure, yet compliance in burn units is consistently below the recommended 80% threshold, partly due to the frequent wound care interactions and gloved procedures required in burn nursing^[38].

Active surveillance cultures—nasopharyngeal, wound, and perianal swabs—enable early identification of MRSA, ESBL/CRE, *C. auris*, and *A. baumannii* colonization before clinical infection becomes manifest, enabling preemptive isolation and targeted decolonization. Outbreak management in burn units requires particularly aggressive responses including environmental sampling, whole-genome sequencing of outbreak strains to confirm transmission chains, enhanced cleaning protocols, and in some cases temporary unit closure, as illustrated by documented *A. baumannii* and *C. auris* outbreaks in burn centres^[39].

8.2 Antimicrobial Stewardship in Burn Care

Antimicrobial stewardship programmes (ASPs) in burn units must address the unique clinical environment of these patients: the extreme physiological alterations that complicate pharmacokinetics; the high rates of colonization with MDR organisms; the prolonged hospitalizations that create sustained antibiotic exposure; and the legitimate clinical uncertainty about infection diagnosis given the confounding effects of burn-induced SIRS on traditional infection markers^[40].

Prospective audit and feedback by an ASP team with burn-specific expertise is the most evidence-based stewardship intervention. PCT-guided protocols for antibiotic de-escalation and duration determination have been validated in burns and reduce antibiotic exposure by 20–30% without worsening outcomes. Anti-fungal stewardship—distinguishing *Candida* colonization from invasive infection and guiding appropriate antifungal initiation, de-escalation, and duration—is equally critical in this high-risk population^[40].

Table 2: Evidence-based infection prevention and control measures in burn units: targeted pathogens, evidence level, and key implementation details. [39, 40]

IPC Measure	Target Pathogen(s)	Evidence Level	Key Details
Hand hygiene (ABHR / soap)	All pathogens	WHO Grade A	Before/after every patient contact; before donning and after removing gloves; compliance audit mandatory in burn units
Contact precautions (gown + gloves)	MRSA, VRE, ESBL-GNB, <i>C. auris</i> , <i>A. baumannii</i>	Strong (RCTs)	Single-room isolation where possible; dedicated equipment; cohort nursing during outbreaks
Active surveillance cultures	MRSA, ESBL/CRE, VRE, <i>C. auris</i>	Strong	Admission nasal/wound swabs for MRSA; rectal swabs for ESBL/CRE in high-risk burn patients; weekly during stay
Wound dressing protocols	All wound pathogens	Strong	Sterile technique; silver-containing dressings (silver sulfadiazine, Mepilex Ag) reduce bacterial burden; frequency guided by wound status
Topical antimicrobial prophylaxis	Gram-positives, gram-negatives, <i>Candida</i>	Strong	Silver sulfadiazine (1%), mafenide acetate, or nanocrystalline silver; choice guided by local resistance patterns
Environmental decontamination	<i>A. baumannii</i> , <i>C. auris</i> , <i>P. aeruginosa</i>	Moderate	Daily cleaning with sporicidal/bactericidal agents; UV-C robot disinfection on terminal cleaning; equipment decontamination between patients
Antimicrobial stewardship (ASP)	All MDR organisms	Strong (meta-analyses)	Culture before antibiotics; de-escalation at 48–72 h; biomarker-guided (PCT) duration; antifungal stewardship essential
VAP prevention bundle	<i>P. aeruginosa</i> , <i>Klebsiella</i> , <i>S. aureus</i>	Strong	HOB elevation 30–45°; oral decontamination (CHX); subglottic suctioning; daily SAT/SBT; circuit management

9. Special Topics

9.1 Multidrug Resistance and the AMR Crisis in Burn Units

Burn units are a special place where the world's antimicrobial resistance crisis meets high acuity critical care medicine. Longer hospitalizations, increased use of antibiotics, more frequent invasive procedures, and more immunocompromised patients provide ideal conditions for the selection, amplification and transmission of MDR organisms in the hospital setting. XDR *P. aeruginosa* and CRA *A. baumannii* have been associated with devastating mortality in burn centres and, with its intrinsic fluconazole resistance, environmental survival and easy nosocomial transmission, *Candida auris* has emerged as a new threat to burn centres [7].

The introduction of whole genome sequencing (WGS) of MDR outbreak strains has revolutionized burn unit epidemiology, with the ability to definitively resolve the transmission chain, identify specific environmental reservoirs (ventilator circuits, sink drains, wound dressing trolleys), and inform targeted burn unit decontamination interventions. Plasmid profiling alongside WGS of *P. aeruginosa* and *K. pneumoniae* isolates from burn patients has demonstrated the horizontal transfer of carbapenemase genes between species within individual burn units, thus supporting the need for the prevention of not only patient-to-patient transmission, but transmission of resistance genes between species in the burn environment [29].

9.2 Wound Care Innovations

In addition to the more conventional topical antimicrobials, there have been a number of novel wound care strategies that are promising in minimizing wound infection rates and improving wound healing in burn patients. Bacteriophage therapy, the use of the lytic phages that target specific bacterial species, has shown promise as a therapy of last resort for refractory XDR *P. aeruginosa* and *S. aureus* burn wound infections and could be an effective treatment

strategy in the future, while preserving commensal microbiota, which are not targeted [41].

New bioengineered skin substitutes containing antimicrobial peptides, antibiotic loaded nanoparticles, and growth factors are making progress in the clinical trials. Anti-virulence approaches that inhibit virulence factor expression and/or the ability of *P. aeruginosa* to form biofilms (such as inhibitors of *las* and *rhl*) do not necessarily exert direct killing pressure and may be more effective at reducing virulence than conventional antibiotics [42].

10. Conclusions

Thus, wound infections with MDR organisms are the major cause of morbidity and mortality in severely burned patients and result from a combination of disrupted skin barrier function, wide-ranging and sustained immunosuppression, and the high risk of acquiring MDR organisms within the intensive care unit (ICU) setting. The microbiology of burn infections has significantly changed over the years, with MDR gram-negative infections, especially those caused by *P. aeruginosa*, *K. pneumoniae* and *A. baumannii*, becoming more prevalent than MRSA infections and the increasing incidence of fungal infection [1, 6].

The cytokine response to burn injury is a double edged sword: the acute phase of burn injury is pro-inflammatory, consisting of TNF- α , IL-1 β , IL-6 and IL-8 and responsible for the SIRS and organ dysfunction characteristic of major burns; the anti-inflammatory phase is anti-inflammatory, dominated by IL-10, and produces the immunological window for secondary infections to establish and flourish. Cytokine profiling including serial IL-6 and PCT measurement has proved to be a useful prognostic and therapeutic guidance tool which should be incorporated into burn unit clinical protocols [22, 25].

A multi-pronged approach with careful microbiological diagnosis prior to antibiotic initiation, pharmacokinetically informed antibiotic dosing with TDM, evidence-based topical wound care management, early skin grafting, burn-

adapted antimicrobial stewardship, and careful infection prevention and control measures is required to optimize clinical outcomes. There is a need for investments in new development strategies such as Phage therapy, Anti-virulence agents and Bioengineered dressings, as well as stewardship efforts to preserve current antimicrobials, for better results in this most vulnerable population^[35, 40, 41].

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