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# PERSONALIZED MANAGEMENT OF SEPSIS

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Sepsis is a heterogeneous syndrome characterized by life-threatening organ dysfunction resulting from a dysregulated host response to infection. Although clinical definitions and severity scores facilitate recognition and prognostic assessment, they do not adequately capture the biological diversity underlying disease trajectories. Personalized management therefore requires integrating clinical characteristics with immune profiling, molecular endotypes, and repeated assessment to identify patients most likely to benefit from specific interventions.

The host response to sepsis involves interactions between inflammation, immune suppression, and metabolic dysfunction. These processes may coexist and evolve over time, leading to recovery, early multiorgan failure, or chronic critical illness with persistent inflammation, immunosuppression, and catabolism. Mechanisms contributing to immune dysfunction include lymphocyte apoptosis, impaired neutrophil activity, expansion of regulatory T cells and myeloid-derived suppressor cells, reduced interferon-gamma production, and decreased monocyte human leukocyte antigen-DR expression. Such abnormalities increase vulnerability to secondary bacterial and fungal infections and viral reactivation, emphasizing the importance of evaluating immune status throughout the disease course.

Clinical phenotyping and molecular endotyping offer complementary approaches to patient stratification. Transcriptomic studies have identified subgroups characterized by immune competence, immunosuppression, acute inflammation, or immunometabolic disturbances, with differing outcomes. Prognostic enrichment identifies patients at increased risk of deterioration or death, whereas predictive enrichment seeks to identify subgroups more likely to respond to a particular treatment. Biomarkers, including ferritin, lymphocyte counts, inflammatory mediators, and monocyte human leukocyte antigen-DR expression, may support this distinction. However, dynamic endotype trajectories indicate that a single measurement may be insufficient for treatment selection.

Emerging therapeutic strategies aim to match immunomodulation to the dominant biological abnormality. Anakinra has been investigated in patients with macrophage activation-like

features, while interferon-gamma has been evaluated in those with sepsis-associated immunosuppression. Similarly, extracorporeal endotoxin removal may offer benefits in selected biological subgroups, but subgroup findings require cautious interpretation and prospective confirmation.

Personalized sepsis management should combine established supportive and infection-directed care with biologically informed stratification and longitudinal reassessment. Translation into practice requires accessible, validated biomarkers, standardized endotype definitions, large clinical and molecular registries, and adequately designed interventional trials. Ultimately, aligning treatment with the patient's evolving immune phenotype may improve therapeutic precision, reduce ineffective interventions, and address both acute organ dysfunction and the persistent consequences of sepsis among survivors.

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