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Severe trauma incites physiologic, immunologic, and metabolic changes that predisposes the injured patient to organ malfunction, systemic inflammatory response syndrome, and an increased risk of infection. Blood loss results in autonomic-mediated cardiovascular responses that increase heart rate, systemic vascular resistance, and maintain arterial blood pressure to vital organs at the expense of blood flow to the gut and skeletal muscle. Central and local factors produce regional redistribution of blood flow among and within tissues, often leading to tissue hypoperfusion and impaired oxygen delivery.

Severe trauma leads to activation of the immune system and the development of both the systemic inflammatory response syndrome (SIRS) and the counter anti-inflamatory response syndrome (CARS). After injury, patients inflammatory system is primed and vulnerable to a secondary insult. A secondary insult or "Second-hit", such as a prolonged operative procedure, results in an amplified systemic inflammatory response syndrome, culminating in multiple system organ failure.