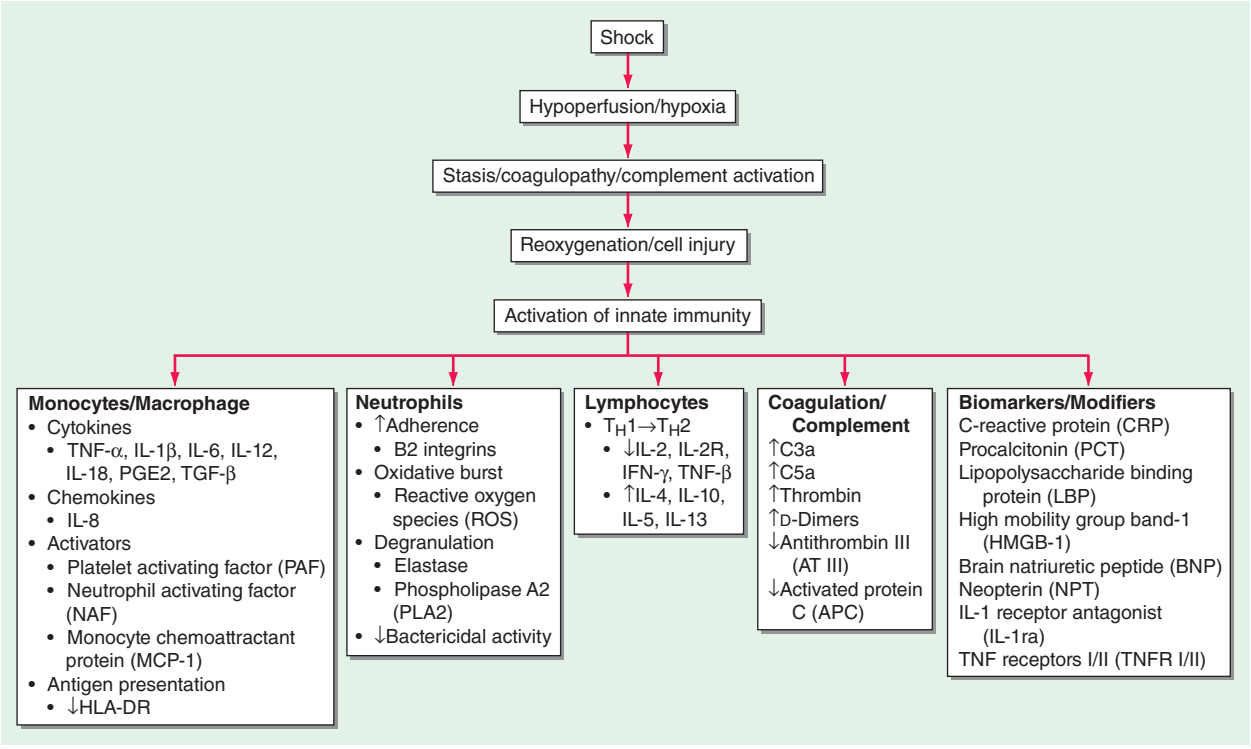

FIGURE 324-2 A schematic of the host immunoinflammatory response to shock. IFN, interferon; IL, interleukin; PG, prostaglandin; TGF, tumor growth factor; TNF, tumor necrosis factor.

hypotension, lactic acidosis, and respiratory failure. Interleukin 1β (IL-1β), originally defined as "endogenous pyrogen" and produced by tissue-fixed macrophages, is critical to the inflammatory response. Both are significantly elevated immediately following trauma and shock. IL-6, also produced predominantly by the macrophage, has a slightly delayed peak response but is the best single predictor of prolonged recovery and development of MOF following shock. Chemokines such as IL-8 are potent neutrophil chemoattractants and activators that upregulate adhesion molecules on the neutrophil to enhance aggregation, adherence, and damage to the vascular endothelium. While the endothelium normally produces low levels of NO, the inflammatory response stimulates the inducible isoform of NO synthase (iNOS), which is overexpressed and produces toxic nitroxyl- and oxygen-derived free radicals that contribute to the hyperdynamic cardiovascular response and tissue injury in sepsis.

Multiple inflammatory cells, including neutrophils, macrophages, and platelets, are major contributors to inflammation-induced injury. Margination of activated neutrophils in the microcirculation is a common pathologic finding in shock, causing secondary injury due to the release of toxic oxygen radicals, lipases (primarily PLA_2), and proteases. Release of high levels of reactive oxygen intermediates/species (ROI/ROS) rapidly consumes endogenous essential antioxidants and generates diffuse oxygen radical damage. Newer efforts to control ischemia/reperfusion injury include treatment with carbon monoxide, hydrogen sulfide, or other agents to reduce oxidant stress. Tissue-fixed macrophages produce virtually all major mediators of the inflammatory response and orchestrate the progression and duration of the inflammatory response. A major source of activation of the monocyte/macrophage is through the highly conserved membrane toll-like receptors (TLRs) that recognize DAMPs, such as HMGB-1, and pathogen-associated molecular patterns (PAMPs), such as endotoxins released following tissue injury, and by pathogenic microbial organisms, respectively. TLRs also appear important in the chronic inflammation seen in Crohn's disease, ulcerative colitis, and transplant rejection. The variability in individual responses is a genetic predisposition that, in part, is due to variants in genetic sequences affecting the function and production of various inflammatory mediators.

TREATMENT SHOCK

MONITORING

Patients in shock require care in an intensive care unit (ICU). Careful and continuous assessment of the physiologic status is necessary. Arterial pressure through an indwelling line, pulse, and respiratory rate should be monitored continuously; a Foley catheter should be inserted to follow urine flow; and mental status should be assessed frequently. Sedated patients should be allowed to awaken ("drug holiday") daily to assess their neurologic status and to shorten duration of ventilator support.

There is ongoing debate as to the indications for using the flow-directed pulmonary artery catheter (PAC; Swan-Ganz catheter) in the ICU. A recent Cochrane analysis showed that the use of a PAC did not alter mortality, length of stay, or cost for adult ICU patients. Most patients in the ICU can be safely managed without the use of a PAC. However, in shock with significant ongoing blood loss, fluid shifts, and underlying cardiac dysfunction, a PAC may be useful. The PAC is placed percutaneously via the subclavian or jugular vein through the central venous circulation and right heart into the pulmonary artery. There are ports both proximal in the right atrium and distal in the pulmonary artery to provide access for infusions and for cardiac output measurements. Right atrial and pulmonary artery pressures (PAPs) are measured, and the pulmonary capillary wedge pressure (PCWP) serves as an approximation of the left atrial pressure. Normal hemodynamic parameters and their derivation are summarized in **Table 272-2** and **Table 324-2**.

Cardiac output is determined by the thermodilution technique, and high-resolution thermistors can also be used to determine right ventricular end-diastolic volume to monitor further the response of the right heart to fluid resuscitation. A PAC with an oximeter port offers the additional advantage of online monitoring of the mixed venous oxygen saturation, an important index of overall tissue perfusion. Systemic and pulmonary vascular resistances are calculated as the ratio of the pressure drop across these vascular beds to the cardiac output **(Chap. 272)**. Determinations of oxygen content in arterial and venous blood, together with cardiac output and hemoglobin concentration, allow calculation of oxygen delivery,