CHAPTER 2

Homeostasis in Massive Multiple Trauma

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INTRODUCTION

The challenges that face clinicians who manage patients with multiple trauma are among the most daunting in medicine. Trauma is a unique disease. Unlike many other diseases, there is a definitive time of onset, followed by a series of time-critical periods when the victim is vulnerable to a number of life-threatening and potentially life-threatening insults.

The survival of these patients depends on some factors that cannot be prevented, such as the degree and nature of the external force causing the injury and the physiologic reserve of the victim. There are, however, a number of preventable factors that directly affect functional survival, such as hypoxia, shock, and infection. For the successful management of traumatized patients during any of these periods, clinicians need to recognize patterns of injuries and to prioritize treatment options so that the patient is not compromised and preventable insults are not missed.

This chapter addresses the pathophysiologic basis of effective trauma management. Many of these principles apply to the management of trauma victims throughout their stay in the hospital. Some of these principles and strategies have been definitively studied in appropriate trials, so that management can be based on evidence. However, for the majority of these strategies, trial-based evidence is limited and clinicians must rely on time-honored physiologic principles and hard-earned experience.

Although this is a chapter in a textbook on orthopaedic anesthesia, it is written from the perspective of the clinician who is presented with traumatized patients during their passage through the health care system. These perspectives are unified by the aim of improving the patient’s survival.

EPIDEMIOLOGY OF TRAUMA

In global terms, trauma poses the greatest threat to human survival. Although patterns of trauma have stabilized in developed or high-income countries, trauma levels are increasing exponentially in developing or low-income countries. This phenomenon is primarily related to increased mechanization in low-income countries, where an expanding population is becoming dependent on vehicular transport for economic survival. This increase in mechanization is not occurring at the same pace as infrastructure development and access to effective health care systems. Adequacy of roads, enforcement of traffic regulations and the use of passenger restraining devices, improvements in vehicular safety, and road safety education are variable and lag behind those in developed countries. Coupled to the increasingly violent environment—owing to economic polarization, war, terrorism, religious fundamentalism, and firearm availability—that predominates in low-income countries, it is not surprising that trauma is regarded as the “silent global epidemic.”

In high-income countries, the incidence of trauma is decreasing, primarily due to the reversal of the adverse phenomena prevalent in low-income countries. Indeed, many regard the rate of trauma death as an index of societal stability and civility.
Globally, trauma remains predominantly a disease of the young. The majority of victims are male, and trauma is the leading cause of death in children. The cost to survivors in all societies in emotional, social, and financial terms is substantial, since the effects of the original injury may persist for many years. Trauma is therefore a major disease confronting all societies.

PATHOPHYSIOLOGIC RESPONSE TO TRAUMA

It is imperative that clinicians have a clear understanding of the pathophysiologic processes that underlie trauma and the systemic responses to these processes.

The physiologic response to trauma, infection, and inflammatory conditions (e.g., pancreatitis and burns) results in a complex neurohumoral phenomenon that has been studied extensively. Despite numerous changes in nomenclature over the last 10 years, the systemic response to injury has been recognized for the last century. This response is characterized by complex neural-endocrine-humoral effects at cellular and organ levels, and the resultant clinical response represents the teleologic reaction to ensure the organism’s survival. Originally described as “fight or flight,” the magnitude of this physiologic response will depend on the severity of the injury and the inherent ability of the host to mount an appropriate response. In the clinical situation, the physiologic reserve of the host will depend on associated comorbidities, medications, and secondary injuries.

Cellular and Neurohumoral Factors

The cellular response to injury results in a nonspecific cascade of numerous molecular effects. The initiating triggers of this response may vary and include direct trauma causing cellular or organ damage, systemic release of toxins from invading microbes, fluctuations in temperature greater than homeostatic limits, and toxicity from drugs. Regardless of the nature of this initiating stimulus, the resultant cellular response is nonspecific and may be regarded as a coordinated endogenous response to augment protective systems that may be depressed after injury (“proinflammatory”) and/or to suppress systems that may cause further cellular or systemic injury (“anti-inflammatory”) (Fig. 2-1).

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![Figure 2-1](image.png)  
Figure 2-1. The systemic response to acute injury.
Although the distinction into pro- and anti-inflammatory mediators assists in conceptualizing this response, there is marked inter- and intraindividual variation in the effects and response of these mediators. A number of cellular systems and mediators of inflammation have been identified and studied.

**Cytokines**
Mediators of inflammation include cytokines, which exist in both circulating and cell-associated forms. These include the family of interleukins (ILs), of which IL-1 and IL-6 have been extensively studied as markers of pro- and anti-inflammatory cytokine release, respectively. Tumor necrosis factors (TNF-α, β, and δ) as well as platelet-activating and inhibiting factors are primary mediators that induce the release of other cellular factors (mostly endothelial), such as nitric oxide, endothelin, and populations of eicosanoids (prostaglandins and leukotrienes). The effects of these mediators are to alter tissue and vascular permeability in order to improve regional blood flow and metabolism. Endothelin and nitric oxide are ubiquitous endothelial compounds that are integral in vasoconstriction and vasodilation, respectively. They form the basis of regional autoregulation—that is, when regional blood flow rates are kept relatively constant in the presence of altered metabolism and perfusion.

**Complement**
Activation of the complement cascade is a fundamental component of cell-mediated and humoral immunity. Apart from the activation of antibodies and cellular responses to injury, activated components of the complement cascade such as C3a and C5a interact with endothelial mediators to alter membrane permeability, both directly and in association with circulating activators such as bradykinin and histamine. In regional circulations, such as in the kidney, complement activation is integral in maintaining renal perfusion and defending glomerular filtration.

**Coagulation**
Regulation of intravascular coagulation is a principal homeostatic mechanism. Rather than simply regarding this system as a series of chemical reactions that are activated in response to hemorrhage, the coagulation system should be regarded as a complex system in a state of fluctuating conformational change, balancing intravascular coagulation and thrombolysis. The interaction between circulating procoagulants (e.g., activated factor VII and von Willebrand factor), anticoagulant proteins (e.g., proteins C and S), opsonic glycoproteins (e.g., fibronectin), and endothelium-derived mediators form the basis for maintaining intravascular integrity and membrane stability. Depletion of these vital homeostatic factors following hemorrhage often result in subsequent coagulopathy and endothelial disruption.

**Neurohumoral Factors**
Under the influence of a number of physiologic stimuli and interactions, autonomic neural control of regional and systemic vasculature and organ function is a principal homeostatic system. Through a series of endogenous conversions, phenylalanine is converted to dopamine within adrenergic nerve terminals. Dopamine is converted to norepinephrine and released into the neural synapse, where it interacts with populations of adrenoreceptors. Under physiologic conditions, norepinephrine is the predominant neuroendocrine agonist. Release and reuptake of norepinephrine from adrenergic terminals is controlled by presynaptic alpha receptors in response to changes in physiologic perturbations, such as changes in posture, altitude, and energy expenditure. Under physiologic conditions of stress or in pathologic states, norepinephrine release is augmented by the release of epinephrine from the adrenal gland via the same presynaptic alpha systems. Teleologically, dopamine and epinephrine may be regarded as norepinephrine precursors, norepinephrine being the predominant endogenous catecholamine.

Catecholamine-mediated physiological responses are complex. Agonists bind to populations of adrenergic receptors, which are largely divided into alpha and beta subgroups. Further subgroups of α (1A, 1B, 2A, 2B, and 2C) and β-receptors (1, 2, and 3) have been identified.

Signal transduction from agonist-receptor occupation to the effector cell is modulated by conformational changes in G proteins associated with these receptors. Under the additional influence of second messengers such as nitric oxide, endothelin, and eicosanoids, these conformational changes promote the release of calcium from intracellular stores and increased membrane calcium permeability. Subsequent phosphorylation of substrate proteins via protein kinases prompts third messengers to trigger a cascade of events leading to specific cardiovascular and metabolic effects.

In addition to adrenergic regulation, other neurohumoral substances have a permissive or regulatory role in maintaining vasomotor tone. These are mediated through the renin-aldosterone-angiotensin axis and local mediators such as vasopressin and corticosteroids. Of these influences, specific vasopressinergic receptors (V1 and V2) have been identified in association with sympathetic terminals and may be responsible for systemic vasoresponsiveness. Similarly, the endogenous release of corticosteroids has been shown to exert an important vasoactive role, thereby augmenting catecholamine-mediated interactions.

**Organ Responses**
The clinical expression of the physiologic response to injury and inflammation outlined above will vary
considerably between and within individuals. Ultimately, the effects on the functions of vital and nonvital organs will determine a person’s response to injury (Fig. 2-2).

Initially, the clinical response to injury is nonspecific. Over the last 20 years, there has been extensive debate to define the systemic inflammatory response syndrome (SIRS), usually in association with infection.\textsuperscript{19,20}

**PART I  GENERAL PRINCIPLES**

**Figure 2-2.** The effects on the functions of vital and nonvital organs will determine the person’s response to injury. Individual variation is vast.

Abbreviations: ALI = acute lung injury; ARDS = acute respiratory distress syndrome; DIC = disseminated intravascular coagulation; FDP = fibrinogen degradation product; NO = nitric or nitrous oxide; PAF = platelet-activating factor; PIF = prolactin-inhibiting factor; TNF = tumor necrosis factor.
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The impetus for this debate was to define baseline clinical features as criteria for including patients in clinical trials, although the use of these criteria has expanded into clinical practice. The SIRS criteria are generic and include at least two clinical features from a list that includes a temperature change (<36 or >38°C; <98.6 or >100.4°F), tachycardia (>90 beats per minute), tachypnea (>30 breaths per minute or an arterial carbon dioxide tension <32 mmHg), and alteration in leukocyte count (<12 or >4 10^9/mm³ or >10 percent band neutrophils). Clearly, there are numerous causes of these physiologic changes, and although they are commonly used as criteria in clinical and research practice, they have limited clinical utility.

An alternative approach is to consider the effects of injury on each organ system and to interpret the resultant changes in the light of the underlying physiologic response and the impact of external injury.

Cardiovascular System

Because of the autonomic responses outlined above, the cardiovascular effects of injury are often the most acute and clinically apparent. The endogenous sympathetic response is directed at maintaining the perfusion of vital organs. Circulatory homeostasis is predicated on the principle that cardiac output is equal to venous return. The assessment and treatment of circulatory failure must consider these two processes.

Cardiac output primarily depends on the heart rate and stroke volumes. Increasing the heart rate will increase cardiac output, so tachycardia is an inevitable sign following trauma. The absence of tachycardia after trauma is therefore always abnormal and suggests sympathetic ablation, either due to adrenergic blocking agents (beta blockers), autonomic neuropathy (e.g., severe diabetes), or high spinal injury (quadriplegia). To eject blood effectively, the heart depends on a critical ventricular mass and contractility. On rare occasions, loss of myocardial contractility after trauma may be due to severe myocardial contusion or rupture.

Although only 20 percent of the circulating blood volume is contained in the arterial (conducting) circulation, stroke volume depends primarily on the amount of blood returned to the heart at the end of diastole. The venous system contains 70 percent of the blood volume and, as such, represents an endogenous blood reservoir. Sympathetic innervation of venous conductance vessels causes venoconstriction, in both major capacitance veins and peripheral veins, resulting in an increased venous return and increased preload. This can represent up to 20 percent of the venous blood volume. This sympathetic response converting the “unstressed” venous volume into a “stressed” venous volume is one of the earliest physiologic responses to injury, and in conjunction with an increase in heart rate and contractility, represents the endogenous cardiovascular response to injury.

Consequently, loss of effective intravascular volume through hemorrhage represents the most common threat to hemodynamic function. An adult can usually tolerate an acute blood loss of up to 20 percent of the blood volume (about 1000 mL in an adult), but this represents the upper limit of physiologic reserve in the majority of patients. Greater blood loss requires volume replacement to maintain effective venous return and cardiac output.

Sudden sympathetic ablation, usually by anesthetic drugs or high doses of analgesics, will result in loss of stressed venous tone, thereby unmasking relative hypovolemia.

Other important physiologic factors that compromise hemodynamic function in the traumatized patient include positive intrapleural pressure (e.g., positive-pressure ventilation or tension pneumothorax), loss of atrial contraction (e.g., atrial fibrillation), and ablation of muscle tone and pump (e.g., neuromuscular blockers or quadriplegia/paraplegia). These factors primarily compromise venous return and must be promptly identified and treated.

During the later stages of trauma, superimposed infection, sepsis, or multiple organ failure will adversely affect on cardiovascular function. Initially a hyperdynamic vasodilated state is recognized, conventionally attributed to pathologic arterial vasodilation or vasoplegia. Although arterial vasodilatation is indeed a feature, the predominant vascular dysfunction is venoplegia, whereby sympathetically mediated venoconstriction is blunted, resulting in relative inability to maintain a stressed volemic response. Consequently, cardiac output becomes dependent on heart rate, resulting in a high-output state, also described as warm shock. As septic shock progresses, sympathetic reserve progressively becomes blunted via quantitative (downregulation) and qualitative (desensitization) processes, resulting in failure to maintain cardiac output. This is conventionally termed “low-output” or “cold” shock, but in effect represents the failure of predominantly adrenergic homeostatic mechanisms to maintain hemodynamic function. Accordingly, treatment strategies are directed at augmenting or replacing failing neurohumoral systems.

Renal System

Apart from blood purification and production of urine, the kidney is an integral homeostatic organ in the response to injury. Fundamental aspects of this response are the defense of mean arterial pressure and water retention. Glomerular filtration and urine production are under intense control by neurohumoral systems, of which the renin-angiotensin-aldosterone neuroendocrine axis
is predominant. Loss of effective intravascular volume or blood pressure causes a reduction in renal perfusion pressure, which triggers the release of renin from the juxtaglomerular apparatus. Apart from converting angiotensinogen to angiotensin and aldosterone, renin augments the adrenal release of epinephrine via second-messenger systems. These powerful endocrine responses cause increased tubular absorption and production of small volumes of concentrated urine. In trauma cases, oliguria should therefore be regarded as a normal physiologic response.

Second, neuroendocrine function, particularly angiotensin-converting enzyme (ACE) and angiotensin II, is integral to maintaining mean arterial pressure. By maintaining efferent arteriolar tone and water retention, the kidney is able to maintain effective renal perfusion pressure in the presence of fluctuating renal blood flow and mean arterial pressure (autoregulation). Furthermore, the kidney has substantial reserve to tolerate ischemia and relative hypoxia. Oliguria (defined as <0.5 mL/kg/h) in the initial period after trauma (up to 48 to 72 h) should therefore not be regarded as renal failure unless urea and creatinine levels are elevated and there is evidence of loss of renal vascular integrity. However, in patients with premorbid hypertension or in those taking ACE inhibitors, endogenous renal reserve to tolerate ischemia may be reduced and renal failure may ensue at an earlier juncture.

Although oliguria after injury may be regarded as a normal clinical sign, spontaneous diuresis during the recovery phase is equally important. The neuroendocrine basis for this reflects the defervescence of the physiologic responses in the acute phase, often heralding the resolution of organ dysfunction, and may be termed a reversal of water retention. Traditionally, the acute response to injury has been described as an initial “ebb” phase, which is followed by a “flow” phase. These observations are based on the neuroendocrine fundamentals outlined above.

**Brain**

Brain injury is the leading cause of death in traumatized patients. The majority of immediate deaths caused by trauma are attributable to lethal head injury sustained at the time of impact. Among patients who reach a hospital alive but subsequently die, the mortality due to brain injury is approximately 90 percent. Of these, the majority have severe primary brain injury; i.e., injury sustained at the time of impact. Secondary brain injuries—defined as systemic insults that occur during the postinjury period—are independent determinants of adverse outcome. Of these insults, hypotension and hypoxia are the most profound. There is a sound physiologic basis for these observations.

Under physiologic conditions, the brain receives 20 percent of the cardiac output. The “luxury perfusion” of the brain reflects the metabolic requirements for brain function. The brain has therefore developed autoregulatory mechanisms to maintain a relatively constant cerebral blood flow when systemic blood pressure fluctuates. In contrast to the kidney, cerebral autoregulation is based on the relative impermeability of the blood-brain barrier to exogenous vasoactive peptides, such as catecholamines; therefore, intense local microvascular regulation is employed, predominantly through endothelial fluxes of endothelin and nitric oxide.

Despite its autoregulatory mechanisms, the brain is extremely vulnerable to the effects of systemic hypotension, particularly after brain injury. Patterns of abnormal cerebral blood flow have been described in these cases. Initially, within 72 h of injury, cerebral blood flow is reduced, often to a critical level of <20 mL/100 g/min. This is well below the autoregulatory threshold or “breakpoint” where cerebral blood flow becomes pressure-passive (35 mL/100 g/min). This breakpoint may be higher in patients with associated systemic hypertension and must be considered during resuscitation and treatment. A number of intrinsic mechanisms have been described for this reduction in cerebral blood flow. They include neurohumorally mediated vasoconstriction, microvascular thrombosis, and traumatic subarachnoid hemorrhage. Importantly, secondary ischemia, in particular hypovolemia due to extracranial trauma and the injudicious use of osmotic diuretics, may aggravate primary and secondary brain injury. Furthermore, lethal ischemic cerebral damage has been described in patients who have not sustained a primary brain injury but suffered exsanguinating hemorrhage from their injuries. Despite surviving the initial trauma, they suffered fatal ischemic damage to the brain.

The maintenance of normal systemic blood pressure and cardiac output therefore form the basis of resuscitation of the patient with head injuries. Prioritization of treatment of extracranial injuries is done by considering the injury most likely to cause extensive hemorrhage or hypotension and treating it in the first instance. In this context, “damage control” surgery is regarded as primarily hemostatic. Provided the patient remains stable, further investigation and treatment of injuries to the head and other parts can proceed.

The use of hyperventilation to reduce increased intracranial pressure in traumatic brain injury has been advocated for many years. Despite guidelines based on evidence against the use of hyperventilation, it is still strongly advocated by some neurosurgeons. Hypocapnia induced by hyperventilation is a potent cerebral vasoconstrictor and has been demonstrated to induce and exacerbate cerebral ischemia in the traumatized brain, particularly during the initial period after head injury. Cerebral ischemia induced by hyperventilation may be regarded as a preventable secondary brain injury.
Similarly, the use of osmotic diuretics, such as mannitol, and hypertonic crystalloid solutions has been advocated to reduce cerebral edema following traumatic brain injury. Although there is a theoretical basis for the use of these solutions, the purported benefit may be related mainly to a transient expansion of intravascular volume which increases cerebral blood flow, rather than a specific rheologic effect. Indeed, hyperosmolar states caused by the overuse of these solutions, particularly in patients with alcohol intoxication, may negate their rheologic benefit. Furthermore, osmotic diuresis may cause hypovolemia, particularly at a period of increased vulnerability of the brain to hypotension.43

The use of hyperventilation and osmotherapy should therefore be restricted and used only as a temporary measure in hemodynamically stable patients in whom there is a high probability of rapidly developing intracranial hypertension and for whom urgent neuroimaging or surgery is considered.44

**Respiratory System**

An open airway is fundamental to the maintenance of oxygenation. At all stages of resuscitation and management, airway patency is mandatory, and this requires constant vigilance. Because of the increased metabolic rate associated with injury, minute ventilation is increased to reduce carbon dioxide levels. Increased minute ventilation also helps to increase oxygenation, although a significant effect on arterial oxygenation is limited at ambient pressure and oxygen concentration. For this reason, all injured patients should receive oxygen at the highest inspired oxygen concentration during the initial resuscitation, since injuries such as tension pneumothorax or pulmonary contusion may cause profound hypoxia. This situation includes patients with chronic obstructive pulmonary disease. Ablation of the hypoxic drive by oxygen is rare in these patients, and the need for supplemental oxygen should always supersede this theoretical concern.45

Apart from direct lung injury—such as pulmonary hemorrhage, contusion, or aspiration pneumonitis—the lungs are also vulnerable to an indirect endothelial injury. The surface area of the lungs is large (>100 m²), and since it receives the entire cardiac output, presents a large endothelial area that is exposed to potential inflammatory insult. Extrapulmonary insults may therefore cause an intense inflammatory response that manifests as an acute lung injury.

Ashbaugh described “shock lung” (later termed the adult respiratory distress syndrome (ARDS)) in 1967, during the Vietnam War, as “a sudden clinical pathophysiological state characterized by severe dyspnea, hypoxia, diffuse bilateral pulmonary infiltrations and stiff lungs following massive acute lung injury, usually in persons with no previous lung injury.”46 Typically, the insult is nonhomogeneous and spares some areas of lung parenchyma. In damaged areas, the lung is atelectatic, edematous, and hemorrhagic. Hypoxia occurs owing to increased intrapulmonary shunting of blood caused by the loss of functional alveoli and the resultant reduction in functional residual capacity. Lung compliance is reduced (<30 mL/cmH₂O) and physiologic dead space is increased, resulting in hypercapnia. Progressive diffuse alveolar and interstitial infiltrates appear on the chest radiograph and have been quantified according to the severity of the injury. Microscopic examination reveals intraalveolar collections of proteinaceous fluid, red blood cells, and inflammatory cells. Microthrombi or white cell aggregates may be seen in small vessels. After 24 to 48 h, hyaline membranes line the alveoli. These are formed by fibrin that has escaped through the capillary walls. As repair of the injury occurs, fibrosis may ensue.47

This syndrome is characterized by an alteration in the permeability of alveolar endothelium and presents as alterations in oxygenation, defined by the ratio of arterial to fractional inspired oxygen tensions (PaO₂/FiO₂), the development of alveolar and interstitial infiltrates, and reductions in pulmonary compliance. Importantly, these physiologic derangements occur in the absence of pulmonary venous hypertension (cardiac failure). A PaO₂/FiO₂ ratio of <350 is used to define acute lung injury (ALI); if it progresses to a PaO₂/FiO₂ ratio <250 mmHg, it is defined as ARDS.48

Although the treatment of ALI/ARDS is largely supportive and directed at resuscitation and the underlying cause, the knowledge that lung injury may be induced by mechanical ventilation has changed the way in which patients who need mechanical ventilation for respiratory failure are managed. Increased alveolar distention associated with positive-pressure ventilation or “volutrauma” has been shown to cause endothelial disruption and acute pulmonary inflammation resulting in an acute lung injury/ARDS. This is distinct from, but often associated with, extraalveolar air or “barotrauma” induced by positive pressure, which may also result in endothelial injury and is often associated with pulmonary interstitial emphysema, subcutaneous emphysema, pneumothorax, pneumomediastinum, or pneumopericardium.49 Accordingly, patients with evidence of ALI/ARDS or who may be at risk of developing it should be ventilated with limited tidal volumes.

**Endocrine System**

Alterations in endocrine function integrated with systemic autonomic responses after trauma have been described. Foremost of these is hyperglycemia, which may be attributed to exaggerated autonomic responses and insulin resistance during the acute-phase response. Hyperglycemia is therefore common, and there is
increasing evidence suggesting that the maintenance of normoglycemia during acute illness leads to improved outcomes.\textsuperscript{30,51} This may be because the overwhelmed endogenous insulin responses are supplemented. The physiologic effects of insulin extend beyond blood glucose homeostasis; they include improved phagocytosis by white blood cells, amino acid utilization, and improved neuronal function.

As outlined above, optimal cardiovascular function is dependent on nonadrenergic neurohormonal influences. Adrenocortical function may be impaired during acute illness; this has been attributed to adrenal medullary infarction following profound hemorrhagic shock, alterations in circulating corticoid-binding globulin, and reduced efficacy or levels of adrenocorticotropic hormone (ACTH). These changes may result in absolute or functional hypoadrenalism, which may manifest as catecholamine-resistant shock, hypoglycemia, anergy, and hypothermia.\textsuperscript{52} In a massively traumatized patient, these signs should prompt one to consider treatment with corticosteroids or to test the adrenal response to ACTH.

Similar reductions in thyroid, posterior pituitary, and gonadal endocrine functions have been described. The clinical relevance of these changes is unclear but should be considered in anergic trauma patients and particularly in patients with preexisting endocrine illness.

**PRINCIPLES OF TRAUMA MANAGEMENT**

On the basis of the above physiologic responses, an integrated plan for treating the traumatized patient may be arrived at. A number of highly regarded and effective management protocols have been developed, such as the Advanced Trauma Life Support (ATLS) initiative of the American College of Surgeons.\textsuperscript{53} These protocols provide a logical and prioritized approach to the early management of patients with severe trauma and have significantly improved the education of doctors and paramedics in the handling and treatment of these patients. Importantly, these protocols direct the attention of clinicians to the most life-threatening trauma, so that correcting vital-organ homeostasis supersedes less threatening but often more dramatic injuries.

The following section is written to complement overarching ATLS principles. In this regard, the reader is encouraged to read these manuals or similar trauma management texts.

What follows is a physiologic approach based on evidence to many of these trauma management principles, providing the rationale on which they are based.

Two phases of management are considered: the initial resuscitation phase followed by the period of stabilization.

**Resuscitation**

The resuscitation period is the conditio sine qua non where the ATLS principles apply.

This phase begins as soon as bystanders or emergency personnel attend to the patient. It extends until the patient is stabilized and transferred to a hospital ward or the intensive care unit (ICU). During this period, the patient may be attended by many people, including paramedics, emergency personnel at the first receiving or referral hospitals, and surgeons/physicians with variable experience and expertise.

Accurate documentation of vital signs—such as blood pressure, pulse rate, oxygen saturation, respiratory rate, temperature, and neurologic function (Glasgow Coma Scale score)—during this period is critical. These signs are important in quantifying initial physiologic function and determining whether the patient has suffered secondary insults. This information is often important for subsequent prognostication. The adequacy of documentation of these early signs is often variable; therefore it should ideally be obtained as soon as possible and directly from the personnel involved.

Initial emphasis is directed at assessing and maintaining airway patency, ensuring adequate oxygenation and ventilation, establishing adequate intravenous lines, and restoring normal hemodynamic function. Neurologic assessment should follow only when cardiorespiratory function has been stabilized.

**Airway Management**

Loss of an open airway at any stage of management represents an acute life-threatening complication. Hypoxia is a prominent cause of secondary brain injury.

The need for an open airway may necessitate endotracheal intubation by emergency personnel under suboptimal circumstances. The intubation of traumatized patients by emergency personnel outside a hospital is a controversial issue, since its success depends on the expertise of the paramedic. The benefits of the early establishment of a definitive airway, oxygenation, and control of carbon dioxide may be offset by the complications of failed intubation, pulmonary aspiration, and delay in transfer to a hospital. Small studies have shown increased mortality in patients intubated before hospitalization, although this practice remains under evaluation.\textsuperscript{54,55}

All traumatized patients with altered consciousness have potentially threatened airways. The emergency intervention required to clear airways will depend on the level of consciousness, adequacy of protective laryngeal reflexes, and the relative risk of aspiration and airway compromise.

All traumatized patients, particularly those with head injury, should be assumed to have an injured cervical
spine and be immobilized in a rigid collar until such an injury is definitively excluded radiologically. During any airway intervention and until injury to the cervical spine is excluded by radiological evidence, in-line immobilization of the cervical spine by a rigid collar or by a dedicated person is mandatory.

The mouth and upper airway must be inspected for foreign bodies, hemorrhage, or dentures and cleared under direct vision using a rigid sucker. Simple maneuvers, such as a chin lift and/or a jaw thrust and the use of oropharyngeal airways or laryngeal masks may make a compromised airway functional and allow efficient oxygenation in patients who still breathe. Nasopharyngeal airways must be used cautiously in patients in whom a cribiform plate fracture is suspected, since these instruments may pass directly into the cranial cavity. They may also cause trauma to the nasal mucosa and bleeding into the nasopharynx and upper airway, leading to further airway compromise. The same caution applies to the insertion of nasotracheal and nasogastric tubes.

The decision to perform endotracheal intubation will depend primarily on the level of consciousness, the degree of respiratory failure (hypoxia or hypercapnia), and the requirements for diagnosis and surgery. The selection of intubation technique will depend on the expertise of the operator. Clearly the most experienced person must perform this lifesaving procedure.

In using anesthetic induction agents, sedation, and muscle relaxants to facilitate intubation, one must consider the effects of these agents on sympathetic tone. As described above, the acute response to injury is characterized by intense sympathetic activity. Anesthetic induction agents such as thiopentone, propofol, and benzodiazepines have a significant dose-dependent sympatholytic effect. In compromised but compensated patients, the administration of these drugs may cause profound hypotension, primarily due to ablation of autonomically mediated stressed venous capacitance as well as reduction in venous return and cardiac output. This phenomenon will be exacerbated in hypovolemic patients. Furthermore, autonomically mediated tachycardia may also be blunted by these anesthetic agents, further compromising systemic blood pressure. The worsening of hypotension due to anesthetic induction drugs must therefore be anticipated in all severely traumatized patients. To minimize the resultant hypotension, accurate measurement of systemic blood pressure (ideally via an intraarterial catheter), preemptive volume replacement, and the early use of vasoactive agents should be considered. This is discussed below.

Agitated or combative patients may best be managed initially by intubation and controlled ventilation until diagnostic and therapeutic interventions are completed.

Unconscious patients should be intubated as soon as possible, as should patients with concomitant maxillofacial trauma or upper airway obstruction due to direct laryngeal trauma. This is best performed at a location where expert anesthesiologists and procedures such as rapid induction and intubation, blind nasal intubation, fiberoptic laryngoscopy, cricothyroidotomy, and tracheostomy are available.

For patients who cannot be intubated or ventilated via a bag and mask, surgical airway access should be provided by urgent cricothyroidotomy. There is little or no role for urgent tracheostomy (either percutaneously or surgically) in this situation.

**Respiratory Management**

As outlined above, oxygen at the highest concentration should be administered to all traumatized patients in the initial period. For patients who still breathe, face-mask oxygen using circuits is suitable. In intubated patients, handheld or mechanical ventilating devices can reliably deliver a fractional inspired oxygen concentration of 1.0 (100%). Handheld, self-inflating devices can effectively ventilate both intubated and nonintubated patients and allow a clinical assessment of lung compliance during inflation, thereby reducing the risk of disconnecting the endotracheal tube or face mask.

Assessment of oxygenation in emergency situations may be difficult in traumatized patients, whose consciousness may be affected by head injuries, alcohol, drugs, or sedatives. All patients should be monitored using pulse oximetry. A saturation of greater than 95% is recommended, as this generally corresponds to an arterial oxygen tension (PaO₂) of at least 75 mmHg (10 kPa). These devices are unreliable in hypoperfused, hypothermic, and agitated patients. However, the demonstration of an oxygen saturation <95% and a pulse waveform even under conditions of poor perfusion indicates hypoxia until proven otherwise.

Mechanically ventilated patients should be ventilated with 100% oxygen until blood gas analysis is obtained. Thereafter, the fractional inspired oxygen concentration may be decreased provided that oxygenation is maintained at a minimum of at least 100 mmHg (13 kPa). Ventilation should be adjusted by using sufficient tidal volumes to obtain normocapnia. Initially this may require tidal volumes of 10 mL/kg, particularly right after endotracheal intubation, when patients are frequently hypocapnic. Once blood gas levels are known, the ventilator should be adjusted to achieve a normal arterial carbon dioxide tension (PaCO₂) (35 to 40 mmHg; 4.5 to 5.0 kPa), using peak airway pressures of less than 35 to 40 cmH₂O, ideally using tidal volumes of 5 to 7 mL/kg. End-tidal capnography should be used whenever possible. This not only provides an approximate PaCO₂ but also shows definitely that the endotracheal tube is correctly placed and allows an assessment of cardiac output.
In combative patients, nondepolarizing muscle relaxants and narcotics such as fentanyl may facilitate ventilation in the immediate postintubation period.

**Circulatory Management**

Prompt restoration of circulating blood volume and a euvolemic state is critical. The initial assessment of circulatory status may be difficult, since the blood pressure may be maintained owing to sympathetic stimulation. Tachycardia, although common in trauma patients, and reduced capillary return are cardinal signs of hypovolemia. Peripheral perfusion may be difficult to assess in hypothermic patients.

Sources of external hemorrhage must be identified and rapidly treated, usually with direct pressure. Causes of refractory hypotension in these patients include acute spinal injury, tension pneumothorax, cardiac tamponade, and severe myocardial contusion; they must be excluded early.

There is no evidence to recommend crystalloid over colloid volume resuscitation; either will suffice. This controversy has been fueled by the conflicting results of metaanalyses of small clinical trials, often of poor quality. A recent large randomized controlled trial demonstrated that saline and albumin were equally effective for the resuscitation of critically ill patients. Some 1 to 2 L of balanced salt solution (lactated Ringer’s or normal saline) or an equivalent volume of synthetic colloid (Hemaccel, Gelfusin, or Hetastarch) should initially be infused in all patients through large-bore peripheral venous lines. Hypertonic saline may theoretically be useful as a small-volume resuscitation fluid, which is effective in expanding intravascular volume, with potentially beneficial effects in head-injured patients. However, hypertonic saline given before the patient reaches a hospital has not been demonstrated to improve outcome.

Blood transfusion must be administered to patients who have lost more than 20 to 30 percent of their blood volume or where further serious hemorrhage is anticipated.

Early and accurate measurement of arterial pressure (ideally through a central artery) and a central venous catheter are essential to guide volume replacement and administer blood and drugs. The placement of these lines must not delay volume resuscitation.

The target for mean arterial pressure should be estimated on the basis of the patient’s premorbid blood pressure, since higher pressures may be necessary in hypertensive or elderly patients. The early use of vasoactive agents may be necessary to achieve this.

Vasoactive agents such as epinephrine, norepinephrine or dopamine or vasopressors such as phenylephrine or metaraminol may be used to defend blood pressure once correction of hypovolemia is under way or achieved. There is no evidence that any vasoactive agent or combinations of vasoactive agents are superior to one another.

In selected patients with penetrating thoracic injury, a “permissive hypotension” strategy has been advocated during resuscitation pending definitive surgical intervention. This strategy is based on the assumption that aggressive hemodynamic resuscitation may increase surgically remediable bleeding in noncompressible areas. Although there is some evidence to support this strategy, it cannot be used in patients with an associated traumatic brain injury or those with blunt trauma.

**Neurologic Assessment**

The assessment of neurologic function is important to quantify the severity of brain injury and provide prognostic information. The level of function may be influenced by associated injuries, hypoxia, hypotension, and drug or alcohol intoxication.

Neurologic assessment of the patient should be done frequently. During the resuscitation phase, neurologic signs should be documented before and after any major intervention (e.g., intubation, correction of blood pressure, patient transport) and at least at hourly intervals.

Neurologic assessment includes observing the best neurologic response to the least noxious stimulus. This includes simple scores such as AVPU (awake, verbal, pain, unresponsive to stimulation) or more integrated scores, such as the Glasgow Coma Scale score and pupillary responses.

**Secondary Survey**

After the initial assessment and when resuscitation is under way, a thorough secondary survey adopting a head-to-toe approach is mandatory.

The principles outlined in the initial assessment form the basis for deciding priorities of interventions in the secondary survey. Causes of hypoxia or hypercapnia—such as pulmonary contusion, and hemothorax/pneumothorax—must be excluded and promptly treated. Hemorrhage, both external and internal, must be aggressively treated until the circulation is stable.

The approach of “damage-control surgery” outlined above is advocated in head-injured patients so as to minimize secondary insults. In the initial 24 to 48 h after injury, only life- or limb-threatening injuries should be treated. After this, patients are transferred to the ICU for stabilization and monitoring. Thereafter, semiformal or formal plastic repairs may be completed. Patients with severe head injury who undergo prolonged emergency surgery should ideally have intracranial pressure monitoring begun as soon as possible.

Routine x-rays of the chest, pelvis, and cervical spine and baseline blood tests (including tests for blood alcohol and other drugs of abuse level when deemed necessary) are part of the secondary survey.
For intubated and ventilated patients, sedation in the acute phase must be titrated against the patient’s hemodynamic stability. High doses of narcotics (e.g., 15 to 25 µg/kg fentanyl) and nondepolarizing muscle relaxants (e.g., vecuronium 8 to 10 mg) will provide sufficient sedation and allow control of ventilation for 1 to 2 h, during which time imaging and other investigations can be performed. Frequent assessment of consciousness is essential, because excessive sympathetic activity may potentiate raised intracranial pressure or myocardial ischemia in a paralyzed but awake patient. Sedation may need to be supplemented with intermittent doses of opiates or benzodiazepines.

**Stabilization**

Depending on the degree of trauma and extent of injuries, patients may be transferred to the operating theater for emergency or definitive surgery. The majority of patients with massive or multiple trauma will be transferred to a high-acuity-care area such as a trauma unit or an ICU.

This section addresses the principles of management of patients who require intensive care for stabilization following trauma resuscitation.

There is no standard or uniform method of managing traumatized patients in the ICU. Local preferences, experience, caseload, and resources determine most practices. After initial resuscitation, intensive care is regarded as a continuation of care in the emergency department or operating theatre.

**Hemodynamic Management**

The defense of perfusion in vital organs forms the basis of hemodynamic management, considering the physiologic principles outlined above.

➤ **MONITORING**

Circulatory dysfunction is commonly defined as a mean arterial pressure ≤60 mmHg for 1 h despite adequate fluid administration, although this may vary between patients and will depend on the etiology. Accurate measurement of systemic blood pressure is essential and should be done via an arterial catheter referenced to the aortic root. A large artery, such as the femoral artery, should be considered in hemodynamically unstable patients, because measurements from radial or dorsalis pedis arteries may underestimate systemic pressure in shocked patients. Given the importance of maintaining adequate systemic pressures, noninvasive measurement of blood pressure is not recommended during the acute phase of monitoring.60

Therapy should be titrated to mean arterial pressure in accordance with the patient’s premorbid blood pressure; i.e., in older patients, higher mean arterial pressure (e.g., 80 mmHg) may be necessary.

Central venous catheters are inserted in the majority of severely traumatized patients requiring intensive care. Volume status should be assessed by electronically transduced measurements of central venous pressure and hourly measurements of urine output. Right atrial pressure monitoring via a central venous catheter provides the best assessment of volume status.66 Accuracy may be affected by tricuspid regurgitation or pulmonary hypertension.

The response of right atrial pressure to a fluid challenge, rather than an absolute number, will yield useful information regarding the patient’s volume status.

Pulmonary artery catheters allow measurement of two independent variables—cardiac output and pulmonary artery pressures—but is rarely indicated in traumatized patients unless there is associated cardiac dysfunction. Measurement of these two variables may be useful in patients with states of low cardiac output or in those with acute pulmonary hypertension, such as ALI/ARDS. Pulmonary artery occlusion pressure may be used as an indirect measurement of left atrial pressure. However, this measurement may be affected by respiratory artifact, positive airway pressure, tachycardia, hypovolemia, and poor ventricular compliance and has limited clinical utility in critically ill patients.

Derived hemodynamic variables, such as systemic vascular resistance, are frequently calculated and used as a surrogate index of afterload. However, the clinical utility of systemic vascular resistance is limited to providing a crude estimate of global vascular tone, as it does not reflect afterload, arteriolar tone, or venous return. Consequently, systemic vascular resistance should not be used as a criterion for the selection of vasoactive drug or as a titratable endpoint.67

Central venous catheters are a major source of nosocomial infection and cause significant morbidity and mortality. There is no agreement about how long such catheters should be left in place or the diagnosis of catheter-induced sepsis.66,68,69 By puncturing the skin, these catheters provide a nidus for infection and a point of entry into the circulation for bacteria.

Generally, catheters inserted during resuscitation should be changed as soon as possible unless strict asepsis was used in their insertion. The incidence of infection increases markedly after 5 days and varies with the site of the catheter, with an increasing rate of infection in subclavian, internal jugular, and femoral venous catheters. How long catheters should be left in situ before replacement remains controversial; such decisions must consider the reason for their use and the patient’s clinical state as well the risk involved in placing new catheters. Catheters should not be changed routinely and should be observed daily or until clinical evidence of infection is apparent. The development of persistent...
or new pyrexia, leukocytosis, and an inflamed insertion site indicate catheter sepsis and warrant a new catheter. Semiquantitative culture of the intradermal portion or tip of the catheter may determine whether an infection was present.

**FLUID MANAGEMENT**

The maintenance of a euvoletic state is essential throughout the intensive care period. This is determined by regular measurements, such as serum sodium and osmolality, urea and creatinine, pulse rate, right atrial and mean arterial pressure, and urine output.

Resuscitative fluids depend on local preferences, since there is no evidence to recommend crystalloids over colloids. Similarly, fluids should be titrated to maintain neutral fluid balance and biochemical normality.

Hemoglobin invariably falls following an acute insult. The lower limit of tolerable hemoglobin levels in critically ill patients has been extensively debated, with increasing evidence that a restrictive transfusion strategy (hemoglobin ≤8 g/L) is associated with improved outcomes compared to a more liberal transfusion strategy (hemoglobin <10 g/L). Rather than using an absolute value, acceptance of hemoglobin of 8 to 10 g/L appears to be physiologically appropriate in acutely traumatized patients, although subgroups of patients, such as those with concomitant cardiac disease, may require maintenance of higher hemoglobin levels.

**VASOACTIVE THERAPY**

Catecholamines such as epinephrine, norepinephrine, or dopamine are frequently used to increase mean arterial pressure. Normally these drugs should be used only when volume resuscitation is actively under way or complete. However, the early use of catecholamines is increasingly being advocated to maintain homeostatic systemic pressure, often to counter the depressant cardiovascular effects of acute injury and the effects of sedation and anesthesia. On a pathobiologic basis, catecholamines are essentially used to increase endogenous mechanisms that may be failing, with norepinephrine being regarded as the principal endogenous catecholamine to defend systemic blood pressure.

Except when very small doses of vasoactive drugs are used, the mean arterial pressure of all patients who receive them should be monitored, ideally with an intraarterial catheter referenced to the aortic root. There is no conclusive evidence to recommend one vasoactive agent over another or any combination of vasoactive agents. In clinical practice, epinephrine, norepinephrine, and dopamine are most commonly used. These drugs have similar pharmacodynamic profiles with equivalent effects on mean arterial pressure and cardiac output and without significant changes in systemic vascular resistance. Increases in cardiac output are matched by increased venous return, which results in a pressor effect.

Prediction of the response of an individual to a catecholamine is problematic because inter- and intraindividual responses to inotropic agents may vary markedly. Although norepinephrine is widely used as an initial inotropic agent, epinephrine is still advocated by many as a first-line agent. However, its use may be associated with metabolic side effects such as hyperlactatemia and hyperglycemia, which may complicate metabolic management. There is, however, no evidence that these side effects are associated with morbidity. Although dopamine is a commonly employed inotrope, its use is questioned due to significant neuroendocrine effects, particularly inhibition of posterior pituitary gland function. Furthermore, the use of dopamine is associated with the highest incidence of tachyarrhythmias, which may be important in patients with ischemic heart disease.

Synthetic catecholamines, such as dobutamine, dopexamine, and isoprenaline, and agents such as milrinone and levosimendan offer little advantage over the endogenous catecholamines. These agents are predominantly vasodilators with moderate and unpredictable inotropic activity, particularly in hypovolemic patients.

**Renal Protection**

By increasing mean arterial pressure, vasoactive agents have an important role in preventing or lessening acute renal failure in critically ill patients. This is important in hypertensive patients, in whom higher mean arterial pressure may be required to maintain renal perfusion, particularly when these patients develop intercurrent causes of circulatory failure.

A “renal” dose of dopamine (2 μg/kg/min) has been advocated for many years as a renal-protective agent by causing renal vasodilatation. However, this has not been substantiated in controlled clinical trials in susceptible patients. Its use as an adjunctive agent with other inotropes in septic shock has also not been proven. In addition, the prolonged use of low-dose dopamine is associated with suppression of anterior and posterior pituitary hormonal secretion and impairment in T-cell function. It is therefore no longer recommended. Equivalent renal protection has been demonstrated with dopamine, norepinephrine, and dobutamine; this effect may be primarily due to their effect in sustaining renal perfusion rather than to a specific renal effect.

Diuretics should be used sparingly in traumatized patients. As outlined above, oliguria is a normal response to injury. The injudicious use of diuretics may therefore not only mask this important clinical sign but
also exacerbate hypovolemia. There is no evidence to support the use of diuretics to prevent acute renal failure by inducing polyuria. Indeed, in the hemodynamically unstable patient, the use of diuretics may be regarded as potentially nephrotoxic.

The use of iodinated intravenous contrast media is associated with acute renal dysfunction, particularly in hemodynamically unstable patients. Contrast-induced nephropathy may be minimized by ensuring adequate hemodynamic resuscitation before contrast administration. Renoprotective effects of intravenous N-acetylcysteine or sodium bicarbonate have been described and should be considered in susceptible patients who receive contrast media.

**SIRS and Septic Shock**

The development of high- or low cardiac output shock will occur in a minority of traumatized patients. Noninfective causes of this syndrome include massive blood transfusion, pancreatitis, ischemic colitis, and drug reactions. Infection usually develops 72 h after injury and may be due to infected wounds, intraabdominal or intrathoracic abscesses, or nosocomial sepsis. Regardless of the cause, the hemodynamic management of this syndrome remains essentially the same.

An increasing body of literature now supports the use of norepinephrine and epinephrine as first-line agents in the systemic inflammatory response syndrome and septic shock, since they maintain tissue perfusion by effectively defending cardiac output and mean arterial pressure. Systemic vascular resistance is not significantly altered by catecholamine infusions in septic shock.

Despite their widespread recent use, the efficacy of dobutamine and isoprenaline in septic shock is questionable; it appears to add little to the efficacy of norepinephrine or epinephrine when used in combination. However, the benefit attributable to a particular catecholamine in preventing mortality due to septic shock has not been established.

A proportion of patients with severe septic shock who require high doses of catecholamines to support the circulation will need less of these drugs when treated with infusions of vasopressin (0.04 U/h). This phenomenon appears to be independent of any direct vasopressor effect; rather, it may be due to a supplemental “catecholamine sparing” strategy. However, its impact on mortality has not been determined in conclusive clinical trials.

The role of steroid supplementation in circulatory failure has been studied for many years. Although immunosuppressive or anti-inflammatory doses have been shown to be ineffective, particularly in septic shock, stress response doses (approximately 100 to 200 mg of hydrocortisone per day) have been shown to improve vasoressponsiveness to catecholamines in patients with refractory shock. Patients who respond to low doses of steroids may have biochemical evidence of hypoadrenalism, defined by a low serum cortisol level or a blunted response to intravenous adrenocorticotropic, or functional hypoadrenalism as part of the multiple organ failure syndrome.

**Respiratory Therapy**

**AIRWAY MANAGEMENT**

Patients should remain intubated only as long as necessary. In patients with head injuries, endotracheal intubation may be prolonged due to their slow recovery of consciousness and adequate glottic reflexes.

Endotracheal intubation may be performed either translaryngeally through the nose or mouth or transtracheally via a tracheostomy. The use of polyvinylchloride tubes with low-pressure, high-volume cuffs decreased the incidence of tracheal mucosal damage and ulceration from nasal or oral endotracheal tubes. Consequently the duration of translaryngeal intubation depends on the degree of underlying head injury, preexisting lung reserve, and concomitant lung function.

Oral intubation is the preferred method for emergencies and allows passage of a tube of a larger diameter (8 mm or more) with easier bronchial toilet. These tubes are more prone to movement and are more difficult to secure. The incidence of nosocomial sinusitis is significantly lower with oral intubation. Nasal intubation provides good support for the endotracheal tube and patients often require less sedation to tolerate the tube. Nasal tubes are also less prone to move in the trachea and therefore cause less tracheal mucosal damage than oral tubes. However, suction through these tubes is more difficult owing to the smaller diameter of the tube and the increased distance from the nasal aditus to the end of the tube. Nasal tubes allow patients to swallow their saliva; it is therefore easier to maintain oral hygiene. Nasal intubation is, however, contraindicated in patients with fractures of the basal skull and cribiform plate.

Tracheostomy is generally indicated in patients when prolonged ventilation due to respiratory failure is anticipated for more than 7 to 10 days, or when a return to full consciousness is not expected for weeks or months. These patients usually have poor protective glottic reflexes and inadequate clearance of secretions and are predisposed to recurrent aspiration and nosocomial pneumonia. Tracheostomy tubes are more comfortable than translaryngeal tubes and allow easier trachobronchial toilet. Tubes with a device that directs a stream of retrograde air through the larynx above the cuff site make speech possible in selected patients.

Tracheostomy should be performed only by experienced operators and when pulmonary reserve is adequate.
to tolerate an operation on the airway. In ventilated patients, this means a fractional inspired oxygen concentration of 0.5 or less to achieve a PaO₂ greater than 80 mmHg and peak inflation pressures of less than 30 cmH₂O. Clotting status should be normal.

Tracheostomy may be performed in the operating room or in the ICU. A number of percutaneous dilatational tracheostomy techniques have been described that can be performed in the ICU to avoid moving the patient. These procedures are quick and allow the passage of a normal 8- or 9-mm tube. Tracheal stenosis is a recognized complication of tracheostomy, but its incidence after the percutaneous procedure compared to surgical tracheostomy is unknown.

Irrespective of the route of intubation, cuffed tubes must be inflated sufficiently to seal the airway in order to prevent aspiration. Cuffs may leak due to changing cuff compliance, tracheal dilatation during prolonged intubation, or tube movement. Excess cuff pressure on the tracheal mucosa may predispose to tracheal ulceration and subsequent stenosis. Frequent volumetric cuff checks and cuff pressure measurements should be performed to ensure a safe seal.

Ventilatory Management

The majority of severely traumatized patients will require mechanical ventilation to ensure adequate oxygenation (PaO₂ > 75 mmHg; 10 kPa) and to maintain an arterial carbon dioxide tension between 36 and 40 mmHg (4.5 to 5.0 kPa). The need for normal oxygenation and carbon dioxide must outweigh the potential hazards of ventilation. Advances in the design of mechanical ventilators and an increased awareness of ventilator-induced lung injury and nosocomial pneumonia have improved ventilator and nosocomial pneumonia have improved ventilator methods and made them safer.

Positive-pressure ventilation is the routine form of mechanical ventilation in current practice. Gas is delivered under positive pressure to a preset inspiratory pressure or tidal volume. Mechanical ventilation should be regarded as lung support that is adapted to the individual patient's respiratory condition.

Complete control of ventilation is usually necessary during the resuscitation period. This requires a mode of ventilation that will override the patient's efforts to breathe. When resuscitation has been completed and cardiorespiratory and neurologic stability are achieved, the patient should be allowed to breathe spontaneously with as little respiratory support as possible. The degree of respiratory support will depend on the improvement or resolution of acute traumatic and systemic processes, level of sedation, and preexisting cardiorespiratory disease.

During the initial period when controlled ventilation is desired, modes such as assist or volume or pressure control may be employed. These modes deliver a preset tidal volume, respiratory rate, and inspiratory pressure. At this stage patients are usually heavily sedated or paralyzed with muscle relaxants. For the majority of patients with normal lungs, either mode will suffice to achieve adequate gaseous exchange. However, patients with acute lung injury (e.g., direct lung injury, aspiration pneumonia, fat embolism syndrome, or neurogenic pulmonary edema or those with extensive bodily trauma) are at risk of developing ventilator-induced lung injury. Accordingly, a protective ventilation strategy should be considered.

The distinction between volume- and pressure-based ventilatory modes is less important in modern practice. These modes deliver tidal volumes and inspiratory pressures in what is considered a safe range, which reduces the risk of ventilator-induced lung injury. Central to this strategy is the use of low tidal volumes (5 to 7 mL/kg) and limited peak inspiratory pressures (<35 to 40 cmH₂O). Under these conditions, mechanical ventilation has been shown to improve survival in patients with severe ALI or ARDS. A consequence of this ventilatory strategy is permissive hypercapnia, in which PaCO₂ is allowed to increase, resulting in acute respiratory acidosis (pH 7.1 to 7.2).

Although controlled ventilation is useful in the above situations, deep sedation may be associated with accumulation of secretions, hypostatic and nosocomial pneumonia, gastroparesis, and neuromuscular weakness.

Assisted ventilation should be instituted as soon as possible. This is determined by reducing sedation requirements and allowing the patient to breathe spontaneously, with sufficient mechanical support to maintain gaseous exchange. Modes such as assist control ventilation (ACV), synchronized intermittent mandatory ventilation (SIMV), pressure support ventilation (PSV), and flow-by ventilation are suitable. These modes allow the patient to generate a small negative airway pressure or flow that activates the inspiratory cycle, the duration of which is determined either by a preset tidal volume, the ratio of inspiration to expiration (I:E ratio), or by reaching a pressure limit. The triggering mechanism must be sensitive enough to detect inspiratory efforts of the patient, increasing the work of breathing, but not so sensitive that the ventilator will cycle in response to fluctuations in airway pressure not initiated by the patient.

Weaning from ventilation should start once cardiorespiratory and neurologic homeostasis has been achieved and no major operations are scheduled. The advent of "noninvasive" modes of ventilation (i.e., positive-pressure ventilation without an endotracheal tube), such as biphasic positive-pressure ventilation (BIPAP), or continuous positive airway pressure (CPAP), has greatly facilitated the weaning of ventilated patients. Noninvasive ventilation is particularly useful in patients with postextubation stridor, moderate chronic obstructive airways disease, asthma, atelectasis, or congestive cardiac failure.
Trials of extubation should be carefully considered so that subsequent hypoxic episodes do not occur, as these are potent secondary insults.

**MAINTENANCE OF VENTILATED PATIENTS**

Inspired gases must be humidified for all ventilated patients because the humidifying functions of the nasopharynx are bypassed by endotracheal intubation. Ideally gas should be humidified to 75 to 100% and at a constant temperature (32 to 36°C; 89.6 to 96.8°F) and should not increase work of breathing, dead space, or resistance in either spontaneous or controlled ventilation.

Humidifiers include water baths and aerosol nebulizers or atomizers. Bacterial contamination of water reservoirs, overhydration, overheating, and electrical hazards may complicate the use of these systems. Most of these complications may be avoided by attaching heat and moisture exchangers to the endotracheal tube. These devices provide safe, efficient humidification and may be combined with a bacterial filter.99

Patients with reactive airways due to asthma, chronic airways disease, or acute bronchospasm from infection or pulmonary edema may benefit from nebulization of beta2 agonists, such as salbutamol, to improve gas exchange and reduce inspired airway pressure. The addition of nebulized anticholinergics, such as ipratropium bromide, may be beneficial in patients with severe airflow obstruction, particularly in the weaning phase. The routine use of these agents in ventilated patients has, however, not been shown to be beneficial.

**NOSOCOMIAL PNEUMONIA**

Patients who require prolonged ventilation are susceptible to respiratory infections. During the later stages of trauma management, the lung is vulnerable to nosocomial infection. The causes for this association include reduced airway defense mechanisms due to endotracheal intubation, impaired mucociliary clearance, aspiration pneumonitis, and hematogenous spread of inflammatory and infective mediators to the lung. The resultant nosocomial pneumonia may induce or exacerbate an acute lung injury and increase morbidity and mortality.

Early pneumonia is defined as respiratory infection present or developing soon after intubation and may arise from aspiration of gastric contents or infection of lobar collapses in the acute stages. Late or true ventilator-associated or nosocomial pneumonia is defined as infection that first occurs 48 h after intubation.100

True ventilator-associated pneumonia causes significant morbidity and mortality, particularly in patients who develop an acute lung injury. In patients who need positive-pressure mechanical ventilation for more than 3 days, the incidence of pneumonia has been reported to be 35 to 70 percent. Nosocomial pneumonia prolongs ventilation and ICU stay significantly, although the incidence of mortality attributable to it remains low.101

Several criteria for a clinical diagnosis of nosocomial pneumonia have been reported.102 These include radiographic evidence of a new or progressive pulmonary infiltrate, fever, leukocytosis, and purulent tracheobronchial secretions. In addition to these clinical criteria, a Gram’s stain of the sputum showing >25 polymorphonuclear leukocytes and <10 squamous epithelial cells per low-power field and the presence of a significant pathogen (by stain or culture) has been advocated. In a previously healthy person, these signs almost invariably indicate pneumonia, and treatment with antibiotics should be started as soon as bacterial sensitivities have been established.

Mechanically ventilated patients frequently develop other conditions that obscure these findings or cause a similar clinical picture, which may be due in part to the systemic inflammatory response to acute injury. Moreover, purulent secretions are invariably present in patients on prolonged mechanical ventilation but are not caused by pneumonia in most. Secretions may originate from the sinuses, stomach, or oropharynx and may accumulate above the endotracheal tube cuff and be aspirated by minor manipulation. In addition, the proximal airways of ventilated patients are colonized early by potentially pathogenic organisms.

No combination of clinical variables is completely accurate in predicting pneumonia in ventilated patients. Postmortem studies have shown that pneumonia is underdiagnosed in patients with acute lung injury but overdiagnosed in acute respiratory failure from other causes.100

Mortality rates in patients who received antimicrobial therapy before the onset of pneumonia are significantly lower than in those who did not. However, the overuse of broad-spectrum antibiotics in patients without infection is potentially harmful because it may facilitate colonization and superinfection with highly virulent organisms.105

To improve the recognition of pneumonia and identify the responsible microbes, a number of techniques have been described. Although a culture from lung tissue is regarded as the gold standard in establishing this diagnosis, open lung biopsy is obviously not feasible in all patients. Numerous bronchoscopic and bronchoscopic methods to obtain lower respiratory secretions and various microbiologic analyses have been described but are beyond the scope of this review. Of these, quantitative cultures of tracheal aspirates and nondirected bronchoalveolar lavage are recommended for the majority of patients. Other systemic sources of infection should also be actively sought and treated. The relative risk of investigations must be balanced against the benefit to the patient, particularly when invasive investigations such as bronchoalveolar lavage are considered.
Effective pulmonary toilet, postural drainage, and the prevention of gastric aspiration is essential. Increased sedation may be necessary during tracheal suctioning to prevent sympathetically mediated swings in blood pressure. Antibiotic coverage should use the least toxic bactericidal agent in appropriate doses and should be guided by monitoring its level if necessary. Antibiotics should be used only when the criteria for nosocomial pneumonia are established and bacteriologic cultures are positive. Sensitivity testing is the best guide to antibiotic choice.

**Acute Respiratory Distress Syndrome/Acute Lung Injury**

As outlined above, the hallmarks of this syndrome relate to increased permeability of the alveolar-capillary endothelium.

In traumatized patients, the causes of ALI/ARDS are many and may be considered as direct or indirect insults. It is important to distinguish between these causes, since their outcomes vary. Some patients with ALI/ARDS develop dysfunction or failure of one or more organ systems sequentially or simultaneously. Other patients develop multiple organ failure without ALI/ARDS, although they may have less severe degrees of parenchymal lung injury. This suggests that ALI/ARDS is the respiratory manifestation of multiple organ failure syndrome, just as distributive or septic shock is the cardiovascular manifestation.

The treatment of patients with ALI/ARDS is supportive and aims to maintain oxygenation. The majority—80 percent—of patients with ARDS die from multiple organ failure or sepsis rather than from respiratory impairment. The underlying cause must be treated and suspected sites of sepsis need to be managed with appropriate antibiotics and surgical drainage. Volume- or pressure-limited ventilation and the effective use of positive end-expiratory pressure form the mainstays of support of these patients in the ICU. Techniques such as prone ventilation, extended- or inverse-ratio pressure-control ventilation, and selected pulmonary vasodilators such as nitric oxide and nebulized prostacyclin are used in selected patients. On rare occasions, when survival cannot be sustained with mechanical ventilation, extracorporeal techniques such as extracorporeal membrane oxygenation (ECMO) with or without low-frequency positive-pressure ventilation and extracorporeal removal of carbon dioxide (LPPV-ECCO₂) have been employed with anecdotal success. No conclusive studies have demonstrated improved outcomes in ARDS with these advanced supportive techniques.

The prognosis of ALI/ARDS depends largely on the cause of the insult and the subsequent development of multiple organ failure. Fat embolism syndrome and neurogenic pulmonary edema may cause a severe but transient ALI/ARDS, which is often associated with a good outcome and probably has little influence on mortality. However, other causes, such as gram-negative sepsis and shock states, are associated with a higher incidence of multiple organ failure with an increased mortality rate on the order of 40 to 60 percent.

**Metabolic Management**

Routine measurement of biochemical variables is essential to keep them all within normal limits. Hyperglycemia is common after massive trauma and is usually centrally mediated and transient. Blood sugar levels should be maintained within normal limits with insulin infusions. Recent studies have demonstrated that the strict maintenance of normoglycemia in critically ill patients is associated with improved survival. Blood sugar levels between 4.4 to 6.1 mmol/L are recommended, using infusions of insulin as required. Concomitant administration of 20% dextrose may be necessary to reduce the risk of hypoglycemia, which may go unrecognized in sedated or unconscious patients. Hypoglycemia is a recognized secondary insult and must be avoided.

**Renal Dysfunction**

Renal dysfunction and failure is common after multiple trauma. As outlined above, oliguria is a normal physiologic response to acute injury in the initial period (up to 48 to 72 h following injury). However, in the traumatized patient, oliguria should also be regarded as a cardinal sign of hypovolemia, for which the appropriate initial treatment is a fluid challenge and/or augmentation of mean arterial pressure with a vasoactive agent. In traumatized patients, this forms the vanguard to protect renal homeostasis. In managing acute trauma, one should always consider premorbid renal function and concomitant medications, in particular ACE inhibitors and nonsteroidal anti-inflammatory agents, which may exacerbate acute renal dysfunction. Anuria is uncommon after trauma and should raise the possibility of prerenal vascular disruption or postrenal (ureteric, vesical, or urethral) obstruction. This is highly probable for injuries such as pelvic fractures, retroperitoneal hematoma, or major abdominal vascular injury.

**Rhabdomyolysis**

Patients with significant soft tissue injury—particularly when it is associated with long bone fractures and crush injury, threatened limbs from acute arterial insufficiency, and prolonged immobility—may develop acute renal dysfunction caused by deposition of myoglobin. Although this is a recognized insult, the association between myonecrosis and acute tubular necrosis is tenuous, since the associated renal deficiency is primarily due to hypotension, shock, and hypovolemia. The treatment of acute renal failure associated with crush injury is therefore directed primarily at restoration of hemodynamic...
function rather than the use of specific antidotes to myoglobin deposition. For the latter condition, urinary alkalization and the use of osmotic diuretics has been advocated for many years, although there is little evidence that these agents are effective. These agents should therefore be used carefully so that hemodynamic function is not compromised.

**Abdominal Compartment Syndrome**

Another important and reversible cause of acute renal dysfunction after trauma is the abdominal compartment syndrome. Increased intraabdominal pressure due to excessive bowel distention, intra- or retroperitoneal hematoma, or tense ascites may cause intrinsic and/or extrinsic renal compression. The resultant reduction in renal preload, exaggerated activation of renin, and postrenal compression. This syndrome should be suspected in susceptible patients who develop marked abdominal distention. This may be quantified by measuring intravesical pressures, for which a value of >20 mmHg suggests abdominal compartment syndrome. These clinical signs and measurements may necessitate surgical decompression of the peritoneal cavity.

Acute renal failure that requires dialysis is associated with a high mortality rate (40 to 60 percent). New continuous renal dialysis techniques such as continuous venovenous hemofiltration make it possible to provide prompt and effective dialysis without the hemodynamic and coagulation disturbances that often complicate conventional intermittent hemodialysis. The indications for dialysis in traumatized patients include clinically significant hyperkalemia, symptomatic fluid overload, and azotemia associated with hypercatabolism. There is insufficient evidence to recommend continuous renal dialysis solely to remove unwanted pro- or anti-inflammatory mediators.

**GENERAL HOMEOSTATIC MANAGEMENT**

**Sedation, Analgesia, and Muscle Relaxants**

There are no standards for sedation and analgesia for traumatized patients; protocols will depend on local preferences and resources. The level of sedation and analgesia required for traumatized patients depends on the degree of coma, hemodynamic stability, and associated injuries.

During the resuscitation phase, sedation should be titrated to cause the least effect on systemic blood pressure. During this period, short-acting narcotics such as fentanyl are useful. These agents are relatively cardiotable and have the additional benefit of tempering the systemic sympathetic surges that frequently occur after injury. Intermediate acting muscle relaxants, such as vecuronium, are useful during this phase to control combative patients after intubation, ventilation, and sedation.

During the intensive care phase, requirements for sedation are different. The aim should be to sedate the patient as lightly as possible to allow clinical assessment of neurologic function and to facilitate mechanical ventilation. The level of sedation will depend on the patient's hemodynamic stability and the degree of intracranial pressure. Infusions of narcotic and benzodiazepines (e.g., fentanyl, morphine, and midazolam) are useful in providing moderate to deep levels of sedation and are effective in controlling surges of intracranial pressure. However, these agents may accumulate, resulting in a delay in the return of consciousness; if used for prolonged periods, they may be associated with the emergence of delirium.

The use of propofol as a sole sedating agent has become popular. It provides deep sedation, which is effective in controlling systemic sympathetic swings. It does not accumulate, and its effects are rapidly reversible on cessation, allowing prompt assessment of neurologic status. Propofol should be used with caution in hemodynamically unstable patients, since it is a potent negative inotrope. The prolonged use of propofol is associated with tachyphylaxis and significant caloric loading from the lipid vector. Concerns have been raised about myocardial depression and sudden cardiac death, particularly if large doses are administered. The routine use of muscle relaxants to facilitate sedation is not recommended. Prolonged use of nondepolarizing muscle relaxants is associated with the development of polyneuromyopathy.

**Nutrition**

The caloric needs of traumatized patients must be addressed as soon as possible following resuscitation. Early enteral feeding is recommended.

The placement of nasogastric or enteral feeding tubes in traumatized patients is usually done via the oral route. If the cribriform plate is not fractured, postpyloric tubes via the oral, nasal, or percutaneous route are recommended, since gastroparesis is common after major trauma, particularly if there is intraabdominal injury. Formulated enteral feeds should be started as soon as possible and increased as tolerated to 1 to 2 mL/kg/h to deliver a total caloric intake of 35 to 40 kcal/kg/day.

In patients who cannot be fed enterally within 2 to 5 days of injury or for extended periods (>4 days) due to gastrointestinal pathology, parenteral nutrition may be required. A normal caloric load is administered as dextrose (2 g/kg/day at 4.1 kcal/g) and synthetic amino acids (1 g/kg of protein per day). Intravenous lipid, administered
as an emulsion of fat (2 g/kg/day at 9 kcal/g) may be given as an additional caloric source and to replenish essential fatty acids.

**Stress Ulcer Prophylaxis**

The incidence of gastric erosions and stress ulceration has markedly decreased with better resuscitation and early enteral feeding. Traumatized patients, including those with brain injury or burns, are at no more risk than other critically ill patients for developing stress ulceration. Increased risk factors for gastric bleeding include critically ill patients who require mechanical ventilation for more than 48 h and those with an associated coagulopathy.\(^{111}\)

There is no difference in the efficacy of \(H_2\) antagonists (e.g., ranitidine) or proton-pump inhibitors. These should be used in susceptible patients until enteral feeding is established, after which they may be discontinued. Patients with a history of peptic ulceration should remain on antacid therapy for the duration of the acute phase.

**Thromboprophylaxis**

Traumatized patients, particularly those who require prolonged ventilation and sedation and those with pelvic or lower limb fractures, are at increased risk for developing thromboembolism. For these patients, treatment with fractionated or low-molecular-weight heparins, with or without compression stockings or calf-compressors, should be considered as soon as possible. The use of anticoagulants is, however, contraindicated for 7 to 10 days after injury in patients with intracranial hemorrhage. When intracranial pathology has stabilized, however, prophylactic anticoagulants may be considered, although there are no evidence-based standards for their use.\(^{112}\) As a general rule, anticoagulants should not be used in head-injured patients with destructive intracranial pathology or hemorrhage, until a CT scan shows resolution of these processes.

Frequent surveillance of the iliofemoral veins using Doppler ultrasound in high-risk patients, such as those with pelvic fractures, should be performed. In patients who develop deep venous thrombosis but cannot be treated with anticoagulants, inferior vena caval filters should be considered.

**Patient Transport**

Patients with multiple trauma frequently require transportation for specialized investigations such as computerized tomography, angiography and ultrasound, or for multiple trips to the operating room. The transport of critically ill patients is associated with an increased risk of accidents and adverse events.\(^{113,114}\) These include loss of airway, ventilator malfunction, temporary loss of monitoring, dislodgment of important drains and catheters, and omission of important medications. The urgency of each intended transfer must therefore be considered and transport undertaken only after the patient has been resuscitated and is hemodynamically stable. Appropriately trained personnel should attend all transported patients, particularly when they are hemodynamically unstable but require urgent transportation.

For patients who undergo multidisciplinary surgical procedures, a trauma specialist should be asked to coordinate the procedures so that life- and limb-threatening injuries receive priority. Underpinning this must be the recognition that severely injured patients, particularly those with traumatic brain injury, are vulnerable to potentially damaging secondary insults, and these must be prevented.

**OUTCOMES**

Once the functions of vital organs recover and patients no longer require intensive support, they may be progressively weaned and organ supports removed. During this period patients require the most emotional and psychosocial support, because the period of resuscitation and intensive care is usually associated with profound retrograde amnesia. Rehabilitation as well as physical, occupational, and speech therapy should begin as soon as possible. Although these aspects only become critical after the acute period, they are often key determinants of functional survival.

Deaths from trauma are related to the degree of external force suffered by the patient. The majority of immediate deaths are due to head injury and major vascular disruption. These are usually nonpreventable and account for up to 40 percent of all deaths due to trauma. Early deaths are usually due to hypoxia secondary to airway compromise or exsanguinating hemorrhage. For patients who survive the initial injury and resuscitation, the outcome will largely depend on their injuries, the time taken to reach proper health care, and the adequacy of resuscitation and definitive treatment. Severely traumatized patients without serious brain injuries who are admitted to major hospitals survive in over 90 percent of cases. However, patients admitted to hospitals with head injuries, have a mortality rate of approximately 30 percent. Late deaths are usually due to complications of the primary injury, such as multiple organ failure, infection, and associated morbidities. Indeed, a proportion of these patients will have active treatment limited or withdrawn due to the burden of the acute injury.

Although mortality is often used as a primary measure of outcome for trauma, functional survival, particularly at 6 and 12 months after injury, is regarded as a more appropriate measure of outcome. It depends on
the patient’s underlying reserve and on how well injuries are repaired and heal.

In conclusion, this chapter has taken the reader through a physiologic journey from the moments of injury to recovery from massive multiple trauma. A consistent theme is that assiduous defense of vital-organ oxygenation and perfusion forms the vanguard in the management of these difficult cases. Most resuscitative and acute management strategies have been simplified and directed at augmenting the physiologic responses to injury. Where these responses are intact and the patient is compensating, close observation and preemptive support are often all that is required. When these systems begin to fail, their replacement by treatment becomes the priority, and the patient’s survival will ultimately depend on his or her physiologic reserve.

REFERENCES