CHAPTER

57

Critical Care

KEY CONCEPTS

1. Brain death criteria can be applied only in the absence of hypothermia, hypotension, metabolic or endocrine abnormalities, neuromuscular blockers, or drugs known to depress brain function.
2. Hyperoxia *and* hypoxia are risk factors, but not the primary causes of retinopathy of prematurity (ROP). Neonates' risk of ROP increases with low birth weight and complexity of comorbidities (eg, sepsis).
3. Pressure control ventilation (PCV) is similar to pressure support ventilation in that peak airway pressure is controlled but is different in that a mandatory rate and inspiratory time are selected. As with pressure support, gas flow ceases when the pressure level is reached; however, the ventilator does not cycle to expiration until the preset inspiration time has elapsed.
4. The disadvantage of conventional PCV is that tidal volume (V_T) is not guaranteed (although there are modes in which the consistent delivered pressure of PCV can be combined with a predefined volume delivery).
5. When compared with orotracheal intubation, nasotracheal intubation may be more comfortable for the patient and more secure (fewer instances of accidental extubation).
6. When left in place for more than 2–3 weeks, both orotracheal and nasotracheal tubes predispose patients to subglottic stenosis. If longer periods of mechanical ventilation are necessary, the tracheal tube should generally be replaced by a cuffed tracheostomy tube.
7. The major effect of positive end-expiratory pressure (PEEP) on the lungs is to increase functional residual capacity (FRC). In patients with decreased lung volume, appropriate levels of either PEEP or continuous positive airway pressure (CPAP) will increase FRC and tidal ventilation above closing capacity, will improve lung compliance, and will correct ventilation/perfusion abnormalities.
8. A higher incidence of pulmonary barotrauma is observed with excessive PEEP or CPAP, particularly at levels greater than 20 cm H_2O.
9. Maneuvers that produce sustained maximum lung inflation such as the use of an incentive spirometer can be helpful in inducing cough as well as preventing atelectasis and preserving normal lung volume.
10. While injury from high inspired oxygen concentrations has not been conclusively demonstrated in humans, V_T of 12 mL/kg was associated with greater mortality than V_T of 6 mL/kg and plateau pressure of less than 30 cm H_2O in patients with acute respiratory distress syndrome.

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11. Early elective tracheal intubation is advisable when there are obvious signs of heat injury to the airway.
12. The criteria developed by the Acute Kidney Injury Network are now most often used to stage acute kidney injury (AKI). AKI is diagnosed by documenting an increase in serum creatinine of more than 50%, or an absolute increase of 0.3 mg/dL, and a reduction in urine output to less than 0.5 mL/kg/h for 6 h or longer, with all findings developing over 48 h or less.
13. Age greater than 70 years, corticosteroid therapy, chemotherapy of malignancy, prolonged use of invasive devices, respiratory failure, kidney failure, head trauma, and burns are established risk factors for nosocomial infections.
14. Systemic venodilation and transudation of fluid into tissues result in a relative hypovolemia in patients with sepsis.

Critical care medicine deals with potentially life-threatening illnesses. Anesthesiologists played a major role in developing this multidisciplinary subspecialty. Relative to most other physicians, anesthesiologists have greater expertise in airway management, mechanical ventilation, drug and fluid resuscitation, and advanced monitoring techniques that are central to effective care in critical illness. Moreover, the emphasis in anesthesia on physiology, pathophysiology, and pharmacology, as well as on rapid diagnosis and treatment of acute physiological derangements, provides an excellent foundation for a career in evaluating and treating patients with critical illness. The critical care physician (or "intensivist") also requires broad knowledge that crosses internal medicine, surgery, pediatrics, neurology, emergency medicine, and palliative care. Unlike most subspecialty education, which tends to emphasize a single organ system, intensive care fellowships provide experience in treating patients with systemic inflammatory response syndrome (SIRS) and the related multiple organ dysfunction syndrome (MODS). The American Boards of Anesthesiology, Internal Medicine, Pediatrics, and Surgery, recognizing these requirements, sponsor specialized training for certification in critical care medicine. Clinicians who have such certification are increasingly recognized by multinational corporations and organizations as making important contributions to the outcomes of hospitalized patients.

This chapter provides an abbreviated survey of critical care medicine. Many topics relevant to critical care are covered in other chapters; only important topics not presented elsewhere will be presented.

Economic, Ethical, & Legal Issues in Critical Care

High-quality critical care is very expensive; poor-quality critical care is even more expensive. Intensive care unit (ICU) beds constitute only 10% of all beds in most hospitals yet account for a large fraction of hospital expenditures. If this cost is justified, clear reductions in morbidity or mortality should be readily demonstrable. Unfortunately, confirmatory studies are few and typically flawed by the use of historical controls. A method of reliably identifying those patients who will benefit most from intensive care is needed. Several scoring systems based on the severity of physiological derangements and preexisting health have been used, such as the Acute Physiology and Chronic Health Evaluation (APACHE) and Therapeutic Intervention Scoring System (TISS), but while all reliably identify "sicker" patients none reliably identifies the very sick but recoverable patients for whom intensive care is intended. Survival is generally inversely related to the severity of illness and number of organ systems

ACRONYMS & ABBREVIATIONS

AC	Assist-control (ventilation)
AKI	Acute kidney injury
AMI	Acute myocardial infarction
APACHE	Acute Physiology and Chronic Health Evaluation
APRV	Airway pressure release ventilation
ARDS	Acute respiratory distress syndrome
CMV	Continuous mandatory ventilation
CPAP	Continuous positive airway pressure
CRRT	Continuous renal replacement therapy
EGD	Esophagogastroduodenoscopy
$FENa^+$	Fractional excretion of filtered sodium
F_{IO_2}	Fraction of inspired oxygen
FRC	Functional residual capacity
HFJV	High-frequency jet ventilation
HFV	High-frequency ventilation
I:E	Inspiratory:expiratory (ratio)
ILV	Independent lung ventilation
IMV	Intermittent mandatory ventilation
IPAP	Inspiratory positive airway pressure
MMV	Mandatory minute ventilation
MODS	Multiple organ dysfunction syndrome
P_{plt}	Plateau pressure
PCV	Pressure control ventilation
PEEP	Positive end-expiratory pressure
PSV	Pressure support ventilation
ROP	Retinopathy of prematurity
RSBI	Rapid shallow breathing index
SIMV	Synchronized intermittent mandatory ventilation
SIRS	Systemic inflammatory response syndrome
TISS	Therapeutic Intervention Scoring System
V_D	Volume of distribution
V_T	Tidal volume

affected. The Society of Critical Care Medicine has established Project Impact, a system that allows ICUs to compare their outcomes and the care they provide against a national and international network of ICUs.

ETHICAL & LEGAL ISSUES

The high cost of critical care medicine has led to economic constraints being applied by governments and third-party payers. At the same time an increased awareness of ethical and legal issues has changed the practice of critical care medicine.

Decisions about when to initiate or terminate treatment can be difficult. Generally, any treatment that can reasonably be expected to reverse illness or restore health is justified, whereas withholding that treatment requires specific ethical justification. Conversely, if treatment will definitely not reverse a disease process or restore health, then the decision to initiate such treatment may not be justified and may be unethical. Until recently, nearly all patients in the United States—even those who were clearly about to die—received maximal treatment (sometimes contrary to the patient's or family's wishes) for fear of the possible legal repercussions of withholding treatment. "Heroic" measures such as chest compressions, drug resuscitation, and mechanical ventilation were continued until the patient died. These complex decisions must involve the patient (or guardian) and the family and must be consistent with hospital policies and state and federal law.

Fortunately, legal guidelines for arriving at these decisions are available in nearly all states. Although laws vary from state to state, they tend to be similar. The greatest conundrums relate to withholding treatment and discontinuing artificial life-support systems. Competent patients (ie, individuals who have the capacity to understand and make medical decisions) have the right to refuse treatment and the right to have life-support machines or devices turned off (or not initiated) if and when they so request. Most states allow competent individuals to prepare an advance directive, usually either a living will or a durable power of attorney for health care, to prevent needless prolongation of life if they become incompetent (eg, severe mental disability, vegetative state, or irreversible coma). Withholding treatment or discontinuing life support from patients who do not have advance directives or cannot provide their own consent requires permission of the spouse, guardian, next of kin, or an individual to whom the patient has given power of attorney for health care. In some cases, clarification from the courts may be necessary. "Do Not Resuscitate" (DNR) or "Allow Natural Death" (AND) orders have been upheld by the courts for patients in whom resuscitation offers no hope of curing or

reversing the disease process responsible for imminent death.

Artificial support of ventilation and circulation complicates legal definitions of death. Until recently, most states required only a determination by a physician that irreversible cessation of ventilatory and circulatory function had occurred. All states have added the concept of brain death to that definition, while some states recognize religious exemptions. In New Jersey, for example, physicians cannot declare brain death "if it would violate the personal religious beliefs of the individual." In addition, although brain death can be established in a pregnant woman, the issue of whether life support can be withdrawn remains subject to both ethical and legal debate. There have been a number of cases of women giving birth to a viable baby weeks or months after having been declared brain dead. These cases involve issues of maternal rights, "fetal rights," and paternal rights and have yet to be resolved.

Brain Death

Brain death is defined as irreversible cessation of all brain function. Spinal cord function below C1 may still be present. Establishing brain death relieves the burden on families of unjustifiable hope and prolonged anxiety; it also prevents waste of medical resources, and potentially allows the retrieval of organs for transplantation.

1 Brain death criteria can be applied only in the absence of hypothermia, hypotension, metabolic or endocrine abnormalities, neuromuscular blockers, and drugs known to depress brain function. A toxicology screen is required if sufficient time since admission (at least 3 days) has not elapsed to exclude a drug effect. Moreover, the patient should be observed long enough to establish with reasonable certainty the irreversible nature of the injury. **Generally accepted clinical criteria for brain death include the following:**

1. Coma
2. Absent motor activity, including no decerebrate or decorticate posturing; spinal cord reflexes may be preserved in some patients
3. Absent brainstem reflexes, including no pupillary, corneal, vestibuloocular (caloric), or gag (or cough) reflexes
4. Absence of ventilatory effort, with the arterial CO_2 tension at least 60 mm Hg or 20 mm Hg above the pretest level.

Repeating the examination (not less than 2 h apart) is optional. In the United States the required number of physician observers varies by state (Florida requires two), as does the level of expertise (Virginia requires a neurologist or neurosurgeon to make the determination). The apnea test should be reserved for last because of its detrimental effects on intracranial pressure. Confirmatory test findings that may be helpful but are not required include an isoelectric electroencephalogram, absence of brainstem auditory evoked potentials, and absence of cerebral perfusion as documented by angiographic, transcranial Doppler, or radioisotopic studies.

Respiratory Care

Respiratory care refers both to the delivery of pulmonary therapy and diagnostic tests and to the allied health profession that has become an integral part of cardiopulmonary diagnostics and critical care. Respiratory therapists' scope of practice encompasses medical gas therapy, delivery of aerosolized medications, airway management, mechanical ventilation, positive airway pressure therapy, critical care monitoring, cardiopulmonary rehabilitation, and the application of various techniques collectively termed *chest physiotherapy*. The latter includes administering aerosols, clearing pulmonary secretions, reexpansion of atelectatic lung, and preserving normal lung function postoperatively or during illness. Diagnostic services may include pulmonary function testing, arterial blood gas analysis, electrocardiography testing, and evaluation of sleep-disordered breathing. The majority of respiratory care procedures are based on clinical practice guidelines developed by the American Association for Respiratory Care using best practice/evidence-based medicine criteria.

MEDICAL GAS THERAPY

The therapeutic medical gases include oxygen at ambient or hyperbaric pressure, helium–oxygen mixtures (heliox), and nitric oxide. Oxygen is made available in high-pressure cylinders, via pipeline systems, from oxygen concentrators, as well as in liquid form. Heliox is occasionally used to partially relieve the increased work of breathing due to partial upper airway obstruction. Nitric oxide is administered as a direct, selective pulmonary vasodilator.

The primary goal of oxygen therapy is to prevent or correct hypoxemia or tissue hypoxia. Table 57–1 identifies classic categories of hypoxia. Oxygen therapy alone may not correct either hypoxemia or hypoxia. Continuous positive airway pressure (CPAP) or positive end-expiratory pressure (PEEP) may be required to recruit collapsed alveoli. Patients with profound hypercapnia may require ventilatory assistance. High concentrations of oxygen may be indicated for conditions requiring removal of entrapped gas (eg, nitrogen) from body cavities or vessels. The short-term inhalation of increased concentrations of oxygen is relatively free of complications.

Supplemental oxygen is indicated for adults, children, and infants (older than 1 month) when Pao_2 is less than 60 mm Hg (8 kPa) or Sao_2 or Spo_2 is less than 90% while at rest breathing room air. In neonates, therapy is recommended if Pao_2 is less than 50 mm Hg (6.7 kPa) or Sao_2 is less than 88% (or capillary Po_2 is less than 40 mm Hg [5.3 kPa]). Therapy may be indicated for patients when clinicians suspect (rather than measure) hypoxemia or hypoxia based on a medical history and physical examination. Patients with myocardial infarction, cardiogenic pulmonary edema, acute lung injury, acute respiratory distress syndrome (ARDS), pulmonary fibrosis, cyanide poisoning, or carbon monoxide inhalation all require supplemental oxygen. Supplemental oxygen is given during the perioperative period because general anesthesia commonly causes a decrease in Pao_2 secondary to increased pulmonary ventilation/perfusion mismatching and decreased functional residual capacity (FRC). Supplemental oxygen should be provided before procedures such as tracheal suctioning or bronchoscopy, which commonly cause arterial desaturation. There is evidence that supplemental oxygen is effective in prolonging survival of patients with chronic obstructive pulmonary disease (COPD) whose resting Pao_2 is lower than 60 mm Hg at sea level. Supplemental oxygen therapy also appears to have a mild beneficial effect on the mean pulmonary arterial pressure and subjective indices of patients' dyspnea.

TABLE 57–1 Classification of hypoxias.[1]

Hypoxia	Pathophysiologic Category	Clinical Example
Hypoxic hypoxia	↓ P_{Barom} or ↓ FIO_2 (<0.21) Alveolar hypoventilation Pulmonary diffusion defect Pulmonary $\dot{V}/\dot{Q}$ mismatch R → L shunt	Altitude, O_2 equipment error Drug overdose, COPD exacerbation Emphysema, pulmonary fibrosis Asthma, pulmonary emboli Atelectasis, cyanotic congenital heart disease
Circulatory hypoxia	Reduced cardiac output Microvascular dysfunction	Severe heart failure, dehydration Sepsis, SIRS
Hemic hypoxia	Reduced hemoglobin content Reduced hemoglobin function	Anemias Carboxyhemoglobinemia, methemoglobinemia
Demand hypoxia Histotoxic hypoxia	↑ Oxygen consumption Inability of cells to utilize oxygen	Fever, seizures Cyanide toxicity, ↑TNF, late sepsis

[1] P_{Barom}, barometric pressure; COPD, chronic obstructive pulmonary disease; $\dot{V}/\dot{Q}$, ventilation/perfusion; R → L, right to left; SIRS, systemic inflammatory response syndrome; TNF, tumor necrosis factor.

AMBIENT OXYGEN THERAPY EQUIPMENT

Classifying Oxygen Therapy Equipment

Oxygen given alone or in a gas can be mixed with air as a partial supplement to patients' tidal or minute volume or serve as the entire source of the inspired volume. This approach provides the basis for classifying devices or systems according to their ability to provide adequate flow levels and a range of fraction of inspired oxygen (F_{IO_2}). Other considerations in selecting therapy include patient compliance, the presence and type of artificial airway, and the need for humidification or an aerosol delivery system.

A. Low-Flow or Variable-Performance Equipment

Oxygen (usually 100%) is supplied at a fixed flow that is only a portion of inspired gas. Such devices are usually intended for patients with stable breathing patterns. As ventilatory demands change, variable amounts of room air will dilute the oxygen flow. Low-flow systems are adequate for patients with

- Minute ventilation less than ~8–10 L/min
- Breathing frequencies less than ~20 breaths/min
- Tidal volumes (V_T) less than ~0.8 L
- Normal inspiratory flow (10–30 L/min).

B. High-Flow or Fixed-Performance Equipment

Inspired gas at a preset F_{IO_2} is supplied continuously at high flow or by providing a sufficiently large reservoir of premixed gas. Ideally, the delivered F_{IO_2} is not affected by variations in ventilatory level or breathing pattern. Profoundly dyspneic and hypoxemic patients may need flows of 100% oxygen in excess of 100 L/min. High-flow systems are indicated for patients who require

- Consistent F_{IO_2}
- Large inspiratory flows of gas (>40 L/min).

1. Variable-Performance Equipment (Table 57–2)

Nasal Cannulas

The nasal cannula is available as either a blind-ended soft plastic tube with an over-the-ear head-elastic or dual-flow with under-the-chin lariat adjustment. Sizes appropriate for adults, children, and infants are available. Cannulas are connected to flowmeters with small-bore tubing and can rapidly be placed on most patients. The tension of attachment should be firm yet comfortable enough to avoid pressure sores on the ears, cheeks, and nose. Patients receiving long-term oxygen therapy most commonly use a nasal cannula. The appliance is usually well tolerated, allowing unencumbered speech, eating, and drinking. Cannulas can be combined with spectacle frames for convenience or to improve acceptance by improving cosmesis. Oxygen-conserving cannulas equipped with inlet reservoirs are available for patients receiving long-term oxygen. Since oxygen flows continuously, approximately 80% of the gas is wasted during expiration.

TABLE 57–2 Oxygen delivery devices and systems.

Device/System	Oxygen Flow Rate (L/min)	F_{IO_2} Range
Nasal cannula	1 2 3 4 5–6	0.21–0.24 0.23–0.28 0.27–0.34 0.31–0.38 0.32–0.44
Simple mask	5–6 7–8	0.30–0.45 0.40–0.60
Mask with reservoir	5	0.35–0.50
Partial rebreathing mask-bag	7 15	0.35–0.75 0.65–1.00
Nonrebreathing mask-bag	7–15	0.40–1.00
Venturi mask and jet nebulizer	4–6 (total flow = 15) 4–6 (total flow = 45) 8–10 (total flow = 45) 8–10 (total flow = 33) 8–12 (total flow = 33)	0.24 0.28 0.35 0.40 0.50

There are valved reservoir devices that permit storage of incoming oxygen until inspiration occurs.

The actual F_{IO_2} delivered to adults with nasal cannulas is determined by oxygen flow, nasopharyngeal volume, and the patient's inspiratory flow (which depends both on V_T and inspiratory time). Oxygen from the cannula can fill the nasopharynx after exhalation, yet with inspiration, oxygen and entrained air are drawn into the trachea. The inspired percent oxygen increases by approximately 1–2% (above 21%) per liter of oxygen flow with quiet breathing in adults. Cannulas can be expected to provide inspired oxygen concentrations up to 30–35% with normal breathing and oxygen flows of 3–4 L/min. However, levels of 40–50% can be attained with oxygen flows of greater than 10 L/min for short periods. Flows greater than 5 L/min are poorly tolerated because of the discomfort of gas jetting into the nasal cavity and because of drying and crusting of the nasal mucosa.

Data from "normal-breathing subjects" may not be accurate for acutely ill tachypneic patients. Increasing V_T and reducing inspiratory time will dilute the small flow of oxygen. Different proportions of mouth-only versus nose-only breathing and varied inspiratory flow can alter F_{IO_2} by up to 40%. In clinical practice, flow should be titrated according to vital signs, pulse oximetry, and arterial blood gas measurements. Some patients with COPD tend to hypoventilate with even modest oxygen flows, yet are hypoxemic on room air. They may do well with cannula flows of less than 1–2 L/min.

Pediatric-sized nasal cannulas are available. Special cannulas allow babies to nurse and produce less trauma of the face and nose than oxygen masks. Because of the inherently reduced minute ventilation of infants, flow requirements to the cannula must be proportionately reduced. This generally requires a pressure-compensated flowmeter accurate at delivering oxygen flows in the less than 1–3 L/min range. Hypopharyngeal oxygen sampling from infants breathing with cannulas has demonstrated mean F_{IO_2} of 0.35, 0.45, 0.6, and 0.68 with flows of 0.25, 0.5, 0.75, and 1.0 L/min, respectively.

Nasal Mask

The nasal mask is a hybrid of the nasal cannula and a face mask. It can be applied to the face by either an over-the-ear lariat or a headband strap. The lower edge of the mask's flanges rests on the upper lip, surrounding the external nose. Nasal masks have been shown to provide supplemental oxygen equivalent to the nasal cannula under low-flow conditions for adult patients. The primary advantage of the nasal mask over nasal cannulas appears to be patient comfort. The nasal mask does not produce sores around the external nares and dry oxygen is not "jetted" into the nasal cavity. The nasal mask should be considered if it improves patient comfort and compliance.

"Simple" Oxygen Mask

The "simple" or oxygen mask is a disposable lightweight plastic device that covers both nose and mouth. It has no reservoir bag. Masks are fastened to the patient's face by adjustment of an elastic headband; some manufacturers provide a malleable metal nose-bridge adjustment device. The seal is rarely complete: usually there is "inboard" leaking. Thus, patients receive a mixture of oxygen and secondarily entrained room air. This varies depending on the size of the leak, oxygen flow, and breathing pattern. Some brands of the simple mask connect tubing to a standard tapered fitting; others have a small room air–entrainment hole at the connection.

The body of the mask functions as a reservoir for both oxygen and expired carbon dioxide. A minimum oxygen flow of approximately 5 L/min is applied to the mask to limit rebreathing and the resulting increased respiratory work. Wearing any mask appliance for long periods of time is uncomfortable. Speech is muffled and drinking and eating are difficult.

It is difficult to predict delivered F_{IO_2} at specific oxygen flow rates. During normal breathing, it is reasonable to expect an F_{IO_2} of 0.3–0.6 with flows of 5–10 L/min, respectively. Oxygen levels can be increased with smaller V_T or slower breathing rates. With higher flows and ideal conditions, F_{IO_2} may approach 0.7 or 0.8.

Masks lacking oxygen reservoirs may be best suited for patients who require concentrations of oxygen greater than cannulas provide, yet need oxygen therapy for fairly short periods of time. Examples

would include medical transport or therapy in the postanesthesia care unit or emergency department. It is not the device of choice for patients with severe respiratory disease who are profoundly hypoxemic, tachypneic, or unable to protect their airway from aspiration.

Masks with Gas Reservoirs

Incorporating a gas reservoir is a logical adaptation to the simple mask. Two types of reservoir mask are commonly used: the partial rebreathing mask and the nonrebreathing mask. Both are disposable, lightweight, transparent plastic under-the-chin reservoirs. The difference between the two relates to use of valves on the mask and between the mask and the bag reservoir. Mask reservoirs commonly hold approximately 600 mL or less of gas volume. The phrase "partial rebreather" is used because "part" of the patient's expired V_T refills the bag. Usually that gas is largely dead space that should not result in significant rebreathing of carbon dioxide.

The nonrebreather uses the same basic system as the partial rebreather but incorporates flap-type valves between the bag and mask and on at least one of the mask's exhalation ports. Inboard leaking is common, and room air will enter during brisk inspiratory flows, even when the bag contains gas. The lack of a complete facial seal and a relatively small reservoir influence the delivered oxygen concentration. The key factor in successful application of the masks is to use a sufficiently high flow of oxygen, so that the reservoir bag is at least partially full during inspiration. Typical minimum flows of oxygen are 10–15 L/min. Well-fitting partial rebreathing masks provide a range of F_{IO_2} from 0.35 to 0.60 with oxygen flows up to 10 L/min. With inlet flows of 15 L/min or more and ideal breathing conditions, F_{IO_2} may approach 1.0. Either style of mask is indicated for patients suspected of having significant hypoxemia, with relatively normal spontaneous minute ventilation. Such patients may include victims of trauma, myocardial infarction, or carbon monoxide exposure. Profoundly dyspneic patients with gasping respiration may be served by a fixed-performance, high-flow oxygen system.

2. Fixed-Performance (High-Flow) Equipment

Anesthesia Bag or Bag-Mask-Valve Systems

The basic design follows that of the nonrebreathing reservoir mask but with more "capable" components. Self-inflating bags consist of a roughly 1.5 L bladder, usually with an oxygen inlet reservoir. Anesthesia bags are 1-, 2-, or 3-L non–self-inflating reservoirs with a tailpiece gas inlet. Masks are designed to provide a comfortable leak-free seal for manual ventilation. The inspiratory/expiratory valve systems may vary. The flow to the reservoir should be kept high so that the bags do not deflate substantially. When using an anesthesia bag, operators may frequently have to adjust the oxygen flow and exhaust valve to respond to changing breathing patterns or demands, particularly when maintaining a complete seal between the mask and face is difficult.

The most common systems for disposable and permanent self-inflating resuscitation bags use a unidirectional gas flow. Although these devices offer the potential for a constant F_{IO_2} greater than 0.9, tailpiece inlet valves will not open for a spontaneously breathing patient. Opening the valves requires negative pressure bag recoil after compression. If this situation is not recognized, clinicians might be misled into thinking the patient is receiving a specific concentration of oxygen when this is not the case.

There are limits to the ability of each system to maintain its fixed-performance characteristics. Delivered F_{IO_2} can approach 1.0 with either anesthesia or self-inflating bags. Spontaneously breathing patients are allowed to breathe only the contents of the system if the mask seal is tight and the reservoir is adequately maintained.

Failure to maintain an adequate oxygen supply in the reservoir and inlet flow is a concern. The spring-loaded valve of anesthesia bags must be adjusted to prevent overdistention of the bag. Self-inflating bags look the same whether or not oxygen flow to the unit is adequate, and they will entrain room air into the bag, thus lowering the delivered F_{IO_2}.

Air-Entraining Venturi Masks

The gas delivery approach with air-entraining masks is different than with an oxygen reservoir. The goal is to create an open system with high flow about the nose and mouth, with a fixed F_{IO_2}. Oxygen is directed by small-bore tubing to a mixing jet; the final oxygen concentration depends on the ratio of air drawn in through entrainment ports. Manufacturers have developed both fixed and adjustable entrainment selections over an F_{IO_2} range. Most provide instructions for the operator to set a minimum flow of oxygen. Table 57–3 identifies total flow at various inlet flows and F_{IO_2}.

Despite the high-flow concept, F_{IO_2} can vary up to 6% from the anticipated setting. The air-entraining masks are a logical choice for patients who require greater F_{IO_2} than can be provided by devices such as the nasal cannula. Patients with COPD who tend to hypoventilate with a moderate F_{IO_2} are candidates for the Venturi mask. Clinicians providing oxygen therapy with Venturi masks should be aware of the previously mentioned problems involving the mask itself. F_{IO_2} can increase if the air entrainment ports are obstructed by the patient's hands, bed sheets, or water condensate. Clinicians should encourage the patient and caregivers to keep the mask on the face continuously. Interruption of oxygen is a serious problem in unstable patients with hypoxemia and or hypercarbia.

Direct analysis of the F_{IO_2} during air-entrainment mask breathing is difficult to perform accurately. Arterial blood gas analysis and the patient's respiratory rate should guide clinicians as to whether the patient's demands are being met by the mask's flow. If that occurs, then inlet oxygen flows may need to be increased or an alternate device selected.

TABLE 57–3 Air-entrainment mask input flow versus total flow at varying F_{IO_2}.[1]

F_{IO_2}	Inlet Oxygen Flow (Minimum)	Total Flow (L/min)
0.24	4	97
0.28	6	68
0.3	6	54
0.35	8	45
0.4	12	50
0.5	12	33
0.7	12	19
0.8	12	16
1.0	12	12

[1] F_{IO_2}, fraction of inspired oxygen.

Air-Entraining Nebulizers

Large-volume, high-output or "all-purpose" nebulizers have been used in respiratory care for many years to provide mist therapy with some control of the F_{IO_2}. These units are commonly placed on patients following extubation for their aerosol-producing properties. Like the air-entraining masks, nebulizers use a pneumatic jet and an adjustable orifice to vary entrained air for varying F_{IO_2} levels. Many commercial devices have an inlet orifice diameter that maximally allows only 15 L/min when the source pressure is 50 psi. This means that on the 100% setting (no air entrainment) output flow is only 15 L/min. Only patients breathing at slow rates and small V_T will receive 100% oxygen. This problem has been addressed by the development of high-flow, high-F_{IO_2} nebulizers. For more common applications that use an F_{IO_2} of 0.3–0.5, room air is entrained, reducing the F_{IO_2} and increasing the total flow output to 40–50 L/min.

Knowledge of the air/oxygen ratio and the input flow rate of oxygen allows the total outflow to be calculated. Nebulizer systems can be applied to the patient with many different devices, including aerosol, tracheostomy dome/collar, face tent, and T-piece adapter. These appliances can all be attached via large-bore tubing to the nebulizer. This open system freely vents inspiratory and expiratory gases around the patient's face or out a distal port of a T-piece adapter. Unfortunately, the lack of any valves allows patients to secondarily entrain room air. It is common practice to use either a reservoir bag before the T-piece or a reservoir tube on the distal side of the T-piece to provide a larger volume of gas than

that coming from the nebulizer. A typical concern of those applying air-entrainment aerosol therapy with controlled oxygen concentration is whether the system will provide adequate flow. Clinicians should observe the mist like a tracer to determine adequacy of flow. When a T-piece is used and the visible mist (exiting the distal port) disappears during inspiration, the flow is inadequate.

Another concern in clinical practice is that excess water in the tubing collects and can obstruct gas flow completely or can offer increased resistance to flow. The latter may increase the F_{IO_2} above the desired setting. Other complications include bronchospasm or laryngospasm in some patients as a consequence of airway irritation from sterile water droplets (condensate of the aerosol). In such circumstances, a heated (nonaerosol) humidification system should be substituted.

High-Flow Air–Oxygen Systems

Dual air–oxygen flowmeters and air–oxygen blenders are commonly used for oxygen administration as well as freestanding continuous positive airway pressure (CPAP) and "add-on" ventilator systems. These systems differ from the air-entraining nebulizers, as their total output flows do not diminish at F_{IO_2} greater than 0.4. With these high-flow systems, the total flow to the patient and F_{IO_2} can be set independently to meet patient needs. This can be done using a large reservoir bag or constant flows in the range of 50 to more than 100 L/min. Clinicians can use a variety of appliances with these systems, including aerosol masks, face tents, or well-fitted nonrebreathing system masks with air–oxygen blenders. Face-sealing mask systems can also be constructed with a reservoir bag and a safety valve to allow breathing if the blender fails. The high flows of gas require use of heated humidifiers of the type commonly used on mechanical ventilators. Humidification offers an advantage for patients with reactive airways. Because of the high flows, such systems are used to apply CPAP or BIPAP for spontaneously breathing patients.

Oxygen Hoods

Although many of the devices previously described have pediatric-sized options, many infants and neonates will not tolerate facial appliances. Oxygen hoods cover only the head, allowing access to the child's lower body while still permitting use of a standard incubator or radiant warmer. The hood is ideal for relatively short-term oxygen therapy for newborns and inactive infants. However, for mobile infants requiring longer term therapy, the nasal cannula, face mask, or full-bed enclosure allow for greater mobility.

Normally, oxygen and air are premixed by an air–oxygen blender and passed through a heated humidifier. Nebulizers should be avoided. Most pneumatic jet-type nebulizers create noise levels (>65 dB) that may cause newborn hearing loss, and cold gas can induce an increase in oxygen consumption. Hoods come in different sizes. Some are simple Plexiglas boxes; others have elaborate systems for sealing the neck opening. There is no attempt to completely seal the system, as a constant flow of gas is needed to remove carbon dioxide (minimum flow >7 L/min). Hood inlet flows of 10–15 L/min are adequate for a majority of patients.

Helium–Oxygen Therapy

Helium–oxygen (heliox) mixtures have a notable, yet limited clinical role. In addition to its uses in industry and deep-sea diving, heliox has a number of medical applications. Helium is premixed with oxygen in several standard blends. The most popular mixture is 79%/21% helium–oxygen, which has a density that is 40% that of pure oxygen. Helium–oxygen mixtures are available in large-sized compressed gas cylinders.

In anesthetic practice, pressures needed to ventilate patients with small-diameter tracheal tubes can be substantially reduced when the 79%/21% mixture is used. Heliox can provide patients with upper airway–obstructing lesions (eg, subglottic edema, foreign bodies, and tracheal tumors) with relief from acute distress until more definitive care can be delivered. The evidence is less convincing in treating lower airway obstruction from COPD or acute asthma. Helium mixtures may also be used as the driving gas for small-volume nebulizers in bronchodilator therapy for asthma. However, with heliox, the nebulizer flow needs to be increased to 11 L/min versus the usual 6–8 L/min with oxygen. Patients'

work of breathing can be reduced with heliox as compared to a conventional oxygen/nitrogen gas mixture.

Hyperbaric Oxygen

Hyperbaric oxygen therapy uses a pressurized chamber to expose the patient to oxygen tensions exceeding ambient barometric pressure (at sea level the ambient pressure is 760 mm Hg). With a one-person hyperbaric chamber, 100% oxygen is usually used to pressurize the chamber. Larger chambers allow for the simultaneous treatment of multiple patients and for the presence of medical personnel in the chamber with patients. Multiplace chambers use air to pressurize the chamber, whereas patients receive 100% oxygen by mask, hood, or tracheal tube. Common indications for hyperbaric oxygen include decompression sickness (the "bends"), certain forms of gas embolism, gas gangrene, carbon monoxide poisoning, and treatment of certain wounds.

3. Hazards of Oxygen Therapy

Oxygen therapy can result in both respiratory and nonrespiratory toxicity. Important factors include patient susceptibility, the F_{IO_2}, and duration of therapy.

Hypoventilation

This complication is primarily seen in patients with COPD who have chronic CO_2 retention. These patients develop an altered respiratory drive that becomes at least partly dependent on the maintenance of relative hypoxemia. Elevation of arterial oxygen tension to "normal" can therefore cause severe hypoventilation in these patients. Conversely, stable, spontaneously breathing patients with profound hypercarbia (P_{aCO_2} > 80 mm Hg) who are being supported with supplemental oxygen should not have supplemental oxygen discontinued, even for short intervals. Oxygen therapy can be indirectly hazardous for patients being monitored with pulse oximetry while receiving opioids for pain. Hypoventilation as a consequence of opioids may fail to cause worrisome change in oxygen saturation, despite respiratory rates as infrequent as 2 per minute, delaying the diagnosis.

Absorption Atelectasis

High concentrations of oxygen can cause pulmonary atelectasis in areas of low $\dot{V}/\dot{Q}$ ratios. As nitrogen is "washed out" of the lungs, the lowered gas tension in pulmonary capillary blood results in increased uptake of alveolar gas and absorption atelectasis. If the area remains perfused but nonventilated, the resulting intrapulmonary shunt can lead to progressive widening of the alveolar-to-arterial (A–a) gradient.

Pulmonary Toxicity

Prolonged high concentrations of oxygen may damage the lungs. Toxicity is dependent both on the partial pressure of oxygen in the inspired gas and the duration of exposure. Alveolar rather than arterial oxygen tension is most important in the development of oxygen toxicity. Although 100% oxygen for up to 10–20 h is generally considered safe, concentrations greater than 50–60% are undesirable for longer periods as they may lead to pulmonary toxicity.

Molecular oxygen (O_2) is unusual in that each atom has unpaired electrons. This gives the molecule the paramagnetic property that allows precise measurements of oxygen concentration. Notably, internal rearrangement of these electrons or their interaction with other atoms (iron) or molecules (xanthine) can produce potentially toxic chemical species. Oxygen toxicity is thought to be due to intracellular generation of highly reactive O_2 metabolites (free radicals) such as superoxide and activated hydroxyl ions, singlet O_2, and hydrogen peroxide. A high concentration of O_2 increases the likelihood of generating toxic species. These metabolites are cytotoxic because they readily react with cellular DNA, sulfhydryl proteins, and lipids. Two cellular enzymes, superoxide dismutase and catalase, protect against toxicity by sequentially converting superoxide first to hydrogen peroxide and then to water. Additional protection may be provided by antioxidants and free radical scavengers; however, clinical evidence supporting the use of these agents in preventing pulmonary toxicity is lacking.

In experimental animals oxygen-mediated injury of the alveolar–capillary membrane produces a syndrome that is pathologically and clinically indistinguishable from ARDS. Tracheobronchitis may also be present initially in some patients. Pulmonary O_2 toxicity in newborn infants is manifested as bronchopulmonary dysplasia.

Retinopathy of Prematurity

Retinopathy of prematurity (ROP), formerly termed *retrolental fibroplasia*, is a neovascular retinal disorder that develops in 84% of premature survivors born at less than 28 weeks' gestation. ROP may include disorganized vascular proliferation and fibrosis and may lead to retinal detachment and blindness. ROP resolves in approximately 80% of these cases without visual loss from retinal detachments or scars. ROP was very common in the 1940s–1950s when unmonitored high (>0.5 F_{IO_2}) oxygen was often administered to premature infants. However, it is now known that hyperoxia *and* hypoxia are risk factors, but not the primary causes of ROP. Neonates' risk of ROP increases with low birth weight and complexity of comorbidities (eg, sepsis). In contrast to pulmonary toxicity, ROP correlates better with arterial than with alveolar O_2 tension. The recommended arterial concentrations for premature infants receiving oxygen are 50–80 mm Hg (6.6–10.6 kPa). If an infant requires arterial O_2 saturations of 96%–99% for cardiopulmonary reasons, fear about causing or worsening ROP is not a reason to withhold the oxygen.

Hyperbaric Oxygen Toxicity

The high inspired O_2 tensions associated with hyperbaric O_2 therapy greatly accelerate O_2 toxicity. The risk and expected degree of toxicity are directly related to the pressures used as well as the duration of exposure. Prolonged exposure to O_2 partial pressures in excess of 0.5 atmospheres can cause pulmonary O_2 toxicity. This may present initially with retrosternal burning, cough, and chest tightness and will result in progressive impairment of pulmonary function with continued exposure. Patients exposed to O_2 at 2 atmospheres or greater are also at risk for central nervous system toxicity that may be expressed as behavior changes, nausea, vertigo, muscular twitching, or convulsions.

Fire Hazard

Oxygen vigorously supports combustion. The potential for oxygen enriched gas mixtures to promote fires and explosions is discussed in Chapter 2.

MECHANICAL VENTILATION

Despite early intervention and appropriate respiratory care, patients with critical illness will often require mechanical ventilation. Mechanical ventilation can replace or supplement normal spontaneous ventilation. In most instances, the problem is primarily that of impaired CO_2 elimination (ventilatory failure). In other instances, mechanical ventilation may be used as an adjunct (usually to positive-pressure therapy; see below) in the treatment of hypoxemia. The decision to initiate mechanical ventilation is made on clinical grounds, but certain parameters have been suggested as guidelines (Table 57–4).

Of the two available techniques, positive-pressure ventilation and negative-pressure ventilation, the former has much wider applications and is

TABLE 57–4 Indicators of the need for mechanical ventilation.

Criterion	Measurement
Direct measurement	
Arterial oxygen tension	<50 mm Hg on room air
Arterial CO_2 tension	>50 mm Hg in the absence of metabolic alkalosis
Derived indices	
Pa_{O_2}/F_{IO_2} ratio	<300 mm Hg
$PA–a_{O_2}$ gradient	>350 mm Hg
V_D/V_T	>0.6
Clinical indices	
Respiratory rate	>35 breaths/min
Mechanical indices	
Tidal volume	<5 mL/kg
Vital capacity	<15 mL/kg
Maximum inspiratory force	>−25 cm H_2O (eg, −15 cm H_2O)

almost universally used. Although negative-pressure ventilation does not require tracheal intubation, it cannot overcome substantial increases in airway resistance or decreases in pulmonary compliance, and it also limits access to the patient.

During positive-pressure ventilation, lung inflation is achieved by periodically applying positive pressure to the upper airway through a tight-fitting mask (noninvasive mechanical ventilation) or through a tracheal or tracheostomy tube. Increased airway resistance and decreased lung compliance can be overcome by manipulating inspiratory gas flow and pressure. The major disadvantages of positive-pressure ventilation are altered ventilation-to-perfusion relationships, potentially adverse circulatory effects, and risk of pulmonary barotrauma and volutrauma. Positive-pressure ventilation increases physiological dead space because gas flow is preferentially directed to the more compliant, nondependent areas of the lungs, whereas blood flow (influenced by gravity) favors dependent areas. Reductions in cardiac output are primarily due to impaired venous return to the heart from increased intrathoracic pressure. Barotrauma is closely related to repetitive high peak inflation pressures and underlying lung disease, whereas volutrauma is related to the repetitive collapse and reexpansion of alveoli.

1. Positive-Pressure Ventilators

Positive-pressure ventilators periodically create a pressure gradient between the machine circuit and alveoli that results in inspiratory gas flow. Exhalation occurs passively. Ventilators and their control mechanisms can be powered pneumatically (by a pressurized gas source), electrically, or by both mechanisms. Gas flow is either derived directly from the pressurized gas source or produced by the action of a rotary or linear piston. This gas flow then either goes directly to the patient (single-circuit system) or, as commonly occurs with operating room ventilators, compresses a reservoir bag or bellows that is part of the patient circuit (double-circuit system).

All ventilators have four phases: inspiration, the changeover from inspiration to expiration, expiration, and the changeover from expiration to inspiration (see Chapter 4). These phases are defined by V_T, ventilatory rate, inspiratory time, inspiratory gas flow, and expiratory time.

Classification of Ventilators

The complexity of modern ventilators defies simple classification. Incorporation of microprocessor technology into the newest generation of ventilators has further complicated this task. Nonetheless, ventilators are most commonly classified according to their inspiratory phase characteristics and their method of cycling from inspiration to expiration.

A. Inspiratory Characteristics

Most modern ventilators behave like flow generators. Constant flow generators deliver a constant inspiratory gas flow regardless of airway circuit pressure. Constant flow is produced by the use of either a solenoid (on–off) valve with a high-pressure gas source (5–50 psi) or via a gas injector (Venturi) with a lower-pressure source. Machines with high-pressure gas sources allow inspiratory gas flow to remain constant despite large changes in airway resistance or pulmonary compliance. The performance of ventilators with gas injectors varies more with airway pressure. Nonconstant flow generators consistently vary inspiratory flow with each inspiratory cycle (such as by a rotary piston); a sine wave pattern of flow is typical.

Constant-pressure generators maintain airway pressure constant throughout inspiration and irrespective of inspiratory gas flow. Gas flow ceases when airway pressure equals the set inspiratory pressure. Pressure generators typically operate at low gas pressures (just above peak inspiratory pressure).

B. Cycling (Changeover from Inspiration to Expiration)

Time-cycled ventilators cycle to the expiratory phase once a predetermined interval elapses from the start of inspiration. V_T is the product of the set inspiratory time and inspiratory flow rate. Time-cycled ventilators are commonly used for neonates and in the operating room.

Volume-cycled ventilators terminate inspiration when a preselected volume is delivered. Many adult ventilators are volume cycled but also have

secondary limits on inspiratory pressure to guard against pulmonary barotrauma. If inspiratory pressure exceeds the pressure limit, the machine cycles into expiration even if the selected volume has not been delivered.

Properly functioning volume-cycled ventilators do not deliver the set volume to the patient. A percentage of the set VT is always lost due to expansion of the breathing circuit during inspiration. Circuit compliance is usually about 3–5 mL/cm H_2O; thus, if a pressure of 30 cm H_2O is generated during inspiration, 90–150 mL of the set VT is lost to the circuit. Loss of VT to the breathing circuit is therefore inversely related to lung compliance. For accurate measurement of the exhaled VT, the spirometer must be placed at the tracheal tube rather than the exhalation valve of the ventilator.

Pressure-cycled ventilators cycle into the expiratory phase when airway pressure reaches a predetermined level. VT and inspiratory time vary, being related to airway resistance and pulmonary and circuit compliance. A significant leak in the patient circuit can prevent the necessary rise in circuit pressure and machine cycling. Conversely, an acute increase in airway resistance, or decrease in pulmonary compliance, or circuit compliance (kink) causes premature cycling and decreases the delivered VT. Pressure-cycled ventilators have been most often used for short-term indications (transport).

Flow-cycled ventilators have pressure and flow sensors that allow the ventilator to monitor inspiratory flow at a preselected fixed inspiratory pressure; when this flow reaches a predetermined level (usually 25% of the initial peak mechanical inspiratory flow rate), the ventilator cycles from inspiration into expiration (see the sections on Pressure Support and Pressure Control Ventilation).

C. Microprocessor-Controlled Ventilators

These versatile machines can be set to function in any one of a variety of inspiratory flow and cycling patterns. The microprocessor allows closed-loop control over the ventilator's performance characteristics. Microprocessor-controlled ventilators are the norm in modern critical care units and on newer anesthesia machines.

Ventilatory Modes

Ventilatory mode is defined by the method by which the ventilator cycles from expiration to inspiration as well as whether the patient is able to breathe spontaneously (**Table 57–5** and **Figure 57–1**). Most modern ventilators are capable of multiple ventilatory modes, and some (microprocessor-controlled ventilators) can combine modes simultaneously. Typical ventilatory modes are regulated to deliver a defined VT or a defined maximal inspiratory pressure. Modern ventilators can provide for breaths that are volume-controlled (machine-initiated inspiration stops when the set volume is delivered), volume-assisted (patient-initiated inspiration stops when the set volume is delivered), pressure-controlled (machine-initiated inspiration at a mandatory inspiratory pressure stops after a defined time has elapsed), pressure-assisted (patient-initiated inspiration at a mandatory inspiratory pressure stops after a defined time has elapsed), or pressure-supported (patient-initiated inspiration continues at a mandatory inspiratory pressure until the inspiratory flow declines to a defined value).

A. Continuous Mandatory Ventilation (CMV)

In this mode, the ventilator cycles from expiration to inspiration after a fixed time interval. The interval determines the ventilatory rate. Typical settings on this mode provide a fixed VT and fixed rate (and, therefore, minute ventilation) regardless of patient effort, because *the patient cannot breathe spontaneously*. Settings to limit inspiratory pressure guard against pulmonary barotrauma, and indeed CMV can be provided in a pressure-limited (rather than volume-limited) way. Controlled ventilation is best reserved for patients capable of little or no ventilatory effort. Awake patients with active ventilatory effort require sedation, possibly with muscle paralysis.

B. Assist-Control (AC) Ventilation

Incorporation of a pressure sensor in the breathing circuit of AC ventilators permits the patient's inspiratory effort to be used to trigger inspiration.

TABLE 57–5 Ventilatory modes.[1]

Mode	I to E Cycling				E to I Cycling		Allows Spontaneous Ventilation	Weaning Mode
	Volume	*Time*	*Pressure*	*Flow*	*Time*	*Pressure*		
CMV	+				+			
AC	+				+	+		
IMV	+				+		+	+
SIMV	+				+	+	+	+
PSV				+		+	+	+
PCV			+		+			
MMV							+	
PC-IRV			+		+			
APRV		+			+		+	
HFJV		+			+		+	

[1]CMV, continuous mandatory ventilation; AC, assist-control ventilation; IMV, intermittent mandatory ventilation; SIMV, synchronized intermittent mandatory ventilation; PSV, pressure support ventilation; PCV, pressure control ventilation; MMV, mandatory minute ventilation; IRV, inverse I:E ratio ventilation; APRV, airway pressure release ventilation; HFJV, high-frequency jet ventilation.

A sensitivity control allows selection of the inspiratory effort required. The ventilator can be set for a fixed ventilatory rate, but each patient effort of sufficient magnitude will trigger the set VT. If spontaneous inspiratory efforts are not detected, the machine functions as if in the control mode. Most often, AC ventilation is used in a volume-limited format, but it can also be provided in a pressure-limited way (see below).

C. Intermittent Mandatory Ventilation (IMV)

IMV allows spontaneous ventilation while the patient is on the ventilator. A selected number of mechanical breaths (with fixed VT) is given to supplement spontaneous breathing. At high mandatory rates (10–12 breaths/min), IMV essentially provides all of the patient's ventilation; at low rates (1–2 breaths/min), it provides minimal mechanical ventilation and allows the patient to breathe relatively independently. The VT and frequency of spontaneous breaths are determined by the patient's ventilatory drive and muscle strength. The IMV rate can be adjusted to maintain a desired minute ventilation. IMV has found greatest use as a weaning technique.

Synchronized intermittent mandatory ventilation (SIMV) times the mechanical breath, whenever possible, to coincide with the beginning of a spontaneous effort. Proper synchronization prevents superimposing (stacking) a mechanical breath in the middle of a spontaneous breath, resulting in a very large VT. As with CMV and AC, settings to limit inspiratory pressure guard against pulmonary barotrauma. The advantages of SIMV include patient comfort, and if used for weaning, the machine breaths provide a backup if the patient becomes fatigued. However, if the rate is too low (4 breaths/min), the backup may be too low, particularly for weak patients who may not be able to overcome the added work of breathing during spontaneous breaths.

IMV circuits provide a continuous supply of gas flow for spontaneous ventilation between mechanical breaths. Modern ventilators incorporate SIMV into their design, but older models must be modified by a parallel circuit, a continuous flow system, or a demand

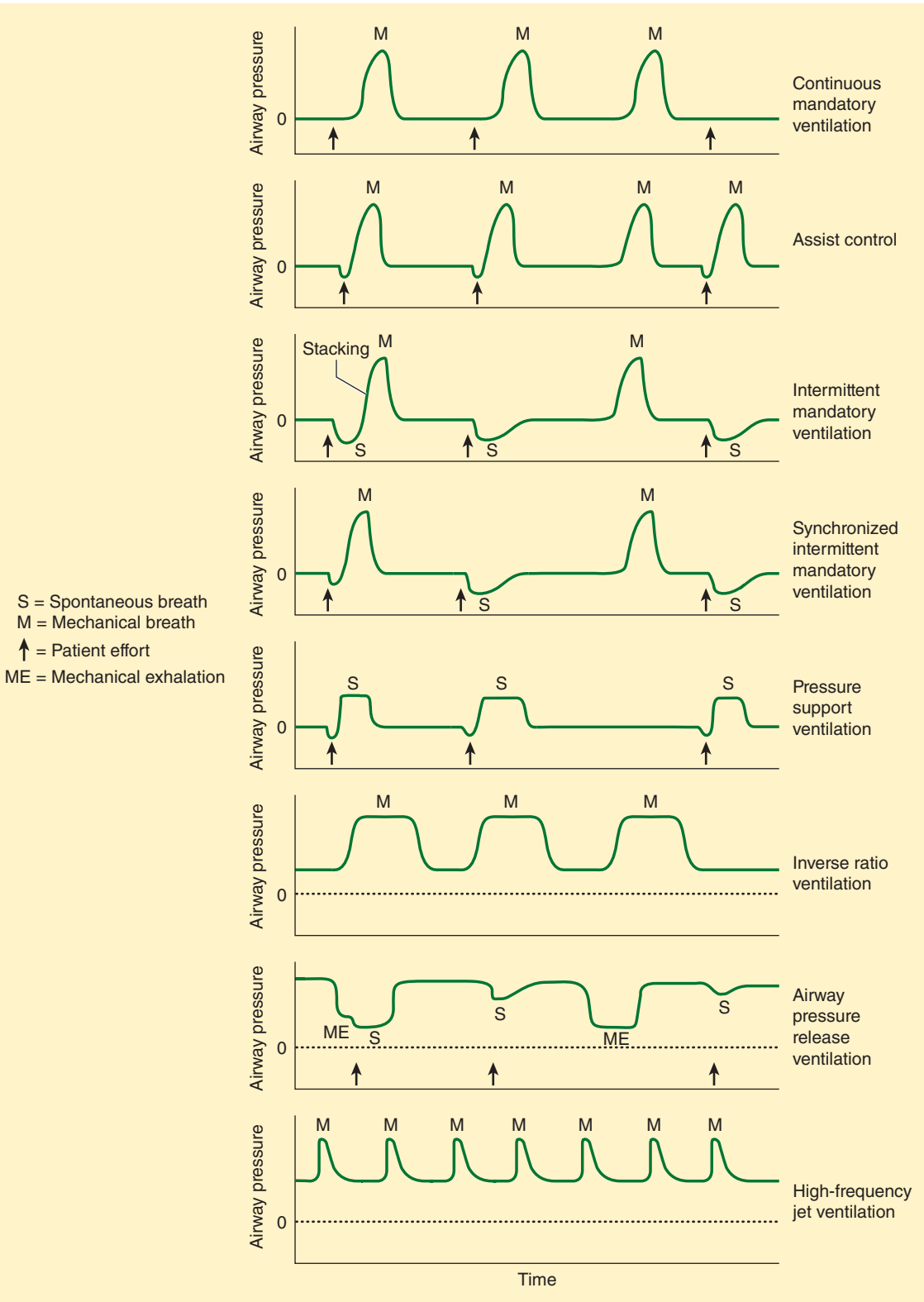

FIGURE 57–1 Airway pressure waveforms of ventilatory modes.

flow valve. Regardless of the system, proper functioning of one-way valves and sufficient gas flow are necessary to prevent an increase in the patient's work of breathing, particularly when PEEP is also used.

The IMV discussion has considered this to be a volume-limited format; however, it can also be provided in pressure-limited format if desired (see below).

D. Mandatory Minute Ventilation (MMV)

With MMV, the patient is able to breathe spontaneously (with pressure support) and also receive SIMV mechanical breaths, while the machine monitors the exhaled minute ventilation. In this mode, the machine continuously adjusts the number of SIMV mechanical breaths so that the sum total of spontaneous and mechanical ventilation equals the desired set minute ventilation. The role of this mode in weaning remains to be defined.

E. Pressure Support Ventilation (PSV)

Pressure support ventilation was designed to augment the V_T of spontaneously breathing patients and overcome any increased inspiratory resistance from the tracheal tube, breathing circuit (tubing, connectors, and humidifier), and ventilator (pneumatic circuitry and valves). Microprocessor-controlled machines have this mode, which delivers sufficient gas flow with every inspiratory effort to maintain a predetermined positive pressure throughout inspiration. When inspiratory flow decreases to a predetermined level, the ventilator's feedback (servo) loop cycles the machine into the expiratory phase, and airway pressure returns to baseline (Figure 57–2). The only setting in this mode is inspiratory pressure. The patient determines the respiratory rate and V_T varies according to inspiratory gas flow, lung mechanics, and the patient's own inspiratory effort. Low levels of PSV (5–10 cm H_2O) are usually sufficient to overcome any added resistance imposed by the breathing apparatus. Higher levels (10–40 cm H_2O) can function as a standalone ventilatory mode if the patient has sufficient spontaneous ventilatory drive and stable lung mechanics. The principal advantages of PSV are its ability to augment spontaneous V_T, decrease the work of breathing, and increase patient comfort. However, if the patient fatigues or lung mechanics change, V_T may be inadequate, and there is no backup rate if the patient's intrinsic respiratory rate decreases or the patient becomes apneic. Pressure support is often used in conjunction with IMV (Figure 57–3). The IMV machine breaths provide backup, and a low level of pressure support is used to offset the increased work of breathing resulting from the breathing circuit and machine.

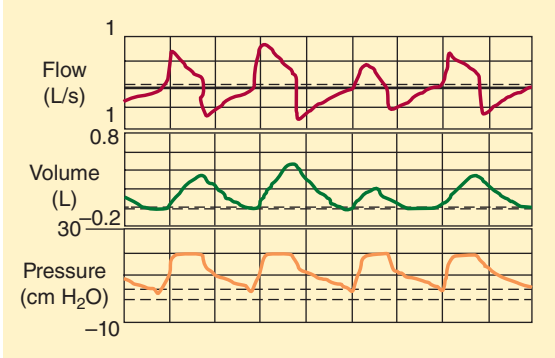

FIGURE 57–2 Pressure support ventilation. The patient initiates a breath; the machine is set to deliver 15 cm H_2O pressure (above 5 cm H_2O of continuous positive airway pressure [CPAP]). When flow ceases, the machine cycles into the expiratory mode.

F. Pressure Control Ventilation (PCV)

3 Pressure control ventilation is similar to PSV in that peak airway pressure is controlled but is different in that a mandatory rate and inspiratory

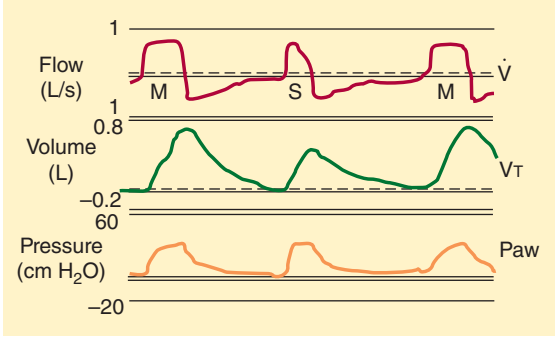

FIGURE 57–3 Intermittent mechanical ventilation with pressure support. M = machine breath → set tidal volume (V_T) delivered. S = spontaneous breath, 15 cm of pressure support over 5 cm of PEEP. V_T depends on patient effort and lung mechanics. V, flow; Paw, partial airway pressure; PEEP, positive end-expiratory pressure.

time are selected. As with pressure support, gas flow ceases when the pressure level is reached; however, the ventilator does not cycle to expiration until the preset inspiration time has elapsed. PCV may be used in both the AC and IMV modes. In AC, all breaths (either machine initiated or patient initiated) are time cycled and pressure limited. In IMV, machine-initiated breaths are time cycled and pressure limited. The patient may breathe spontaneously between the set rate, and the VT of the spontaneous breaths is determined by the patient's pulmonary muscle strength. The advantage of PCV is that by limiting inspiratory pressure, the risks of barotrauma and volutrauma may be decreased. Also, by extending inspiratory time, better mixing and recruitment of collapsed or flooded alveoli may be achieved, provided adequate PEEP levels are used.

4 The disadvantage of conventional PCV is that VT is not guaranteed (although there are modes in which the consistent delivered pressure of PCV can be combined with a predefined volume delivery). Any change in compliance or resistance will affect the delivered VT. This is a major issue in patients with acute lung injury because if the compliance decreases and the pressure limit is not increased, adequate VT may not be attained. PCV has been used for patients with acute lung injury or ARDS, often with a prolonged inspiratory time or inverse I:E ratio ventilation (IRV) (see below) in an effort to recruit collapsed and flooded alveoli. The disadvantage of using IRV with PCV is that the patient needs to be heavily sedated and often paralyzed to tolerate this particular ventilatory mode.

With PCV, pressure and inspiratory time are preset, whereas airflow and volume are variable and dependent on the patient's resistance and compliance. With volume ventilation, on the other hand, inspiratory time is also preset but flow and VT are also preset, and in this circumstance the inspiratory pressure can be very high.

G. Inverse I:E Ratio Ventilation (IRV)

IRV reverses the normal inspiratory:expiratory time ratio of 1:3 or greater to a ratio of greater than 1:1. This may be achieved by adding an end-inspiratory pause, by decreasing peak inspiratory flow during volume-cycled ventilation (CMV), or by setting an inspiratory time such that inspiration is longer than expiration during PCV (PC-IRV). Intrinsic PEEP may be produced during IRV and is caused by air trapping or incomplete emptying of the lung to the baseline pressure prior to the initiation of the next breath. This air trapping increases FRC until a new equilibrium is reached. This mode does not allow spontaneous breathing and requires heavy sedation or neuromuscular blockade. IRV with PEEP is effective for improving oxygenation in patients with decreased FRC.

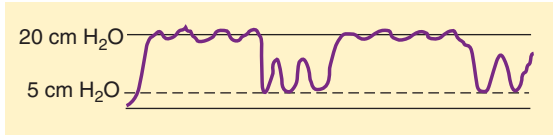

FIGURE 57–4 Airway pressure release ventilation.

H. Airway Pressure Release Ventilation (APRV)

APRV or bilevel ventilation is a mode in which a relatively high PEEP is used, despite the patient being allowed to breathe spontaneously. Intermittently, the PEEP level decreases to help augment the elimination of CO_2 (**Figure 57–4**). The inspiratory and expiratory times, high and low PEEP levels, and spontaneous respiratory activity determine minute ventilation. Initial settings include a minimum PEEP of 10–12 cm H_2O and a release level of 5–10 cm H_2O. Advantages of APRV appear to be less circulatory depression and pulmonary barotrauma as well as less need for sedation. This technique appears to be an attractive alternative to PC-IRV for overcoming problems with high peak inspiratory pressures in patients with reduced lung compliance.

I. High-Frequency Ventilation (HFV)

Three forms of HFV are available. High-frequency positive-pressure ventilation involves delivering a small "conventional" VT at a rate of 60–120 breaths/min. High-frequency jet ventilation (HFJV) utilizes a small cannula at or in the airway through which a pulsed jet of high-pressure gas is delivered at a set frequency of 120–600 times/min (2–10 Hz). The jet of gas may entrain air (Bernoulli effect), which may augment VT. High-frequency oscillation employs a

driver (usually a piston) that creates to-and-fro gas movement in the airway at rates of 180–3000 times/min (3–50 Hz).

These forms of ventilation all produce VT at or below anatomic dead space. The exact mechanism of gas exchange is unclear but is probably a combination of effects (including convective ventilation, asymmetrical velocity profiles, Taylor dispersion, pendelluft, molecular diffusion, and cardiogenic mixing). Jet ventilation has found widest use in the operating room. It may be used for laryngeal, tracheal, and bronchial procedures and can be lifesaving in emergency airway management when tracheal intubation and conventional positive-pressure ventilation are unsuccessful (see Chapter 19). In the ICU, HFJV may be useful in managing some patients with bronchopleural and tracheoesophageal fistulas when conventional ventilation has failed. Occasionally, HFJV or high-frequency oscillation is used in patients with ARDS to try to improve oxygenation. Inadequate heating and humidification of inspired gases during prolonged HFV, however, can be a problem. Initial settings for HFJV in the operating room are typically a rate of 120–240 breaths/min, an inspiratory time of 33%, and a drive pressure of 15–30 psi. Mean airway pressure should be measured in the trachea at least 5 cm below the injector to avoid an artifactual error from gas entrainment. Carbon dioxide elimination is generally increased by increasing the drive pressure, whereas adequacy of oxygenation relates to the mean airway pressure. An intrinsic PEEP effect is seen during HFJV at high drive pressures and inspiratory times greater than 40%.

J. Differential Lung Ventilation

This technique, also referred to as independent lung ventilation, may be used in patients with severe unilateral lung disease or those with bronchopleural fistulae. Use of conventional positive-pressure ventilation and PEEP in such instances can aggravate ventilation/perfusion mismatching or, in patients with fistula, result in inadequate ventilation of the unaffected lung. In patients with restrictive disease of one lung, overdistention of the normal lung can lead to worsening hypoxemia or barotrauma. After separation of the lungs with a double-lumen tube, positive-pressure ventilation can be applied to each lung independently using two ventilators. When two ventilators are used, the timing of mechanical breaths is often synchronized, with one ventilator, the "master," setting the rate for the "slave" ventilator.

2. Care of Patients Requiring Mechanical Ventilation

Tracheal Intubation

Tracheal intubation for mechanical ventilation is most commonly undertaken in ICU patients to manage pulmonary failure. Both nasotracheal and orotracheal intubation appear to be relatively safe for at least 2–3 weeks. When compared with orotracheal intubation, nasotracheal intubation may be more comfortable for the patient and more secure (fewer instances of accidental extubation). Nasal intubation, however, has significant adverse events associated with its use, including nasal bleeding, transient bacteremia, submucosal dissection of the nasopharynx or oropharynx, and sinusitis or otitis media (from obstruction of sinus outflow or of the auditory tubes). Nasal intubation will also generally necessitate use of a smaller diameter tube than orotracheal intubation, and this can make it more difficult to clear secretions and can limit fiberoptic bronchoscopy to use of smaller devices.

Intubation usually can be carried out without the use of sedation or muscle paralysis in agonal and unconscious patients. However, topical anesthesia of the airway and sedation are helpful in patients who still have active airway reflexes. More vigorous and uncooperative patients require varying degrees of sedation; administration of a paralytic agent also greatly facilitates orotracheal intubation. Small doses of relatively short-acting agents are generally used; popular agents include midazolam, etomidate, dexmedetomidine, and propofol. Succinylcholine or a nondepolarizing neuromuscular blocker can be used for paralysis after a hypnotic is given.

The time of tracheal intubation and initiation of mechanical ventilation can be a period of great hemodynamic instability. Hypertension or hypotension and bradycardia or tachycardia may be encountered.

Responsible factors include activation of autonomic reflexes from stimulation of the airway, myocardial depression and vasodilation from sedative-hypnotic agents, straining by the patient, withdrawal of intense sympathetic activity, and reduced venous return due to positive pressure in the airways. Careful monitoring is required during and immediately following intubation.

6 When left in place for more than 2–3 weeks, both orotracheal and nasotracheal tubes predispose patients to subglottic stenosis. If longer periods of mechanical ventilation are necessary, the tracheal tube should generally be replaced by a cuffed tracheostomy tube. If it is anticipated that a tracheal tube will be required for more than 2 weeks, a tracheostomy may be performed soon after intubation. There is a trend to earlier tracheostomy in victims of trauma, particularly those with major head injuries. While earlier tracheostomy does not reduce mortality, it does tend to reduce the incidence of pneumonia, the duration of mechanical ventilation, and the length of stay.

Initial Ventilator Settings

Depending on the type of pulmonary failure, mechanical ventilation is used to provide either partial or full ventilatory support. For full ventilatory support, CMV, AC, or PCV is generally employed with a respiratory rate of 10–12 breaths/min and a V_T of 8–10 mL/kg; lower V_T (6–8 mL/kg) may be necessary to avoid high peak inflation pressures (>35–40 cm H_2O) and pulmonary barotrauma and volutrauma. High airway pressures that overdistend alveoli (transalveolar pressure >35 cm H_2O) have been shown experimentally to promote lung injury. Likewise, compared with a V_T of 12 mL/kg, a V_T of 6 mL/kg and plateau pressure (P_{plt}) less than 30 cm H_2O have been associated with reduced mortality in patients with ARDS. Partial ventilatory support is usually provided by low SIMV settings (<8 breaths/min), either with or without pressure support. Lower P_{plt} (<20–30 cm H_2O) can help preserve cardiac output, may be less likely to alter normal ventilation/perfusion relationships, and is the current recommendation.

Patients breathing spontaneously on SIMV must overcome the additional resistances of the tracheal tube, demand valves, and breathing circuit of the ventilator. These imposed resistances increase the work of breathing. Smaller tubes (<7.0 mm i.d. in adults) increase resistance and should be avoided whenever possible. The simultaneous use of pressure support of 5–15 cm H_2O during SIMV can compensate for tube and circuit resistance.

The addition of 5–8 cm H_2O of PEEP during positive-pressure ventilation preserves FRC and gas exchange. This "physiological" PEEP is purported to compensate for the loss of a similar amount of intrinsic PEEP (and decrease in FRC) in patients following tracheal intubation. Periodic sigh breaths (large V_T) are not necessary when a PEEP of 5–8 cm H_2O accompanies V_T of appropriate volumes.

Sedation & Paralysis

Sedation and paralysis may be necessary in patients who become agitated and "fight" the ventilator. Repetitive coughing ("bucking") and straining can have adverse hemodynamic effects, can interfere with gas exchange, and may predispose to pulmonary barotrauma and self-inflicted injury. Sedation with or without paralysis may also be desirable when patients continue to be tachypneic despite high mechanical respiratory rates (>16–18 breaths/min).

Commonly used sedatives include opioids (morphine or fentanyl), benzodiazepines (usually midazolam), propofol, and dexmedetomidine. These agents may be used alone or in combination and are often administered by continuous infusion. Nondepolarizing paralytic agents are used in combination with sedation when sedation alone and all other means to ventilate the patient have failed.

Monitoring

Patients on mechanical ventilation require continuous monitoring for adverse hemodynamic and pulmonary effects from positive pressure in the airways. Continuous electrocardiography and pulse oximetry are useful. Direct intraarterial pressure monitoring also allows frequent sampling of arterial blood for respiratory gas analysis (both a convenience and a disadvantage, given the large number of unnecessary laboratory tests that are often performed on patients with critical illness). Accurate recording of fluid intake and output is necessary to assess fluid

balance. An indwelling urinary catheter will lead to an increased risk of urinary tract infections and should be avoided when possible, but it is helpful for monitoring urinary output. Central venous (and rarely pulmonary artery) pressure monitoring are used in hemodynamically unstable patients. Frequent chest radiographs are commonly obtained to confirm tracheal tube and central venous catheter positions, evaluate for evidence of pulmonary barotrauma or pulmonary disease, and determine whether there are signs of pulmonary edema.

Airway pressures (baseline, peak, plateau, and mean), inhaled and exhaled VT (mechanical and spontaneous), and fractional concentration of oxygen should be closely monitored. Monitoring these parameters not only allows optimal adjustment of ventilator settings but helps detect problems with the tracheal tube, breathing circuit, and ventilator. For example, an increasing P_{plt} for a set VT can indicate worsening compliance. A declining blood pressure and increasing P_{plt} from dynamic hyperinflation (autoPEEP) can be quickly diagnosed by disconnecting the patient from the ventilator. Inadequate suctioning of airway secretions and the presence of large mucus plugs are often manifested as increasing peak inflation pressures (a sign of increased resistance to gas flow) and decreasing exhaled VT. An abrupt increase in peak inflation pressure together with sudden hypotension strongly suggests a pneumothorax.

3. Discontinuing Mechanical Ventilation

There are two phases to discontinuing mechanical ventilation. In the first, "readiness testing," so-called weaning parameters and other subjective and objective assessments are used to determine whether the patient can sustain progressive withdrawal of mechanical ventilator support. The second phase, "weaning" or "liberation," describes the way in which mechanical support is removed.

Readiness testing should include determining whether the process that necessitated mechanical ventilation has been reversed or controlled. Complicating factors such as bronchospasm, heart failure, infection, malnutrition, metabolic acidosis or alkalosis, anemia, increased CO_2 production due to increased carbohydrate loads, altered mental status, and sleep deprivation should be adequately treated. Underlying lung disease and respiratory muscle wasting from prolonged disuse often complicate weaning. Patients who fail to wean despite apparent readiness often have COPD or chronic heart failure.

Weaning (or liberation) from mechanical ventilation should be considered when patients no longer meet general criteria for mechanical ventilation (see Table 57–4). In general, this occurs when patients have a pH greater than 7.25, show adequate arterial oxygen saturation while receiving FIO_2 less than 0.5, are able to spontaneously breathe, are hemodynamically stable, and have no current signs of myocardial ischemia. Additional mechanical indices have also been suggested (**Table 57–6**). Useful weaning parameters include arterial blood gas tensions, respiratory rate, and rapid shallow breathing index (RSBI, see below). Intact airway reflexes and a cooperative patient are also mandatory prior to completion of the weaning and extubation unless the patient will retain a cuffed tracheostomy tube. Similarly, adequate oxygenation (arterial oxygen saturation >90% on 40–50% O_2 with <5 cm H_2O of PEEP) is imperative prior to extubation. When the patient is weaned from mechanical ventilation and extubation is planned, the RSBI is frequently used to help predict who can be successfully weaned from mechanical ventilation and extubated. With the patient breathing spontaneously on a T-piece, the VT (in liters) and respiratory rate (f) are measured:

$$\text{RSBI} = \frac{f(\text{breaths/min})}{\text{VT(L)}}$$

TABLE 57–6 Mechanical criteria for weaning/extubation.

Criterion	Measurement
Inspiratory pressure	<–25 cm H_2O
Tidal volume	>5 mL/kg
Vital capacity	>10 mL/kg
Minute ventilation	<10 mL
Rapid shallow breathing index	<100

Patients with an RSBI less than 100 can be successfully extubated. Those with an RSBI greater than 120 should retain some degree of mechanical ventilator support.

The common techniques to wean a patient from the ventilator include SIMV, pressure support, or periods of spontaneous breathing alone on a T-piece or on low levels of CPAP. Mandatory minute ventilation has also been suggested as an ideal weaning technique, but experience with it is limited. Finally, many institutions use "automated tube compensation" to provide just enough pressure support to compensate for the resistance of breathing through an endotracheal tube. Newer mechanical ventilators have a setting that will automatically adjust gas flows to make this adjustment. In practice in adults breathing through conventionally sized tubes (7.5–8.5), the adjustment will typically amount to pressure support of 5 cm H_2O and PEEP of 5 cm H_2O.

Weaning with SIMV

With SIMV the number of mechanical breaths is progressively decreased (by 1–2 breaths/min) as long as the arterial CO_2 tension and respiratory rate remain acceptable (generally <45–50 mm Hg and <30 breaths/min, respectively). If pressure support is concomitantly used, it should generally be reduced to 5–8 cm H_2O. In patients with acid–base disturbances or chronic CO_2 retention, arterial blood pH (>7.35) is more useful than CO_2 tension. Blood gas measurements can be checked after a minimum of 15–30 min at each setting. When an IMV of 2–4 breaths is reached, mechanical ventilation is discontinued if arterial oxygenation remains acceptable.

Weaning with PSV

Weaning with PSV alone is accomplished by gradually decreasing the pressure support level by 2–3 cm H_2O while V_T, arterial blood gas tensions, and respiratory rate are monitored (using the same criteria as for IMV). The goal is to try to ensure a V_T of 4–6 mL/kg and an *f* of less than 30 with acceptable Pao_2 and $Paco_2$. When a pressure support level of 5–8 cm H_2O is reached, the patient is considered weaned.

Weaning with a T-Piece or CPAP

T-piece trials allow observation while the patient breathes spontaneously without any mechanical breaths. The T-piece attaches directly to the tracheal tube or tracheostomy tube and has corrugated tubing on the other two limbs. A humidified oxygen–air mixture flows into the proximal limb and exits from the distal limb. Sufficient gas flow must be given in the proximal limb to prevent the mist from being completely drawn back at the distal limb during inspiration; this ensures that the patient is receiving the desired oxygen concentration. The patient is observed closely during this period; obvious new signs of fatigue, chest retractions, tachypnea, tachycardia, arrhythmias, or hypertension or hypotension should terminate the trial. If the patient appears to tolerate the trial period and the RSBI is less than 100, mechanical ventilation can be discontinued permanently. If the patient can also protect and clear the airway, the tracheal tube can be removed.

If the patient has been intubated for a prolonged period or has severe underlying lung disease, sequential T-piece trials may be necessary. Periodic trials of 10–30 min are initiated and progressively increased by 5–10 min or longer per trial as long as the patient appears comfortable and maintains acceptable arterial blood gas measurements.

Many patients develop progressive atelectasis during prolonged T-piece trials. This may reflect the absence of a normal "physiological" PEEP when the larynx is bypassed by a tracheal tube. If this is a concern, spontaneous breathing trials on low levels (5 cm H_2O) of CPAP can be tried. The CPAP helps maintain FRC and prevent atelectasis.

POSITIVE AIRWAY PRESSURE THERAPY

Positive airway pressure therapy can be used in patients who are breathing spontaneously as well as those who are mechanically ventilated. The principal indication for positive airway pressure therapy is a decrease in FRC resulting in absolute or relative hypoxemia. By increasing transpulmonary distending pressure, positive airway pressure therapy can increase FRC, improve (increase) lung compliance,

and reverse ventilation/perfusion mismatching. Improvement in the latter parameter will show as a decrease in venous admixture and an improvement in arterial O_2 tension.

Positive End-Expiratory Pressure

Application of positive pressure during expiration as an adjunct to a mechanically delivered breath is referred to as PEEP. The ventilator's PEEP valve provides a pressure threshold that allows expiratory flow to occur only when airway pressure exceeds the selected PEEP level.

Continuous Positive Airway Pressure

Application of a positive-pressure threshold during both inspiration and expiration with spontaneous breathing is referred to as CPAP. Constant levels of pressure can be attained only if a high-flow (inspiratory) gas source is provided. When the patient does not have an artificial airway, tightly fitting full-face masks, nasal masks, nasal "pillows" (ADAM circuit), or nasal prongs (neonatal) can be used. Because of the risks of gastric distention and regurgitation, CPAP masks should be used only on patients with intact airway reflexes and with CPAP levels less than 15 cm H_2O (less than lower esophageal sphincter pressure in normal persons). Expiratory pressures above 15 cm H_2O require an artificial airway.

CPAP versus PEEP

The distinction between PEEP and CPAP is often blurred in the clinical setting because patients may breathe with a combination of mechanical and spontaneous breaths. Therefore, the two terms are often used interchangeably. In the strictest sense, "pure" PEEP is provided as a ventilator-cycled breath. In contrast, a "pure" CPAP system provides only sufficient continuous or "on-demand" gas flows (60–90 L/min) to prevent inspiratory airway pressure from falling perceptibly below the expiratory level during spontaneous breaths (**Figure 57–5**). Some ventilators with demand valve–based CPAP systems may not be adequately responsive and result in increased inspiratory work of breathing.

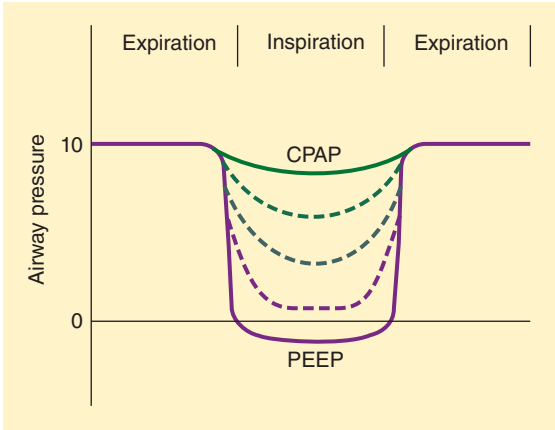

FIGURE 57–5 Airway pressure during positive end-expiratory pressure (PEEP) and continuous positive airway pressure (CPAP). Note that by increasing inspiratory gas flows, PEEP progressively becomes CPAP.

This situation can be corrected by adding low levels of (inspiratory) PSV if in a volume-targeted mode or changing to a pressure-targeted mode. In clinical practice, controlled ventilation, PSV, and CPAP/PEEP support can be delivered by most modern ICU ventilators. Manufacturers have also developed specific devices to deliver bilevel inspiratory positive airway pressure (IPAP) with expiratory positive airway pressure (EPAP) in either a spontaneous or time-cycled fashion. The term *bilevel positive airway pressure* (BiPAP) has become a commonly used phrase, adding to the confusion of airway pressure terminology.

Pulmonary Effects of PEEP & CPAP

7 The major effect of PEEP and CPAP on the lungs is to increase FRC. In patients with decreased lung volume, appropriate levels of either PEEP or CPAP will increase FRC and tidal ventilation above closing capacity, will improve lung compliance, and will correct ventilation/perfusion abnormalities. The resulting decrease in intrapulmonary shunting improves arterial oxygenation. The principal mechanism of action for both PEEP and CPAP appears to be expansion of partially collapsed alveoli. Recruitment (reexpansion) of collapsed alveoli occurs at PEEP or CPAP levels above the inflection point, defined as the pressure level on

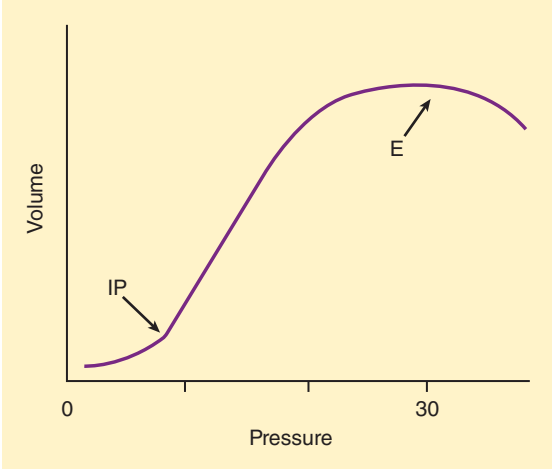

FIGURE 57–6 Pressure–volume curve for pulmonary system (eg, lung, thoracic). Inflection point (IP) above which the majority of alveoli are recruited. E, result of excessive pressure when alveoli are overdistended and pulmonary compliance decreases.

a pressure–volume curve at which collapsed alveoli are recruited (open); with small changes in pressure there are large changes in volume (Figure 57–6). Although neither PEEP nor CPAP decreases total extravascular lung water, studies suggest that they do redistribute extravascular lung water from the interstitial space between alveoli and endothelial cells toward peribronchial and perihilar areas. Both effects can potentially improve arterial oxygenation.

Excessive PEEP or CPAP, however, can overdistend alveoli (and bronchi), increasing dead space ventilation and reducing lung compliance; both effects can significantly increase the work of breathing. By compressing alveolar capillaries, overdistention of normal alveoli can also increase pulmonary vascular resistance and right ventricular afterload.

8 A higher incidence of pulmonary barotrauma is observed with excessive PEEP or CPAP, particularly at levels greater than 20 cm H_2O. Disruption of alveoli allows air to track interstitially along bronchi into the mediastinum (pneumomediastinum). From the mediastinum, air can then rupture into the pleural space (pneumothorax) or the pericardium (pneumopericardium) or can dissect along tissue planes subcutaneously (subcutaneous emphysema) or into the abdomen (pneumoperitoneum or pneumoretroperitoneum). A bronchopleural fistula is the result of failure of an air leak to seal (close). Although barotrauma must be considered in any discussion of CPAP and PEEP, in fact, it may be more clearly associated with higher peak inspiratory pressures that result with increasing level of PEEP or CPAP. Other factors that may increase the risk of barotrauma include underlying lung disease, stacking of breaths (from too frequent breaths or too short expiratory times) so that intrinsic PEEP (dynamic hyperinflation or autoPEEP) develops, large V_T (>10–15 mL/kg), and younger age.

Adverse Nonpulmonary Effects of PEEP & CPAP

Nonpulmonary adverse effects are primarily circulatory and are related to transmission of the elevated airway pressure to the contents of the chest. Fortunately, transmission is directly related to lung compliance; thus, patients with decreased lung compliance (most patients requiring PEEP) are least affected.

Progressive reductions in cardiac output are often seen as mean airway pressure and, secondarily, mean intrathoracic pressure rise. The principal mechanism appears to be intrathoracic pressure–related inhibition of return of venous blood to the heart. Other mechanisms may include leftward displacement of the interventricular septum (interfering with left ventricular filling) because of the increase in pulmonary vascular resistance (increased right ventricular afterload) from overdistention of alveoli, leading to an increase in right ventricular volume. Left ventricular compliance may therefore be reduced; when this occurs, to achieve the same cardiac output may require a higher filling pressure. An increase in intravascular volume will usually at least partially offset the effects of CPAP and PEEP on cardiac output. Circulatory depression is most often associated with end-expiratory pressures greater than 15 cm H_2O.

PEEP-induced elevations in central venous pressure and reductions in cardiac output decrease both renal and hepatic blood flow. Circulating levels of antidiuretic hormone and angiotensin are usually elevated. Urinary output, glomerular filtration, and free water clearance decrease.

Increased end-expiratory pressures, because they impede blood drainage from the brain and blood return to the heart, may increase intracranial pressure in patients whose ventricular compliance is decreased. Therefore, in patients on mechanical ventilation for acute lung injury and who have evidence of increased intracranial pressure, the level of PEEP must be carefully chosen to balance oxygenation requirements against potential adverse effects on intracranial pressure.

Optimum Use of PEEP & CPAP

The goal of positive-pressure therapy is to increase oxygen delivery to tissues, while avoiding the adverse sequelae of excessively increased (>0.5) F_{IO_2}. The latter is best accomplished with an adequate cardiac output and hemoglobin concentration. Ideally, mixed venous oxygen tensions or the arteriovenous oxygen content difference should be followed. The salutary effect of PEEP (or CPAP) on arterial oxygen tension must be balanced against any detrimental effect on cardiac output. Volume infusion or inotropic support may be necessary and should be guided by hemodynamic measurements.

At optimal PEEP the beneficial effects of PEEP exceed any detrimental risks. Practically, PEEP is usually added in increments of 3–5 cm H_2O until the desired therapeutic end point is reached. The most commonly suggested end point is an arterial oxygen saturation of hemoglobin of greater than 88–90% on a nontoxic inspired oxygen concentration (≤50%). Many clinicians favor reducing the inspired oxygen concentration to 50% or less because of the potentially adverse effect of greater oxygen concentrations on the lung. Alternatively, PEEP may be titrated to the mixed venous artery oxygen saturation ($S\bar{v}O_2$ > 50–60%). Monitoring lung compliance and dead space has also been suggested.

OTHER RESPIRATORY CARE TECHNIQUES

Other respiratory care techniques, including administration of aerosolized water or bronchodilators and clearing of pulmonary secretions, preserve or improve pulmonary function.

An aerosol mist is a gas or gas mixture containing a suspension of liquid particles. Aerosolized water may be administered to loosen inspissated secretions and facilitate their removal from the tracheobronchial tree. Aerosol mists are also used to administer bronchodilators, mucolytic agents, or vasoconstrictors (metered-dose inhalers are preferred for administration of bronchodilators). A normal cough requires an adequate inspiratory capacity, an intact glottis, and adequate muscle strength (abdominal muscles and diaphragm). Aerosol mists with or without bronchodilators may induce cough as well as loosen secretions. Instillation of hypertonic saline has been used as a mucolytic and to induce cough. Additional effective measures include chest percussion or vibration therapy and postural drainage of the various lung lobes.

9 Maneuvers that produce sustained maximum lung inflation such as the use of an incentive spirometer can be helpful in inducing cough as well as preventing atelectasis and preserving normal lung volume. Patients should be instructed to inhale approximately 15–20 mL/kg and to hold it for 2–3 s before exhalation.

When thick and copious secretions are associated with obvious atelectasis and hypoxemia, more aggressive measures may be indicated. These include suctioning the spontaneously breathing patient via a nasopharyngeal catheter or flexible bronchoscope, or performing the same two maneuvers through a tracheal tube. When there is atelectasis without retention of secretions, a brief period of CPAP by mask or positive-pressure ventilation through a tracheal tube is often very effective.

Respiratory Failure

Respiratory failure may be defined as impairment of normal gas exchange severe enough to require acute therapeutic intervention. Definitions based on arterial blood gases (see Table 57–1) may not apply to patients with chronic pulmonary diseases. For example, dyspnea and progressive respiratory acidosis may be present in patients with chronic CO_2 retention. Arterial blood gases typically follow one of several patterns in patients with respiratory failure (Figure 57–7). At one extreme, the derangement

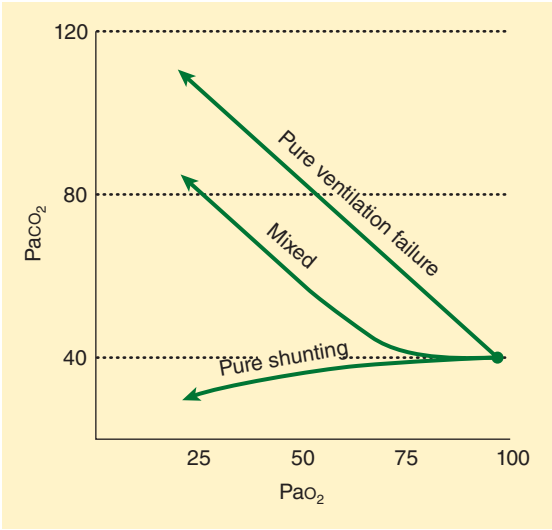

FIGURE 57–7 Arterial gas tension (room air) patterns during acute respiratory failure.

primarily affects oxygen transfer from the alveoli into blood, giving rise to hypoxemia (hypoxic respiratory failure); unless severe ventilation/perfusion mismatching is present, CO_2 elimination in these instances is typically normal or even enhanced. At the other extreme, the disorder primarily affects CO_2 elimination (pure ventilatory failure), resulting in hypercapnia; mismatching of ventilation to perfusion is typically absent or minimal. Hypoxemia, however, can occur with pure ventilatory failure when arterial CO_2 tension reaches 75–80 mm Hg in patients breathing room air (see the alveolar gas equation in Chapter 23). Few patients with respiratory failure display a pattern as "pure" as these extreme examples.

Treatment

Regardless of the disorder, the treatment of respiratory failure is primarily supportive while the reversible components of underlying disease are treated. Hypoxemia is treated with oxygen therapy and positive airway pressure (if FRC is decreased), whereas hypercarbia (ventilatory failure) is treated with mechanical ventilation. Other general measures may include using aerosolized bronchodilators, intravenous antibiotics, and diuretics for fluid overload, therapy to improve cardiac function, and nutritional support.

PULMONARY EDEMA

Pathophysiology

Pulmonary edema results from transudation of fluid, first from pulmonary capillaries into interstitial spaces and then from the interstitial spaces into alveoli. Fluid within the interstitial space and alveoli is collectively referred to as extravascular lung water. The movement of water across the pulmonary capillaries is similar to what occurs in other capillary beds and can be expressed by the Starling equation:

$$Q = K \times [(Pc' - Pi) - \sigma(\pi c' - \pi i)]$$

where Q is net flow across the capillary; Pc′ and Pi are capillary and interstitial hydrostatic pressures, respectively; πc′ and πi are capillary and interstitial oncotic pressures, respectively; K is a filtration coefficient related to effective capillary surface area per mass of tissue; and σ is a reflection coefficient that expresses the permeability of the capillary endothelium to albumin. Albumin is particularly important in this context because water loss to the interstitium will increase when albumin is also lost to the interstitium. A σ with a value of 1 implies that the endothelium is completely impermeable to albumin, whereas a value of 0 indicates free passage of albumin and other particles/molecules. The pulmonary endothelium normally is partially permeable to albumin, such that interstitial albumin concentration is approximately one half that of plasma; therefore, under normal conditions πi must be about 14 mm Hg (one half that of plasma). Pulmonary capillary hydrostatic pressure is dependent on vertical height in the lung (gravity) and normally varies from 0 to 15 mm Hg (average, 7 mm Hg). Because Pi is thought to be normally about –4 to –8 mm Hg, the forces favoring transudation of fluid (Pc′, Pi, and πi) are usually almost balanced by the forces favoring reabsorption (πc′). The net amount of fluid that normally moves out of pulmonary capillaries is small (about 10–20 mL/h in adults) and is rapidly removed by pulmonary lymphatics, which return it into the central venous system.

The alveolar epithelial membrane is usually permeable to water and gases but is impermeable to albumin (and other proteins). A net movement of water from the interstitium into alveoli occurs only when the normally negative Pi becomes positive (relative to atmospheric pressure). Fortunately, because of the lung's unique ultrastructure and its capacity to increase lymph flow, the pulmonary interstitium usually accommodates large increases in capillary transudation before Pi becomes positive. When this reserve capacity is exceeded, pulmonary edema develops.

Pulmonary edema is often divided into four stages:

Stage I: Only interstitial pulmonary edema is present. Patients often become tachypneic as pulmonary compliance begins to decrease. The chest radiograph reveals increased interstitial markings and peribronchial cuffing.

Stage II: Fluid fills the interstitium and begins to fill the alveoli, being initially confined to the angles between adjacent septa (crescentic filling). Near-normal gas exchange may be preserved.

Stage III: Many alveoli are completely flooded and no longer contain gas. Flooding is most prominent in dependent areas of the lungs. Blood flow through the capillaries of flooded alveoli results in a large increase in intrapulmonary shunting. Hypoxemia and hypocapnia (the latter due to dyspnea and hyperventilation) are characteristic.

Stage IV: Marked alveolar flooding spills into the airways as froth. Gas exchange is compromised due to both shunting and airway obstruction, leading to progressive hypercapnia and severe hypoxemia.

Causes of Pulmonary Edema

Pulmonary edema usually results from either an increase in the net hydrostatic pressure across the capillaries (hemodynamic or cardiogenic pulmonary edema) or an increase in the permeability of the alveolar–capillary membrane (increased permeability edema or noncardiogenic pulmonary edema). If a pulmonary artery catheter is present, the distinction can be based on the pulmonary artery occlusion pressure, which if greater than 18 mm Hg indicates that hydrostatic pressure is involved in forcing fluid across the capillaries into the interstitium and alveoli. The protein content of the edema fluid can also help differentiate the two. Fluid due to hemodynamic edema has a low protein content, whereas that due to permeability edema has a high protein content.

Less common causes of edema include prolonged severe airway obstruction (negative pressure pulmonary edema), sudden reexpansion of a collapsed lung, high altitude, pulmonary lymphatic obstruction, and severe head injury, although the same mechanisms (ie, changes in hemodynamic parameters or capillary permeability) also account for these diagnoses. Pulmonary edema associated with airway obstruction may result from an increase in the transmural pressure across pulmonary capillaries associated with a markedly negative interstitial hydrostatic pressure. Neurogenic pulmonary edema appears to be related to a marked increase in sympathetic tone, which causes severe pulmonary hypertension. The latter can disrupt the alveolar–capillary membrane.

1. Increased Transmural Pressure Pulmonary Edema ("Cardiogenic" Pulmonary Edema)

Significantly increased Pc′ can increase extravascular lung water and result in pulmonary edema. As can be seen from the Starling equation, a decrease in $\pi c'$ may accentuate the effects of any increase in Pc′. Two major mechanisms increase Pc′; namely, pulmonary venous hypertension and a markedly increased pulmonary blood flow. Any elevation of pulmonary venous pressure is transmitted passively backward to the pulmonary capillaries and secondarily increases Pc′. Pulmonary venous hypertension usually results from left ventricular failure, mitral stenosis, or left atrial obstruction. Increases in pulmonary blood flow that exceed the capacity of the pulmonary vasculature will also raise Pc′. Marked increases in pulmonary blood flow can be the result of large left-to-right cardiac or peripheral shunts, hypervolemia (fluid overload), or extremes of anemia or exercise.

Treatment

Management of cardiogenic pulmonary edema involves decreasing the pressure in the pulmonary capillaries. Generally, this includes measures to improve left ventricular function, correct fluid overload with diuretics, or reduce pulmonary blood flow. Pharmacological treatment of acute cardiogenic pulmonary edema has included oxygen, morphine, diuretics (especially loop diuretics), vasodilators such as nitrates or angiotensin-converting enzyme (ACE) inhibitors (although these decrease both preload and afterload), and inotropes such as dobutamine or milrinone. Vasodilators, particularly nitrates, have proved useful. By reducing preload, pulmonary congestion is relieved; by reducing afterload, cardiac output may be improved. Positive airway pressure therapy is also a useful adjunct for improving oxygenation. When pulmonary edema is a consequence of acute coronary ischemia and left ventricular failure, intraaortic balloon counterpulsation or other assist devices may be used.

2. Increased Permeability Pulmonary Edema (Noncardiogenic Pulmonary Edema): Acute Lung Injury & ARDS

Extravascular lung water increases in patients with increased permeability pulmonary edema due to enhanced permeability or disruption of the capillary–alveolar membrane. The protective effect of plasma oncotic pressure is lost as increased amounts of albumin "leak" into the pulmonary interstitium; normal—or even low—capillary hydrostatic pressures are unopposed and result in transudation of fluid into the lungs. Permeability edema is seen with acute lung injury (P:F ratio $\leq$300 [P = Pao_2 and F = FIo_2]) and is often associated with sepsis, trauma, and pulmonary aspiration; when severe (P:F ratio < 200), it is referred to as the acute respiratory distress syndrome (ARDS).

Pathophysiology

Acute lung injury and ARDS represent the pulmonary manifestation of the systemic inflammatory response syndrome (SIRS). Central to the pathophysiology of acute lung injury and ARDS is severe injury of the capillary–alveolar membrane. Regardless of the type of injury, the lung responds to the ensuing inflammatory response in a similar fashion. The released secondary mediators increase pulmonary capillary permeability, induce pulmonary vasoconstriction, and alter vascular reactivity such that hypoxic pulmonary vasoconstriction is abolished. Destruction of alveolar epithelial cells is prominent. Alveolar flooding, with decreased surfactant production (due to loss of type II pneumocytes), result in collapse. The exudative phase of ARDS may persist for a varying period; it is often followed by a fibrotic phase (fibrosing alveolitis), which in some cases leads to permanent scarring.

Clinical Manifestations

The diagnosis of acute lung injury or ARDS requires the exclusion of significant underlying left ventricular dysfunction combined with a P:F ratio of less than 300 (acute lung injury) or less than 200 (ARDS), and the presence of diffuse infiltrates on chest radiograph. The lung is often affected in a nonhomogeneous pattern, although dependent areas tend to be most affected.

Acute lung injury and ARDS are commonly seen in the settings of sepsis or trauma. Patients present with severe dyspnea and labored respirations. Hypoxemia due to intrapulmonary shunting is a universal finding. Although dead space ventilation is increased, arterial CO_2 tension is typically decreased because of a marked increase in minute ventilation. Ventilatory failure may be seen initially in severe cases or may eventually develop due to respiratory muscle fatigue or marked destruction of the capillary–alveolar membrane. Pulmonary hypertension and low or normal left ventricular filling pressures are characteristic hemodynamic findings.

Treatment

In addition to intensive respiratory care, treatment should be directed at reversible processes such as sepsis or hypotension. Hypoxemia is treated with oxygen therapy. Milder cases may be treated with a CPAP mask, but most patients require intubation

and at least some degree of mechanical ventilatory support. **Increased P_{plt} pressures (>30 cm H_2O) and high VT (>6 mL/kg), however, should also be avoided because overdistention of alveoli can induce iatrogenic lung injury, as can high FIO$_2$(>0.5).** While injury from high FIO$_2$ has not been conclusively demonstrated in humans, as was previously noted, VT of 12 mL/kg was associated with greater mortality than VT of 6 mL/kg and P_{plt} of less than 30 cm H_2O in patients with ARDS. Thus, reduced tidal volumes are associated with the greatest improvement in outcome after ARDS of any intervention subjected to a randomized clinical trial.

10

If possible, the FIO$_2$ should be maintained at 0.5 or less, primarily by increasing PEEP above the inflection point (see Figure 57–6). Other maneuvers to improve oxygenation include the use of inhaled nitric oxide, inhaled prostacyclin or prostaglandin E_1 (PGE_1), and ventilation in the prone position. These three techniques improve oxygenation in many patients with acute lung injury, but they are not risk free and they have not been associated with an improvement in survival. A recent meta-analysis has concluded that moderate doses of corticosteroids likely improve morbidity and mortality outcomes in ARDS, but the underlying data remain controversial.

Morbidity and mortality from ARDS usually arise from the precipitating cause or from complications rather than from the respiratory failure itself. Among the most common serious complications are sepsis, renal failure, and gastrointestinal hemorrhage. Nosocomial pneumonia is particularly common in patients with a protracted course and is often difficult to diagnose; antibiotics are generally indicated when there is a high index of suspicion (fever, purulent secretions, leukocytosis, and change in chest radiograph). Protected specimen brushings and bronchoalveolar lavage sampling via a flexible bronchoscope may be useful. Breach of mucocutaneous barriers by various catheters, malnutrition, and altered host immunity contribute to a frequent incidence of infection. Kidney failure may result from various combinations of volume depletion, sepsis, or nephrotoxins. Kidney failure substantially increases the mortality rate for ARDS (to >60%). Prophylaxis for gastrointestinal hemorrhage with sucralfate, antacids, H_2 blockers, or proton pump inhibitors is recommended.

DROWNING & NEAR-DROWNING

Drowning, with or without aspiration of water, is death while submerged in water. Near-drowning, with or without aspiration, is suffocation while submerged with (at least temporary) survival. Survival depends on the intensity and duration of the hypoxia and on the water temperature.

Pathophysiology

Both drowning and near-drowning can occur whether or not inhalation (aspiration) of water occurs. If water does not enter the airways, the patient primarily suffers from asphyxia; however, if the patient inhales water, marked intrapulmonary shunting also takes place. Ninety percent of drowning patients aspirate fluid: fresh water, seawater, brackish water, or other fluids. Although the amount of liquid aspirated is generally small, marked ventilation/perfusion mismatching can result from fluids in the airways and alveoli, reflex bronchospasm, and loss of pulmonary surfactant. Aspiration of gastric contents can also complicate drowning before or after loss of consciousness or during resuscitation.

The hypotonic water aspirated following fresh water drowning is rapidly absorbed by the pulmonary circulation; water cannot usually be recovered from the airways. If a significant amount is absorbed (>800 mL in a 70-kg adult), transient hemodilution, hyponatremia, and even hemolysis may occur. In contrast, aspiration of salt water, which is hypertonic, draws out water from the pulmonary circulation into the alveoli, flooding them. Thus, hemoconcentration and hypernatremia may occasionally occur following saltwater drowning. Hypermagnesemia and hypercalcemia have also been reported following near-drowning in salt water.

Patients who suffer from cold water drowning lose consciousness when core body temperature decreases below 32°C. Ventricular fibrillation occurs at about 28–30°C, but relative to normothermic

drowning, the hypothermia has a protective effect on the brain and may improve outcome provided that resuscitation measures are successful.

Clinical Manifestations

Nearly all patients with a true near-drowning episode will have hypoxemia, hypercarbia, and metabolic acidosis. Patients may also suffer from other injuries, such as spine fractures following diving accidents. Neurological impairment is generally related to duration of submersion and severity of asphyxia. Cerebral edema complicates prolonged asphyxia. Acute lung injury and ARDS develop in many patients following resuscitation.

Treatment

Initial treatment of near-drowning is directed at restoring ventilation, perfusion, oxygenation, and acid–base balance as quickly as possible. Immediate measures include establishing a clear and unobstructed airway, administering oxygen, and initiating cardiopulmonary resuscitation. In-line stabilization of the cervical spine is necessary when intubating patients who suffer from near-drowning following a dive. Although salt water can often be drained out of the lungs by gravity, this practice should not delay institution of cardiopulmonary resuscitation; abdominal thrusts may promote aspiration of gastric contents. Resuscitation efforts are always continued until the patient is fully assessed and under treatment in a hospital, particularly following cold water drowning. Complete recovery is possible in such instances even after prolonged periods of asphyxia. Management includes tracheal intubation, positive-pressure ventilation, and PEEP. Bronchospasm should be treated with bronchodilators, electrolyte abnormalities corrected, and acute lung injury and ARDS treated as discussed above. Hypothermia should be corrected gradually over a few hours.

SMOKE INHALATION

Smoke inhalation is the leading cause of death from fires. Affected persons may or may not have sustained a burn. Burn victims who suffer from smoke inhalation have a mortality rate significantly greater than other comparably burned patients without smoke inhalation. Any exposure to smoke in a fire requires a presumptive diagnosis of smoke inhalation until proved otherwise. A suggestive history might include loss of consciousness or disorientation in a patient exposed to a fire, or a burn acquired in a closed space.

Pathophysiology

The consequences of smoke inhalation are complex because they can involve three types of injuries: heat injury to the airways, exposure to toxic gases, and a chemical burn with deposition of carbonaceous particulates in the lower airways. The pulmonary response to smoke inhalation is equally complex and depends on the duration of the exposure, composition of the material that burned, and presence of any underlying lung disease. Combustion of many synthetic materials produces toxic gases such as carbon monoxide, hydrogen cyanide, hydrogen sulfide, hydrogen chloride, ammonia, chlorine, benzene, and aldehydes. When these gases react with water in the airways, they can produce hydrochloric, acetic, formic, and sulfuric acids. Carbon monoxide and cyanide poisoning are common.

After smoke inhalation direct mucosal injury may result in edema, inflammation, and sloughing. Loss of ciliary activity impairs the clearance of mucus and bacteria. Manifestations of acute lung injury and ARDS typically appear 2–3 days after the injury and seem related to the delayed development of SIRS rather than the acute smoke inhalation itself.

Clinical Manifestations

Patients may initially have few if any symptoms after smoke inhalation. Suggestive physical findings include facial or intraoral burns, singed nasal hairs, cough, carbonaceous sputum, and wheezing. The diagnosis usually can be confirmed when flexible bronchoscopy of the upper airway and the tracheobronchial tree reveals erythema, edema, mucosal ulcerations, and carbonaceous deposits. Arterial blood gases initially may be normal or reveal only mild hypoxemia and metabolic acidosis

due to carbon monoxide. The chest radiograph is often normal on presentation.

Heat injury to the airways is usually confined to supraglottic structures in the absence of prolonged exposure to steam. Progressive hoarseness and stridor are ominous signs of impending airway obstruction, which may develop over 12–18 h. Fluid resuscitation of any burn injury will frequently aggravate the edema.

Carbon monoxide poisoning is usually defined as greater than 15% carboxyhemoglobin in the blood. The diagnosis is made by cooximetric measurements of arterial blood. Carbon monoxide has 200–300 times the affinity of oxygen for hemoglobin. When a CO molecule combines with hemoglobin to form carboxyhemoglobin, it decreases the affinity of the other binding sites for oxygen, shifting the hemoglobin dissociation curve to the right. The net result is a marked reduction in the oxygen-carrying capacity of blood.

Carbon monoxide dissociates very slowly from hemoglobin with a half-life of approximately 2–4 h. Clinical manifestations result from tissue hypoxia from impaired oxygen delivery. Levels greater than 20–40% carboxyhemoglobin are associated with neurological impairment, nausea, fatigue, disorientation, and shock. Lower levels may also produce symptoms because carbon monoxide also binds cytochrome c and myoglobin. Compensatory mechanisms include increased cardiac output and peripheral vasodilation.

Cyanide toxicity may occur in patients exposed to fumes from fires that contain synthetic materials, particularly those containing polyurethane. The cyanide, which may be inhaled or absorbed through mucosal surfaces and skin, binds the cytochrome system of enzymes and inhibits cellular production of adenosine triphosphate (ATP). Patients present with neurological impairment and lactic acidosis; they typically have arrhythmias, increased cardiac output, and marked vasodilation.

A chemical burn of the respiratory mucosa follows inhalation of large amounts of carbonaceous material, particularly when combined with toxic fumes. Inflammation of the airways results in bronchorrhea and wheezing. Bronchial edema and sloughing of the mucosa lead to obstruction of the lower airways and atelectasis. Progressive ventilation/perfusion mismatching can lead to marked hypoxemia over the course of 24–48 h. Development of the systemic inflammatory response syndrome can lead to acute lung injury or ARDS.

Treatment

Fiberoptic bronchoscopy usually establishes the diagnosis of an inhalation injury. Bronchoscopy is usually carried out with a tracheal tube loaded over the bronchoscope so that intubation can quickly be performed if edema threatens the patency of the airway. Early elective tracheal intubation is advisable when there are obvious signs of heat injury to the airway. Patients with hoarseness and stridor require immediate intubation; emergency cricothyrotomy or tracheostomy is necessary if oral or nasal intubation is unsuccessful.

The presence of clinically important carbon monoxide or cyanide poisoning, as evidenced by obtundation or coma, also requires prompt tracheal intubation and ventilation with oxygen. The diagnosis of carbon monoxide poisoning requires cooximetry: pulse oximeters cannot reliably differentiate between carboxyhemoglobin and oxyhemoglobin. The half-life of carboxyhemoglobin is reduced to 1 h with 100% oxygen; some clinicians advocate hyperbaric oxygen therapy if the patient does not respond to 100% oxygen. The diagnosis of cyanide poisoning is difficult because reliable measurements of cyanide are not readily available (normal levels are <0.1 mg/L). The enzyme rhodanase normally converts cyanide to thiocyanate, which is subsequently eliminated by the kidneys. Treatment for severe cyanide toxicity consists of administering sodium nitrite, 300 mg intravenously as a 3% solution over 3–5 min, followed by sodium thiosulfate, 12.5 g intravenously in the form of a 25% solution over 1–2 min. Sodium nitrite converts hemoglobin to methemoglobin, which has a higher affinity for cyanide than cytochrome oxidase; the cyanide, which is slowly released from cyanomethemoglobin, is converted by rhodanase to the less toxic thiocyanate.

Marked hypoxemia due to intrapulmonary shunting should be managed with tracheal intubation, oxygen therapy, bronchodilators, positive-pressure ventilation, and PEEP. Corticosteroids are

ineffective and increase the rate of infections. As with other forms of acute lung injury, nosocomial infectious pneumonias are common.

Acute Myocardial Infarction

Acute myocardial infarction (AMI) is a serious complication of ischemic heart disease, with an overall mortality rate of 25%. More than one half of these deaths occur shortly after onset, usually due to arrhythmias (ventricular fibrillation). With recent advances in interventional cardiology, the in-hospital mortality rate has been reduced to less than 10–15%. Pump (ventricular) failure is now the leading cause of death after AMI in hospitalized patients.

Most myocardial infarctions occur in patients with more than one severely narrowed (>75% narrowing of the cross-sectional area) coronary artery. A transmural infarction occurs in an area distal to a complete occlusion. Patients who die within 24 hours after AMI may demonstrate only coronary atherosclerosis on necropsy examination of the heart. The occlusion is nearly always due to thrombosis at a stenotic atheromatous plaque. Coronary emboli or severe spasm is less commonly the cause. The size and location of the infarct depend on the distribution of the obstructed vessel and whether collateral vessels have formed. Anterior, apical, and septal infarcts of the left ventricle are usually due to thrombosis in the left anterior descending circulation; lateral and posterior left ventricular infarcts result from occlusions in the left circumflex system, whereas right ventricular and posterior–inferior left ventricular infarcts result from thrombosis in the right coronary artery. In contrast, subendocardial (nontransmural, or "non–Q wave") infarctions more often occurs in the setting of reduced myocardial perfusion due to hypotension or intimal hemorrhage, and less commonly follows coronary plaque rupture and thrombosis.

Following brief episodes of severe ischemia, persisting myocardial dysfunction with only a slow and incomplete return of contractility can be observed. This phenomenon of "stunning" is often thought to occur in areas adjacent to infarcted myocardium and can contribute to ventricular dysfunction following AMI. Relief of the ischemia in these areas can restore contractile function, albeit not immediately. Stunning may be observed following aortic cross-clamping during cardiopulmonary bypass and present as a reduced cardiac output upon attempted separation from bypass (see Chapter 22). When severe hypokinesis or akinesis is observed in the setting of severe chronic ischemia, the myocardium in these noninfarcted but poorly contractile areas may be said to be "hibernating." This diagnosis can be confirmed by observing viable tissue with positron emission tomography, or by showing that the hypocontractile myocardium responds to dobutamine during stress echocardiography.

The immediate treatment of AMI is the administration of oxygen, aspirin (160–325 mg), nitroglycerin (sublingual or spray), morphine (2–4 mg intravenously every 5 min) until the pain is relieved, and in most cases of an ST-segment elevation MI (STEMI) movement of the patient to the cardiac catheterization laboratory. The mnemonic "MONA (*m*orphine, *o*xygen, *n*itroglycerin, and *a*spirin) greets all patients" succinctly states this approach. Because the prognosis following AMI is generally inversely proportionate to the extent of necrosis, the focus in management of an evolving myocardial infarction remains on reperfusion. Based on local resources, timing, and anatomic findings during angiography, angioplasty, stenting, or coronary artery bypass surgery may be preferred. Guidelines for treatment of AMI change on a nearly annual basis and are regularly published by the American College of Cardiology/American Heart Association and by the European Society of Cardiology; we strongly recommend that they be consulted.

Patients with ST-segment depression or dynamic T-wave changes (non–Q wave infarction; unstable angina) benefit from antithrombin (heparin) and antiplatelet (aspirin) therapy. All patients without contraindications (such as acute heart failure) should receive β blockers. Other medications and treatments such as ACE inhibitors, statins, and cessation of smoking are the key to secondary prevention. Patients who have recurrent angina should be given nitrates. If angina persists or if there is a contraindication to β blockers, calcium channel blockers should be administered. Persistent or

recurrent angina signals the need for angiography, if it has not already been performed.

Intraaortic balloon counterpulsation is usually reserved for hemodynamically compromised patients with refractory ischemia. Temporary pacing following AMI is indicated for Mobitz type II and complete heart block, a new bifascicular block, and bradycardia with hypotension. Emergency treatment of arrhythmias constantly evolves and we recommend that the guidelines for Advanced Cardiac Life Support be followed. In general, ventricular tachycardia, if treated medically is best managed with amiodarone (150 mg intravenous bolus over 10 min). Synchronized cardioversion may be used in patients with ventricular tachycardia and with a pulse. Patients with a stable narrow-complex supraventricular tachycardia should be treated with amiodarone. Patients with paroxysmal supraventricular tachycardia, whose ejection fraction is preserved, should be treated with a calcium channel blocker, a β blocker, or DC cardioversion. Medically unstable hypotensive patients should receive cardioversion.

Patients with ectopic or multifocal atrial tachycardia should not receive DC cardioversion; instead they should be treated with calcium channel blockers, a β blocker, or amiodarone.

Acute Kidney Injury & Failure

Acute kidney injury (AKI) is a rapid deterioration in renal function that is not immediately reversible by altering factors such as blood pressure, intravascular volume, cardiac output, or urinary flow. The hallmark of AKI is azotemia and frequently oliguria. Azotemia may be classified as prerenal, renal, and postrenal. Moreover, the diagnosis of renal azotemia is one of exclusion; thus, prerenal and postrenal causes must always be excluded. However, not all patients with acute azotemia have kidney failure. Likewise, urine output of more than 500 mL/d does not imply that renal function is normal. Basing the diagnosis of AKI on creatinine levels or an increase in blood urea nitrogen (BUN) is also problematic because creatinine clearance is not always a good measure of glomerular filtration rate. The criteria developed by the Acute Kidney Injury Network are now most often used to stage AKI (see Chapter 30). AKI is diagnosed by documenting an increase in serum creatinine of more than 50%, or an absolute increase of 0.3 mg/dL, and a reduction in urine output to less than 0.5 mL/kg/h for 6 h or longer, with all findings developing over 48 h or less.

PRERENAL AZOTEMIA

Prerenal azotemia results from hypoperfusion of the kidneys; if untreated, it progresses to AKI. Renal hypoperfusion typically the result of decreased arterial perfusion pressure, markedly increased venous pressure, or renal vasoconstriction (Table 57–7). Decreased perfusion pressure is usually associated with the release of norepinephrine, angiotensin II, and arginine vasopressin (or antidiuretic hormone). These hormones constrict cutaneous muscle and splanchnic vasculature and promote salt and water retention. The synthesis of vasodilating prostaglandins (prostacyclin and PGE_2) and nitric oxide in the kidneys and the intrarenal action of angiotensin II

TABLE 57–7 Potentially reversible causes of azotemia.

Prerenal
Decreased renal perfusion
Hypovolemia
Reduced cardiac output
Hypotension
Abdominal compartment syndrome
Increased renal vascular resistance
Neural
Humoral/Pharmacological
Thromboembolic
Postrenal
Urethral obstruction
Bladder outlet obstruction
Neurogenic bladder
Bilateral ureteral obstruction
Intrinsic
Calculi
Tumor
Blood clots
Papillary necrosis
Extrinsic
Abdominal or pelvic tumor
Retroperitoneal fibrosis
Postsurgical (ligation)

TABLE 57–8 Urinary indices in azotemia.

Index	Prerenal	Renal	Postrenal
Specific gravity	>1.018	<0.012	Variable
Osmolality (mmol/kg)	>500	<350	Variable
Urine/plasma urea nitrogen ratio	>8	<3	Variable
Urine/plasma creatinine ratio	>40	<20	Variable
Urine/sodium (mEq/L)	<10	>40	Variable
Fractional excretion of sodium (%)	<1	>3	Variable
Renal failure index	<1	>1	Variable

help maintain glomerular filtration. Use of cyclooxygenase inhibitors (eg, ketorolac for postoperative pain control) or ACE inhibitors in the setting of marked prerenal azotemia can precipitate AKI. The diagnosis of prerenal azotemia is usually suspected from the clinical setting and confirmed by urinary laboratory indices (Table 57–8). Treatment of prerenal azotemia is directed at correcting intravascular volume deficits, improving cardiac function, restoring a normal blood pressure, and reversing increases in renal vascular resistance. The hepatorenal syndrome is discussed in Chapter 33.

POSTRENAL AZOTEMIA

Azotemia due to urinary tract obstruction is termed postrenal azotemia. Obstruction of urinary flow from both kidneys is usually necessary for azotemia and oliguria/anuria in these conditions. Complete obstruction eventually develops into AKI and kidney failure, whereas prolonged partial obstruction leads to chronic renal impairment. Rapid diagnosis and relief of acute obstruction usually restore normal renal function, often accompanied by a diuresis. Obstruction may be diagnosed by a physical examination (the upper margin of the bladder can be percussed) or ultrasound (showing a distended bladder) or suggested by a radiograph of the abdomen (revealing bilateral renal calculi), but is definitively diagnosed by demonstrating dilation of the urinary tract proximal to the site of obstruction on imaging studies. Treatment depends on the site of obstruction. Obstruction at the bladder outlet can be relieved with catheterization of the bladder or suprapubic cystostomy, whereas ureteral obstruction requires nephrostomy or ureteral stents.

REVERSIBLE AZOTEMIA VERSUS AKI

It is important to differentiate prerenal and postrenal azotemia from renal azotemia. Exclusion of postrenal azotemia requires physical diagnosis and imaging, whereas exclusion of prerenal azotemia depends on the response to treatments aimed at improving renal perfusion. Diagnosis and treatment may be facilitated by analysis of urine (see Table 57–8); urinary composition in postrenal azotemia is variable and depends on the duration and severity of obstruction. In prerenal azotemia, tubular concentrating ability is preserved and reflected by a low urinary sodium concentration and high urine/serum creatinine ratio. Calculation of the fractional excretion of filtered sodium ($FENa^+$) may also be extremely useful in the setting of oliguria:

$$FENa^+ = \frac{\text{Urine sodium/serum sodium}}{\text{Urine creatinine/serum creatinine}} \times 100\%$$

$FENa^+$ is less than 1% in oliguric patients with prerenal azotemia but typically exceeds 3% in patients with oliguric AKI. Values of 1–3% may be present in patients with nonoliguric AKI. The renal failure index, which is the urinary sodium concentration divided by the urine/plasma creatinine ratio, is a sensitive index for diagnosing kidney failure. The use of diuretics increases urinary sodium excretion and invalidates indices that rely on urinary sodium concentration as a measure of tubular function. Moreover, intrinsic kidney diseases that primarily affect renal vasculature or glomeruli may not affect tubular function and therefore are associated with indices that are similar to prerenal azotemia. Measurement of a 3-h creatinine clearance can estimate the residual glomerular filtration rate but may underestimate the degree of renal impairment if the serum creatinine concentration is still rising.

Etiology of AKI

Causes of AKI are listed in Table 57–9. Up to 50% of cases follow major trauma or surgery; in the majority of instances, ischemia and nephrotoxins are responsible. AKI associated with ischemia is often termed *acute tubular necrosis*. Postischemic acute tubular necrosis follows certain surgical procedures more frequently than others: open abdominal aortic aneurysm resection, cardiac surgery with cardiopulmonary bypass, and operations to relieve obstructive jaundice. Aminoglycosides, amphotericin B, radiographic contrast dyes, cyclosporine, and cisplatin are the most commonly implicated exogenous nephrotoxins. Amphotericin B, contrast dyes, and cyclosporine also appear to produce direct intrarenal vasoconstriction. Hemoglobin and myoglobin are potent nephrotoxins when they are released during intravascular hemolysis and rhabdomyolysis, respectively. Cyclooxygenase inhibitors, particularly nonsteroidal antiinflammatory drugs, may play an important role in at least some patients. Inhibition of prostaglandin synthesis by the latter group of agents decreases prostaglandin-mediated renal vasodilation, allowing unopposed renal vasoconstriction. Other factors predisposing to AKI include preexisting renal impairment, advanced age, atherosclerotic vascular disease, diabetes, and dehydration.

TABLE 57–9 Causes of acute kidney injury.

Renal ischemia
Hypotension
Hypovolemia
Impaired cardiac output
Abdominal compartment syndrome
Nephrotoxins
Endogenous pigments
Hemoglobulin (hemolysis)
Myoglobin (rhabdomyolysis from crush injury and burns)
Radiographic contrast agents
Drugs
Antibiotics (aminoglycosides, amphotericin)
Nonsteroidal antiinflammatory drugs
Chemotherapeutic agents (cisplatin, methotrexate)
Tubular crystals
Uric acid
Oxalate
Sulfonamides
Heavy metal poisoning
Organic solvents
Myeloma protein
Intrinsic kidney disease
Glomerular disease
Interstitial nephritis

Pathogenesis of AKI

The sensitivity of the kidneys to injury may be explained by their very high metabolic rate and ability to concentrate potentially toxic substances. The pathogenesis of AKI is complex and probably has both a vascular endothelial and a renal epithelial (tubular) basis. Inadequate oxygen deliver to the kidney is the likely triggering event, leading to afferent arteriolar constriction, decreased glomerular permeability, increased vascular permeability, altered coagulation, inflammation, leukocyte activation, direct epithelial cell injury, and tubular obstruction from intraluminal debris or edema. All can decrease glomerular filtration. A backleak of filtered solutes through damaged portions of renal tubules may allow reabsorption of creatinine, urea, and other nitrogenous wastes.

Oliguric versus Nonoliguric AKI

AKI is often classified as oliguric (urinary volume <400 mL/d), anuric (urinary volume <100 mL/d), or nonoliguric (urinary volume >400 mL/d). Nonoliguric AKI accounts for up to 50% of cases. Urinary sodium concentrations in patients with nonoliguric AKI are typically lower than those in oliguric patients. In some studies, nonoliguric patients also appear to have a lower complication rate and to require shorter hospitalizations. In another study of AKI patients who required dialysis, nonoliguric AKI patients had a delayed initiation of dialysis, a longer hospital stay, and an increased likelihood of death. It was speculated that it might be possible to convert oliguric AKI into nonoliguric AKI by administering mannitol, furosemide, "renal" doses of dopamine (1–2 mcg/kg/min), or fenoldopam. Theoretically, the resulting increase in urinary output might be therapeutic by preventing tubular obstruction. However, recent studies have found increased mortality in patients with AKI who received diuretics, and a meta-analysis showed no improvement in mortality

or decrease in need for dialysis; therefore diuretics should not be routinely administered in AKI.

Treatment of AKI

AKI accounts for approximately 15% of ICU admissions. Despite advances in critical care medicine, the mortality rate for AKI remains approximately 50% and management is primarily supportive. Diuretics continue to be useful for conventional medical indications (eg, pulmonary edema or rhabdomyolysis). AKI due to glomerulonephritis or vasculitis may respond to glucocorticoids. Standard treatment for oliguric and anuric patients includes restriction of fluid, sodium, potassium, and phosphorus. Daily weight measurements help guide fluid therapy. Sodium and potassium intake is limited to 1 mEq/kg/d. Hyponatremia can be treated with water restriction. Hyperkalemia may require administration of an ion-exchange resin (sodium polystyrene), glucose and insulin, calcium gluconate, or sodium bicarbonate. Sodium bicarbonate therapy may also be necessary for metabolic acidosis when the serum bicarbonate level decreases to less than 15 mEq/L. Hyperphosphatemia requires dietary phosphate restriction and phosphate binders such as sevelamer, aluminum hydroxide, calcium carbonate, calcium acetate. The dosages of renally excreted drugs should be adjusted to the estimated glomerular filtration rate or measured creatinine clearance to prevent accumulation.

Renal replacement therapy may be employed to treat or prevent uremic complications (see Table 30–6). A double-lumen catheter placed in the internal jugular, subclavian, or femoral vein is usually used. The high morbidity and mortality rates associated with AKI would seem to argue for early dialysis, but supporting studies are controversial. Dialysis does not appear to hasten recovery but may in fact aggravate kidney injury if hypotension occurs or too much fluid is removed.

Because of concern that intermittent hemodialysis associated with hypotension may perpetuate renal injury, continuous renal replacement therapy (CRRT; continuous venovenous hemofiltration or continuous venovenous hemodialysis, which removes fluid and solutes at a slow controlled rate) has been used in critically ill patients with uremic AKI who do not tolerate the hemodynamic effects of intermittent "standard" hemodialysis. The main problem associated with CRRT is the expense, as the membrane is prone to clot formation and, therefore, must be periodically replaced. Despite this limitation, many experts believe CRRT is the best way to manage uremic ICU patients with AKI. The indications for CRRT are being expanded from oliguria and uremia to metabolic acidosis, fluid overload, and hyperkalemia. Nevertheless, recent clinical trials have failed to show benefit of continuous technique over intermittent hemodialysis in these critically ill patients.

The nutritional management of AKI with uremia continues to evolve, and there is now consensus among nephrologists, intensivists, and nutritionists that nutrition should be provided, and 1.0–1.5 g/kg/d of protein can be given, particularly for patients on CRRT.

Infections & Sepsis

The systemic inflammatory response to infection, termed *sepsis syndrome* (Figure 57–8), does not necessarily indicate the presence of bacteremia. Moreover, the inflammatory response is not unique to severe infections: similar manifestations may be encountered with noninfectious illnesses.

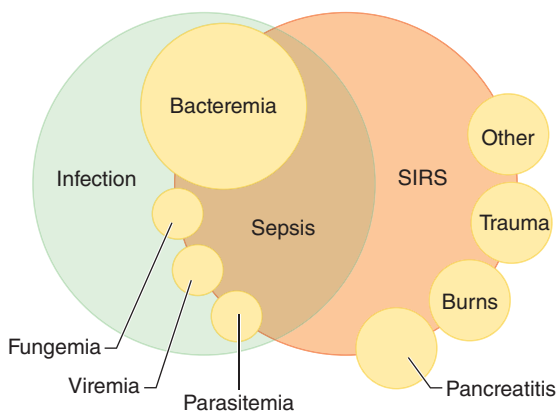

FIGURE 57–8 The relationship among infection, sepsis, and the systemic inflammatory response syndrome (SIRS). (Modified from the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992;20:864.)

The use of the term *systemic inflammatory response syndrome* (SIRS) has been suggested by the Society of Critical Care Medicine (SCCM), European Society of Intensive Care Medicine (ESICM), American College of Chest Physicians (ACCP), American Thoracic Society (ATS), and Surgical Infection Society (SIS) (Table 57–10). A combined conference of the preceding long list of societies classified sepsis based on predisposition, insult, infection, response, and organ dysfunction. Severe sepsis exists when these features are associated with organ dysfunction. The term *multiple organ dysfunction syndrome* (MODS) has been suggested to describe dysfunction of two or more organs associated with sepsis. *Septic shock* is defined as acute circulatory failure in a patient with sepsis or, more specifically, systolic blood pressure less than 90 mm Hg that is not responsive to volume resuscitation and requiring vasopressors for life support.

PATHOPHYSIOLOGY OF SIRS

A mild systemic inflammatory response to an injury, infection, or other bodily insult may normally have salutatory effects. However, a marked or prolonged response, such as that associated with severe infections, is often deleterious and can result in widespread organ dysfunction. Although gram-negative organisms account for most cases of infection-related SIRS, many other infectious agents are capable of inducing the same syndrome. These organisms either elaborate toxins or stimulate release of substances that trigger this response. The most commonly recognized initiators are the lipopolysaccharides, which are released by gram-negative bacteria. Lipopolysaccharide is composed of an O polysaccharide, a core, and lipid A. The O polysaccharide distinguishes between different types of gram-negative bacteria, whereas lipid A, an endotoxin, is responsible for the compound's toxicity. The resulting response to endotoxin involves a complex interaction between macrophages/monocytes, neutrophils, lymphocytes, platelets, and endothelial cells that can affect nearly every organ.

The central mechanism in initiating SIRS appears to be the abnormal secretion of cytokines. These low-molecular-weight peptides and

TABLE 57–10 Diagnostic criteria for sepsis.[1–3]

Infection,[4] documented or suspected, and some of the following:
General variables
Fever (core temperature >38.3°C)
Hypothermia (core temperature <36°C)
Heart rate >90/min or >2 SD above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance (>20 mL/kg over 24 h)
Hyperglycemia (plasma glucose >120 mg/dL or 7.7 mmol/L) in the absence of diabetes
Inflammatory variables
Leukocytosis (WBC count >12,000/μL)
Leukopenia (WBC count <4000/μL)
Normal WBC count with >10% immature forms
Plasma C-reactive protein >2 SD above the normal value
Plasma procalcitonin >2 SD above the normal value
Hemodynamic variables
Arterial hypotension[5] (SBP <90 mm Hg, MAP <70, or an SBP decrease >40 mm Hg in adults or <2 SD below normal value for age)
$S\bar{v}O_2$ > 70%[5]
Cardiac index[5] >3.5 L/min per m^2
Organ dysfunction variables
Arterial hypoxemia (Pao_2/Fio_2 < 300)
Acute oliguria (urine output <0.5 mL/kg/h or 45 mmol/L for at least 2 h)
Creatinine increase > 0.5 mg/dL
Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count < 100,000/μL)
Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 mmol/L)
Tissue perfusion variables
Hyperlactatemia (>1 mmol/L)
Decreased capillary refill or mottling

[1]Reprinted, with permission, from Levy MM, Fink MP, Marshall JC, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 2003;31:1250.

[2]WBC, white blood cell; SBP, systolic blood pressure; MAP, mean arterial blood pressure; $S\bar{v}O_2$, mixed venous oxygen saturation; INR, international normalized ratio; aPTT, activated partial thromboplastin time.

[3]Diagnostic criteria for sepsis in the pediatric population are signs and symptoms of inflammation plus infection with hyper- or hypothermia (rectal temperature >38.4°C or <35°C), tachycardia (may be absent in hypothermia patients), and at least one of the following indications of altered organ function: altered mental status, hypoxemia, increased serum lactate level, or bounding pulses.

[4]Infection defined as a pathological process induced by a microorganism.

[5]$S\bar{v}O_2$ >70% (normally, 75–80%) and cardiac index 3.5–5.5 are normal in children; therefore, neither should be used as a sign of sepsis in newborns or children.

glycoproteins function as intercellular mediators regulating such biological processes as local and systemic immune responses, inflammation, wound healing, and hematopoiesis. The most important cytokines released during SIRS are interleukin-6, adrenomedullin, soluble CD_{14}, the adhesion molecule sELAM-1, macrophage inflammatory protein-1α, extracellular phospholipase A_2, and C-reactive protein. The resulting inflammatory response includes release of potentially harmful phospholipids, attraction of neutrophils, and activation of the complement, kinin, and coagulation cascades.

Increased phospholipase A_2 levels release arachidonic acid from cell membrane phospholipids. Cyclooxygenase converts arachidonic acid to thromboxane and prostaglandins, whereas lipoxygenase converts arachidonic acid into leukotrienes (slow-reacting substances of anaphylaxis). Increased phospholipase A_2 and acetyltransferase activities result in the formation of another potent proinflammatory compound, platelet-activating factor. Attraction and activation of neutrophils releases a variety of proteases and free radical compounds that damage vascular endothelium. Activation of monocytes causes them to express increased amounts of tissue factor, which in turn can activate both the intrinsic and extrinsic coagulation cascades.

INFECTIONS IN THE ICU

Infections are a leading cause of death in ICUs. Serious infections may be "community acquired" or subsequent to hospital admission for an unrelated illness. The term *nosocomial infection* describes hospital-acquired infections that develop at least 48 h following admission. The reported incidence of nosocomial infections in ICU patients has ranged between 10% and 50%, but with recent attention to aseptic placement of central venous catheters and earlier removal of bladder catheters the incidence of bloodstream infections has markedly declined. Nearly universal elevation of the head of bed has also led to a marked reduction in ventilator-associated pneumonia.

Strains of bacteria resistant to commonly used antibiotics are often responsible for infections in patients with critical illness. Host immunity plays an important role in determining not only the course of an infection but also the types of organisms that can cause infection. Thus, organisms that normally do not cause serious infections in immunocompetent patients can produce life-threatening infections in those who are immunocompromised (**Table 57–11**).

Critically ill patients frequently have abnormal host defenses from advanced age, malnutrition, drug therapy, loss of integrity of mucosal and skin barriers, and underlying diseases. Thus, age greater than 70 years, corticosteroid therapy, chemotherapy of malignancy, prolonged use of invasive devices, respiratory failure, kidney failure, head trauma, and burns are established risk factors for nosocomial infections. Patients with burns involving more than 40% of body surface area have significantly increased risk of mortality from infections. Topical antibiotics delay but do not prevent wound infections. After burns, early removal of the necrotic eschar followed by skin grafting and wound closure appears to reverse immunological defects and reduce infections.

Most nosocomial infections arise from the patient's endogenous bacterial flora. Furthermore, many critically ill patients eventually become colonized with resistant bacterial strains. Infections of the urinary tract account for many nosocomial infections. Urinary infections are usually due to gram-negative organisms and are typically associated with the indwelling catheters or urinary obstruction. Community-acquired and ventilator-associated pneumonias are problems in the ICU. Intravascular catheter-related infections are now relatively rare causes of ICU infections. Surgical site and other wound infections are, however, seen.

Nosocomial pneumonias are usually caused by gram-negative organisms. Gastrointestinal bacterial overgrowth with translocation into the portal circulation and retrograde colonization of the upper airway from the gastrointestinal tract as a result of aspiration are possible mechanisms of entry for these bacteria. Preservation of gastric acidity inhibits overgrowth of gram-negative organisms in the stomach and their subsequent migration into the oropharynx. Tracheal intubation does not provide effective protection because patients commonly aspirate gastric fluid containing bacteria despite a properly

TABLE 57-11 Pathogens commonly associated with serious infections in ICU patients.[1]

Infection or Site	Pathogens
Pneumonia	
Community-acquired (nonimmunocompromised host)	*Streptococcus pneumoniae* *Haemophilus influenzae* *Moraxella catarrhalis* *Mycoplasma pneumoniae* *Legionella pneumophila* *Chlamydia pneumoniae* Methicillin-resistant *Staphylococcus aureus* (MRSA) Influenza virus
Health care–associated	MRSA *Pseudomonas aeruginosa* *Klebsiella pneumoniae* *Acinetobacter* species *Stenotrophomonas* species *L. pneumophila*
Immunocompromised host	
Neutropenia	Any pathogen listed above *Aspergillus* species *Candida* species
Human immunodeficiency virus	Any pathogen listed above *Pneumocystis carinii* *Mycobacterium tuberculosis* *Histoplasma capsulatum* Other fungi Cytomegalovirus
Solid organ transplant or bone marrow transplant	Any pathogen listed above (Can vary depending on timing of infection to transplant)
Cystic fibrosis	*H. influenzae (early)* *S. aureus* *P. aeruginosa* *Burkholderia cepacia*
Lung abscess	*Bacteroides* species *Peptostreptococcus* species *Fusobacterium* species *Nocardia* (in immunocompromised patients) Amebic (when suggestive by exposure)
Empyema	
Usually acute	*S. aureus* *S. pneumoniae* Group A streptococci *H. influenzae*
Usually subacute or chronic	Anaerobic bacteria *Enterobacteriaceae* *M. tuberculosis*
Meningitis	
	S. pneumoniae *Neisseria meningitidis* *Listeria monocytogenes* *H. influenzae*
Neonates	*Escherichia coli* Group B streptococci
Postsurgical or post-trauma	*S. aureus* *Enterobacteriaceae* *P. aeruginosa*
Brain abscess	
	Streptococci *Bacteroides* species
Postsurgical or post-trauma	*Enterobacteriaceae* *S. aureus*
Immunocompromised or HIV infected	*Nocardia* *Toxoplasma gondii*
Encephalitis	
	West Nile virus Herpes simplex virus Arbovirus Rabies virus *Bartonella henselae*
Endocarditis	
	Streptococcus viridans *Enterococcus* species *S. aureus* *Streptococcus bovis*
Intravenous drug user, prosthetic valves	MRSA
Prosthetic valve	*Candida* species
Catheter-associated bacteremia	
	Candida species *S. aureus* *Enterococcus* species *Enterobacteriaceae* *P. aeruginosa*
Pyelonephritis	
	Enterobacteriaceae *E. coli* *Enterococcus* species
(This group catheter-associated, postsurgical)	*P. aeruginosa* *Acinetobacter* species

(*continued*)

TABLE 57-11 Pathogens commonly associated with serious infections in ICU patients.[1] (continued)

Infection or Site	Pathogens
Peritonitis	
Primary or spontaneous	*Enterobacteriaceae* *S. pneumoniae* *Enterococcus* species Anaerobic bacteria (rare)
Secondary (bowel perforation)	*Enterobacteriaceae* *Bacteroides* species *Enterococcus* species *P. aeruginosa* (uncommon)
Tertiary (bowel surgery, hospitalized on antibiotics)	*P. aeruginosa* MRSA *Acinetobacter* species *Candida* species
Skin structure infections	
Cellulitis	Group A streptococci *S. aureus* *Enterobacteriaceae* (diabetics)
Decubitus ulcer	Polymicrobial *Streptococcus pyogenes* *Enterococcus* species *Enterobacteriaceae* Anaerobic streptococci *P. aeruginosa* *S. aureus* *Bacteroides* species
Necrotizing fasciitis	*Streptococcus* species *Clostridia* species Mixed aerobic/anaerobic bacteria
Muscle infection	
Myonecrosis (gas gangrene)	*Clostridium perfringens* Other *Clostridia* species
Pyomyositis	*S. aureus* Group A streptococci Anaerobic bacteria Gram-negative bacteria (rare)
Septic shock	
Community-acquired	*S. pneumoniae* *N. meningitidis* *H. influenzae* *Escherichia coli* *Capnocytophaga* (with splenectomy)
Health care–associated	MRSA *P. aeruginosa* *Acinetobacter* species *Candida* species
Toxic shock syndrome	*S. aureus* *Streptococcus* species
Regional illness or special circumstances	Rickettsial species *Ehrlichia* species *Babesia* species *B. henselae* (immunocompromised hosts) *Yersinia pestis* *Francisella tularensis* *Leptospira* *Salmonella enteritidis* *Salmonella typhi*

[1]Reproduced, with permission, from Gabrielli A, Layon AJ, Yu M: *Civetta, Taylor & Kirby's Critical Care,* 4th ed. Lippincott Williams & Wilkins, 2009; Table 104.3, Chapter 104.

functioning cuff; nebulizers and humidifiers can also be sources of infection. Selective decontamination of the gut with nonabsorbable antibiotics may reduce the incidence of infection but does not change outcome. Elevating the head of the bed more than 30° reduces the likelihood of ventilator-associated pneumonia. Enteral nutrition reduces bacterial translocation across the gut and reduces the likelihood of sepsis (see Chapter 53).

Wounds are common sources of sepsis in postoperative and trauma patients; restricting antibiotic prophylaxis to the immediate perioperative time appears to decrease the incidence of postoperative infections in some groups of patients. Although more commonly seen in postoperative patients, intraabdominal infections due to perforated ulcer, diverticulitis, appendicitis, and acalculous cholecystitis can also develop in critically ill nonsurgical patients. Intravascular catheter-related infections are most commonly caused by *Staphylococcus epidermidis, Staphylococcus aureus,* streptococci, *Candida* species, and gram-negative rods. Bacterial sinusitis may be an unrecognized source of sepsis in patients ventilated through nasotracheal tubes. The diagnosis is suspected from purulent drainage and confirmed by imaging and cultures.

SEPTIC SHOCK

The SCCM/ESICM/ACCP/ATS/SIS Consensus Conference defined **septic shock** as sepsis associated with hypotension (systolic blood pressure <90 mm Hg, mean arterial pressure <60 mm Hg, or systemic blood pressure <40 mm Hg from baseline) despite adequate fluid resuscitation. Septic shock is usually characterized by inadequate tissue perfusion and widespread cellular dysfunction. In contrast to other forms of shock (hypovolemic, cardiogenic, neurogenic, or anaphylactic), cellular dysfunction in septic shock is not necessarily related to the hypoperfusion. Instead, metabolic blocks at the cellular and microcirculation levels may contribute to impaired cellular oxidation.

Pathophysiology

An infectious process that induces a severe or protracted SIRS can result in septic shock. In hospitalized patients septic shock most commonly follows gram-negative infections in either the genitourinary tract or the lungs, but identical presentations can be seen with other pathogens. In up to 50% of cases of severe sepsis no organisms can be cultured from blood. Hypotension is due to a decreased circulating intravascular volume resulting from a diffuse capillary leak. Patients may also have myocardial depression. Activation of platelets and the coagulation cascade can lead to the formation of fibrin-platelet aggregates, which further compromise tissue blood flow. Hypoxemia from ARDS accentuates tissue hypoxia. The release of vasoactive substances and formation of microthrombi in the pulmonary circulation increase pulmonary vascular resistance.

Hemodynamic Subsets

The circulation in patients with septic shock is often described as either hyperdynamic or hypodynamic. In reality, both represent the same process, but their expression depends on preexisting cardiac function and intravascular volume and the patient's response.

14 Systemic venodilation and transudation of fluid into tissues result in relative hypovolemia in patients with sepsis. Hyperdynamic septic shock is characterized by normal or elevated cardiac output and profoundly reduced systemic vascular resistance. Decreased myocardial contractility is often demonstrable by echocardiography even in hyperdynamic patients with increased cardiac output. Mixed venous oxygen saturation is characteristically increased in the absence of hypoxemia and likely reflects the increased cardiac output and the cellular metabolic defect in oxygen utilization.

It used to be accepted wisdom that hypodynamic septic shock, characterized by decreased cardiac output with low or normal systemic vascular resistance, was usually seen later in the course of shock. This view is false; hypodynamic shock often occurs early in the course of septic shock. It is more likely to be seen in severely hypovolemic patients and in those with underlying cardiac disease. Myocardial depression is prominent. Mixed venous oxygen saturation is reduced in these patients, and pulmonary hypertension is often prominent. Elevation of pulmonary vascular resistance widens the normal pulmonary artery diastolic-to-wedge pressure gradient; large gradients have been associated with a higher mortality rate. The increase in pulmonary vascular resistance may contribute to right ventricular dysfunction.

Clinical Manifestations

Manifestations of septic shock appear to be primarily related to host response rather than the infective agent. Septic shock classically presents with an abrupt onset of chills, fever, nausea (and often vomiting), decreased mental status, tachypnea, hypotension, and tachycardia. The patient may appear flushed and feel warm (hyperdynamic) or pale with cool and often cyanotic extremities (hypodynamic). In old, debilitated patients and in infants, the diagnosis often is less obvious and hypothermia may be seen.

Leukocytosis with a leftward shift to premature cell forms is typical, but leukopenia can be seen with overwhelming sepsis and is an ominous sign. Progressive metabolic acidosis (usually lactic acidosis) is typically partially compensated by a concomitant respiratory alkalosis. Elevated lactate levels reflect both increased production resulting from poor tissue perfusion and decreased uptake by the liver and kidneys. Hypoxemia may herald the onset of ARDS. Oliguria due to the combination of hypovolemia, hypotension, and a systemic inflammatory insult

will often progress to kidney failure. Elevations in serum aminotransferases and bilirubin are due to hepatic dysfunction. Insulin resistance is uniformly present and produces hyperglycemia. Thrombocytopenia is common and is often an early sign of sepsis. Laboratory evidence of disseminated intravascular coagulation (DIC) is often present but is rarely associated with a bleeding diathesis. The latter responds only to control of the sepsis. Stress ulceration of gastric mucosa is common. Respiratory and kidney failure are the leading causes of death in septic patients.

Neutropenic patients (absolute neutrophil count 500/μL) may develop macular or papular lesions that can ulcerate and become gangrenous (ecthyma gangrenosum). These lesions are commonly associated with *Pseudomonas* septicemia but can be caused by other organisms. Perirectal abscesses can develop very quickly in neutropenic patients with few external signs; conscious patients may complain only of perirectal pain.

Treatment

Septic shock is a medical emergency that requires immediate intervention. Treatment is threefold: (1) control and eradication of the infection by appropriate and timely intravenous antibiotics, drainage of abscesses, debridement of necrotic tissues, and removal of infected foreign bodies; (2) maintenance of adequate perfusion with intravenous fluids and inotropic and vasopressor agents; and (3) supportive treatment of complications such as ARDS, kidney failure, gastrointestinal bleeding, and DIC.

Antibiotic treatment usually is initiated before pathogens are identified but only after adequate cultures are obtained (commonly, blood, urine, wounds, and sputum). Pending the results of cultures and tests of antibiotic sensitivity, combination therapy with two or more antibiotics is generally indicated. Typically, the combination of a penicillin/β-lactamase inhibitor or third-generation cephalosporin with an aminoglycoside is used. The choice depends on which organisms are seen with the greatest frequency in one's medical center. Additional diagnostic studies may be indicated (eg, thoracentesis, paracentesis, lumbar puncture, or imaging), depending on the history and physical examination.

Empiric antibiotic therapy in immunocompromised patients should be based on pathogens that are generally associated with the immune defect (see Table 57–11). Vancomycin is added if intravascular catheter-related infection is suspected. Clindamycin or metronidazole may be given to neutropenic patients if a rectal abscess is suspected. Many clinicians initiate therapy for a presumed fungal infection when an immunocompromised patient continues to experience fever despite antibiotic therapy. Granulocyte colony-stimulating factor or granulocyte–macrophage colony-stimulating factor may be used to shorten the period of neutropenia; granulocyte transfusion may occasionally be used in refractory gram-negative bacteremia. Diffuse interstitial infiltrates on a chest radiograph may suggest unusual bacterial, parasitic, or viral pathogens; many clinicians initiate empiric therapy with trimethoprim-sulfamethoxazole and erythromycin in such instances. Nodular infiltrates on a radiograph suggest a fungal pneumonia and may warrant antifungal therapy. Antiviral therapy should be considered in septic patients who are more than 1 month post–bone marrow or solid organ transplantation.

In general, therapy should follow the most recent SCCM/ESICM "surviving sepsis" guidelines. The presence of inadequate perfusion is determined by measurement of blood lactate. "Goal-directed" hemodynamic support is also recommended by many groups. Tissue oxygenation and perfusion are supported with oxygen, intravenous fluids, inotropes, and vasopressors. Central venous pressure is maintained at greater than 8 mm Hg and central venous oxygen saturation is maintained at greater than 70%. Packed red blood cell transfusions are given to keep hemoglobin levels greater than 8 g/dL, especially when central venous pressure and central venous oxygen saturation are below targets. Marked "third-spacing" has long been regarded as characteristic of septic shock, but currently there is debate regarding the existence of the third space and the administration of large volumes of intravenous fluid as to which is cause and which is effect. Colloid solutions more rapidly restore intravascular volume compared with crystalloid solutions but otherwise offer no proven additional benefit. **Vasopressor therapy is generally initiated if hypotension**

(mean arterial pressure <65 mm Hg) or elevated blood lactate levels persist following administration of intravenous fluids. Suggested choices are norepinephrine or dopamine; other positive inotropic drugs (eg, dobutamine) are indicated only when the $S\bar{V}O_2$ falls below 70% despite fluids and vasopressor therapy. Patients with persisting elevations of lactate or persisting low central venous oxygen saturations, despite treatment, should receive a week-long course of steroids (200–300 mg/d of hydrocortisone or the equivalent in divided doses or by infusion). Blood glucose should be controlled with a target value of less than 180 mg/dL. In patients with hypotension that is refractory to norepinephrine plus dopamine or dobutamine, vasopressin may be administered to improve blood pressure. Severe acidosis may decrease the efficacy of inotropes and should therefore generally be corrected (pH > 7.20) with bicarbonate or THAM infusion in patients with refractory hypotension and lactic acidosis. "Renal" doses of dopamine or fenoldopam may increase urinary output but have not been shown to improve or protect kidney function or patient outcomes. Clinical trials of naloxone, opsonins (fibronectin), inhibitors of the coagulation cascade (drotrecogin alfa), and monoclonal antibodies directed against lipopolysaccharide in septic shock have been disappointing.

Gastrointestinal Hemorrhage

Acute gastrointestinal hemorrhage is a common reason for admission to the ICU. Older age (>60 years), comorbid illnesses, hypotension, marked blood loss (>5 units), and recurrent hemorrhage (rebleeding) after 72 h are associated with increased mortality. Management consists of stabilizing the patient with rapid identification of the site of bleeding. Although volume resuscitation is similar, the clinician must attempt to differentiate between upper and lower gastrointestinal bleeding. A history of hematemesis indicates bleeding proximal to the ligament of Treitz. Melena often indicates bleeding proximal to the cecum. Hematochezia (bright red blood from the rectum) indicates either very brisk upper gastrointestinal bleeding (likely to be associated with hypotension) or more commonly lower gastrointestinal bleeding. The presence of maroon stools usually localizes the bleeding to the area between the distal small bowel and the right colon.

Two large-bore intravenous cannulas should be placed, and blood should be sent for laboratory analysis (including hemoglobin, platelet count, prothrombin time, and activated partial thromboplastin time). The patient should also be cross-matched for at least 4 units of red cells. Fluid resuscitation guidelines are discussed in Chapter 51. Serial hemoglobin or hematocrit measurements are useful but may not accurately reflect true blood loss. Intraarterial blood pressure monitoring can be helpful. Central venous cannulation is useful for both venous access and pressure measurements. Placement of a nasogastric tube may help identify an upper gastrointestinal source if bright red blood or "coffee grounds"–appearing material can be aspirated; inability to aspirate blood, however, does not rule out an upper gastrointestinal source.

Upper Gastrointestinal Bleeding

Lavage through a nasogastric tube can help assess the rate of bleeding and facilitate esophagogastroduodenoscopy (EGD). EGD should be performed whenever possible to diagnose the cause of bleeding. Arteriography should be performed if the site of bleeding cannot be visualized with endoscopy. Both EGD and arteriography can also be used therapeutically to stop the bleeding. In unselected patients the more common causes of upper gastrointestinal bleeding, in decreasing order of likelihood, are duodenal ulcer, gastric ulcer, erosive gastritis, and esophageal varices. Erosive gastritis may be due to stress, alcohol, aspirin, nonsteroidal antiinflammatory drugs, and corticosteroids. Less common causes of upper gastrointestinal bleeding include angiodysplasia, erosive esophagitis, Mallory–Weiss tear, gastric tumor, and aortoenteric fistula.

Bleeding from peptic ulcers (gastric or duodenal) can be coagulated via EGD. Surgery is generally indicated for severe hemorrhage (>5 units) and recurrent bleeding. H_2-receptor blockers and proton pump inhibitors are ineffective in stopping hemorrhage but may reduce the likelihood of rebleeding. Selective arteriography of the bleeding

vessel allows localized infusion of vasopressin (0.15–0.20 units/min) or embolization.

Erosive gastritis is better prevented than treated. Proton pump inhibitors, H_2-receptor blockers, antacids, and sucralfate are all effective for prevention. In the past some have advocated that all patients with critical illness receive a proton pump inhibitor. However, overuse of proton pump inhibitors is associated with an increased incidence of hospital-acquired pneumonia. Data show that patients who require mechanical ventilation for more than 48 h or who are coagulopathic derive the greatest benefit from prophylaxis. Other groups of patients showing relative benefit from prophylaxis include those with AKI, sepsis, liver failure, hypotension, traumatic brain injury, a history of prior gastrointestinal hemorrhage, recent major surgery, or those receiving large-dose corticosteroid therapy. Once bleeding has begun, there is generally no specific therapy other than embolization or coagulation.

Endoscopic therapy, either with bipolar electrocoagulation or heater probes, is the most effective nonsurgical treatment that reduces blood transfusions, rebleeding, hospital stay, and the need for urgent surgery. Sedation or anesthesia to facilitate these procedures is associated with an increased risk of aspiration. Intravenous vasopressin infusions (0.3–0.8 units/min) are not as effective; concomitant infusion of nitroglycerin with vasopressin can help reduce portal pressure and may reduce the incidence of cardiac complications. Intravenous propranolol can also lower portal venous pressure and may reduce variceal bleeding. Balloon tamponade (Sengstaken–Blakemore, Minnesota, or Linton tubes) may be used as adjunctive therapy but usually requires concurrent tracheal intubation to protect the airway against aspiration.

Lower Gastrointestinal Bleeding

Common causes of lower gastrointestinal bleeding include diverticulosis, angiodysplasia, neoplasms, inflammatory bowel disease, ischemic colitis, infectious colitis, and anorectal disease (hemorrhoids, fissure, or fistula). Rectal examination, anoscopy, and sigmoidoscopy can usually diagnose the more distal lesions. As with EGD, colonoscopy usually allows definitive diagnosis and is often useful therapeutically. Radionuclide techniques can be used to identify the source of bleeding when colonoscopy cannot be carried out because of inadequate preparation.

Cauterization of the site of bleeding is often possible via colonoscopy. When colonoscopy is unavailable or not possible because of brisk bleeding, selective arteriography can be used to identify the source, which is either embolized or infused with vasopressin. Surgical treatment is reserved for severe or recurrent hemorrhage.

Head Trauma

The diagnosis and management of traumatic brain injury is described in Chapter 39.

End-of-Life Care

In the United States, death is a taboo subject for many, and most people avoid preparing for it until late in their own lives, and some not even then. Many attend to last wills and testaments, estate planning, and taxes, but less than 15% of the adult population is prepared to make advance decisions about restrictions on life-supporting measures. Yet surveys consistently show a strong preference for a dignified, comfortable, and peaceful death at home and a strong wish to avoid dying in a hospital, particularly in an ICU.

The quandary about what to do is particularly vexing when it concerns a surgical patient who sought relief from symptoms, improved functionality, and a better quality of life, but who ends up with a bad outcome requiring ongoing life-supporting measures with little prospect of achieving the goals of the operation.

A substantial number of physicians cannot discuss such difficult situations in a humane, nonadversarial manner or deal with the anger, despair, and other emotions of family members and friends whose expectations have not been met. Good communication skills are the essential foundation. Communications with the family, friends, and all caregivers must be timely, consistent (having only one physician serve as the spokesman has great advantages), accurate, clear to laypersons, advisory without being dictatorial, focused on what is best for

the patient, and aligned with the patient's wishes. A gradual stepwise approach over time allows family members and friends time to digest the information; get beyond their normal, initial reactions to the bad news; and make the difficult decision to withdraw intensive support.

Finally, it is important to recognize two ethical principles that are relevant here. The first is the principle of double effect. All medical interventions have potential benefits as well as burdens and risks. If the doses of morphine or sedative drug required to relieve pain and agitation result in unintended side effects, we accept them, even if the result is death. *This is not euthanasia.* The second principle is that withdrawal of medical therapies and interventions is no different from withholding them: both may be done to respect the patient's autonomy. There is a broad religious consensus that heroic measures are not mandated to support a heartbeat at the end of life.

CASE DISCUSSION

An Obtunded Young Woman

A 23-year-old woman is admitted to the hospital obtunded with slow respirations (7 breaths/min). Blood pressure is 90/60 mm Hg and the pulse is 90 beats/min. She was found at home in bed with empty bottles of diazepam, acetaminophen with codeine, and fluoxetine lying next to her.

How is the diagnosis of a drug overdose made?

The presumptive diagnosis of a drug overdose usually must be made from the history, circumstantial evidence, and any witnesses. Signs and symptoms may not be helpful. Confirmation of a suspected drug overdose or poison ingestion usually requires delayed laboratory testing for the suspected agent in body fluids. Intentional overdoses (self-poisoning) are the most common mechanism and typically occur in young adults who are depressed. Ingestion of multiple drugs is common. Benzodiazepines, antidepressants, aspirin, acetaminophen, and alcohol are the most commonly ingested agents.

Accidental overdoses frequently occur in intravenous drug abusers and children. Commonly abused substances include opioids, stimulants (cocaine and methamphetamine), and hallucinogens (phencyclidine [PCP]). Younger children occasionally accidentally ingest caustic household alkali (eg, drain cleaner), acids, and hydrocarbons (eg, petroleum products), in addition to unsecured medications of all types. Organophosphate poisoning (parathion and malathion) usually occurs in adults following agricultural exposure. Overdoses and poisoning less commonly occur as an attempted homicide.

What are appropriate steps in managing this patient?

Regardless of the type of drug or poison ingested, the principles of initial supportive care are the same. Airway patency with adequate ventilation and oxygenation must be obtained. Unless otherwise contraindicated, oxygen therapy (100%) should be administered. Hypoventilation and obtunded airway reflexes require tracheal intubation and mechanical ventilation. Many clinicians routinely administer naloxone (up to 2 mg), dextrose 50% (50 mL), and thiamine (100 mg) intravenously to all obtunded or comatose patients until a diagnosis is established; this may help exclude or treat opioid overdose, hypoglycemia, and Wernicke–Korsakoff syndrome, respectively. The dextrose can be omitted if a glucose determination can be obtained by a fingerstick. In this case, intubation should be performed prior to naloxone because the respiratory depression is likely due to both the codeine and the diazepam.

Blood, urine, and gastric fluid specimens should be obtained and sent for drug screening. Blood is also sent for routine hematological and chemistry studies (including liver function). Urine is usually obtained by bladder catheterization, and gastric fluid can be aspirated from a nasogastric tube; the latter should be placed after intubation to avoid pulmonary aspiration. Alternatively, emesis material may be tested for drugs in conscious persons.

Hypotension should generally be treated with intravenous fluids unless the patient is obviously in pulmonary edema; an inotrope or vasopressor

may be necessary in some instances. Seizure activity may be the result of hypoxia or a pharmacological action of a drug (tricyclic antidepressants) or poison. Seizure activity is unlikely in this patient because she ingested diazepam, a potent anticonvulsant.

Should flumazenil be administered?

Flumazenil should generally not be administered to patients who overdose on both a benzodiazepine and an antidepressant and those who have a history of seizures. Reversal of the benzodiazepine's anticonvulsant action can precipitate seizure activity in such instances. Moreover, as is the case with naloxone and opioids, the half-life of flumazenil is shorter than that of benzodiazepines. Thus, it is often preferable to ventilate the patient until the benzodiazepine effect dissipates, the patient regains consciousness, and the respiratory depression resolves.

Should any other antidotes be given?

Because the patient also ingested an unknown quantity of acetaminophen (paracetamol) administration of *N*-acetylcysteine (NAC; Mucomyst) should be considered. Acetaminophen toxicity is due to depletion of hepatic glutathione, resulting in the accumulation of toxic metabolic intermediates. Hepatic toxicity is usually associated with ingestion of more than 140 mg/kg of acetaminophen. NAC prevents hepatic damage by acting as a sulfhydryl donor and restoring hepatic glutathione levels. If the patient is suspected of having ingested a toxic dose of acetaminophen, an initial dosage of NAC (140 mg/kg orally or by nasogastric tube) should be administered even before plasma acetaminophen levels are obtained; additional doses are given according to the measured plasma level. If the patient cannot tolerate oral or gastric administration of NAC, if the patient is pregnant, or if the risk of hepatotoxicity is high, NAC should be given intravenously.

What measures might limit drug toxicity?

Toxicity might be reduced by decreasing drug absorption or enhancing elimination. Gastrointestinal absorption of an ingested substance can be reduced by emptying stomach contents and administering activated charcoal. Both methods can be effective up to 12 h following ingestion. If the patient is intubated, the stomach is lavaged carefully to avoid pulmonary aspiration. Emesis may be induced in conscious patients with syrup of ipecac 30 mL (15 mL in a child). Gastric lavage and induced emesis are generally contraindicated for patients who ingest caustic substances or hydrocarbons because of a high risk of aspiration and worsening mucosal injury.

Activated charcoal 1–2 g/kg is administered orally or by nasogastric tube with a diluent. The charcoal irreversibly binds most drugs and poisons in the gut, allowing them to be eliminated in stools. In fact, charcoal can create a negative diffusion gradient between the gut and the circulation, allowing the drug or poison to be effectively removed from the body.

Alkalinization of the serum with sodium bicarbonate for tricyclic antidepressant overdose is beneficial because, by increasing pH, protein binding is enhanced; if seizures occur the alkalinization prevents acidosis-induced cardiotoxicity.

What other methods can enhance drug elimination?

The easiest method of increasing drug elimination is forced diuresis. Unfortunately, this method is of limited use for drugs that are highly protein bound or have large volumes of distribution. Mannitol or furosemide with saline may be used. Concomitant administration of alkali (sodium bicarbonate) enhances the elimination of weakly acidic drugs such as salicylates and barbiturates; alkalization of the urine traps the ionized form of these drugs in the renal tubules and enhances urinary elimination. Hemodialysis is usually reserved for patients with severe toxicity who continue to deteriorate despite aggressive supportive therapy.

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