16 - Critical Care Medicine

Chapter 222. Approach to the Critically Ill Patient

Introduction

Critical care medicine specializes in caring for the most seriously ill patients. These patients are best treated in an ICU staffed by experienced personnel. Some hospitals maintain separate units for special populations (eg, cardiac, surgical, neurologic, pediatric, or neonatal patients). ICUs have a high nurse:patient ratio to provide the necessary high intensity of service, including treatment and monitoring of physiologic parameters.

Supportive care for the ICU patient includes provision of adequate nutrition (see p. 21) and prevention of infection, stress ulcers and gastritis (see p. 131), and pulmonary embolism (see p. 1920). Because 15 to 25% of patients admitted to ICUs die there, physicians should know how to minimize suffering and help dying patients maintain dignity (see p. 3480).

Patient Monitoring and Testing

Some monitoring is manual (ie, by direct observation and physical examination) and intermittent, with the frequency depending on the patient's illness. This monitoring usually includes measurement of vital signs (temperature, BP, pulse, and respiration rate), quantification of all fluid intake and output, and often daily weight. BP may be recorded by an automated sphygmomanometer; a transcutaneous sensor for pulse oximetry is used as well.

Other monitoring is ongoing and continuous, provided by complex devices that require special training and experience to operate. Most such devices generate an alarm if certain physiologic parameters are exceeded. Every ICU should strictly follow protocols for investigating alarms.

Blood Tests

Although frequent blood draws can destroy veins, cause pain, and lead to anemia, ICU patients typically have routine daily blood tests to help detect problems early. Generally, patients need a daily set of electrolytes and a CBC. Patients with arrhythmias should also have Mg, phosphate, and Ca levels measured. Patients receiving TPN need weekly liver enzymes and coagulation profiles. Other tests (eg, blood culture for fever, CBC after a bleeding episode) are done as needed.

Point-of-care testing uses miniaturized, highly automated devices to do certain blood tests at the patient's bedside or unit (particularly ICU, emergency department, and operating room). Commonly available tests include blood chemistries, glucose, ABGs, CBC, cardiac markers, and coagulation tests. Many are done in < 2 min and require < 0.5 mL blood.

Cardiac Monitoring

Most critical care patients have cardiac activity monitored by a 3-lead system; signals are usually sent to a central monitoring station by a small radio transmitter worn by the patient. Automated systems generate alarms for abnormal rates and rhythms and store abnormal tracings for subsequent review.

Some specialized cardiac monitors track advanced parameters associated with coronary ischemia, although their clinical benefit is unclear. These parameters include continuous ST-segment monitoring and heart rate variability. Loss of normal beat-to-beat variability signals a reduction in autonomic activity and possibly coronary ischemia and increased risk of death.

Pulmonary Artery Catheter Monitoring

Use of a pulmonary artery catheter (PAC) is becoming less common in ICU patients. This balloon-tipped, flow-directed catheter is inserted via central veins through the right side of the heart into the pulmonary artery. The catheter typically contains several ports that can monitor pressure or inject fluids. Some PACs

also include a sensor to measure central (mixed) venous O_2 saturation. Data from PACs are used mainly to determine cardiac output and preload. Preload is most commonly estimated by the pulmonary artery occlusion pressure (see p. 2245). However, preload may be more accurately determined by right ventricular end-diastolic volume, which is measured using fast-response thermistors gated to heart rate.

Despite longstanding use, PACs have not been shown to reduce morbidity and mortality. Rather, PAC use has been associated with excess mortality. This finding may be explained by complications of PAC use and misinterpretation of the data obtained. Nevertheless, some physicians believe PACs, when combined with other objective and clinical data, aid in the management of certain critically ill patients. As with many physiologic measurements, a changing trend is typically more significant than a single abnormal value. Possible indications for PACs are listed in Table 222-1.

Procedure: The PAC is inserted through a special catheter in the subclavian or internal jugular vein with the balloon deflated. Once the catheter tip reaches the superior vena cava, partial inflation of the balloon permits blood flow to guide the catheter. The position of the catheter tip is usually determined by pressure monitoring (see Table 222-2 for intracardiac and great vessel pressures) or occasionally by fluoroscopy. Entry into the right ventricle is indicated by a sudden increase in systolic pressure to about 30 mm Hg; diastolic pressure remains unchanged from

[**Table 222-1.** Potential Indications for Pulmonary Artery Catheterization]

right atrial or vena caval pressure. When the catheter enters the pulmonary artery, systolic pressure does not change, but diastolic pressure rises above right ventricular end-diastolic pressure or central venous pressure (CVP); ie, the pulse pressure narrows. Further movement of the catheter wedges the balloon in a distal pulmonary artery. A chest x-ray confirms proper placement.

The systolic pressure (normal, 15 to 30 mm Hg) and diastolic pressure (normal, 5 to 13 mm Hg) are recorded with the catheter balloon deflated. The diastolic pressure corresponds well to the occlusion pressure, although diastolic pressure can exceed occlusion pressure when pulmonary vascular resistance is elevated secondary to primary pulmonary disease (eg, pulmonary fibrosis, pulmonary hypertension).

Pulmonary artery occlusion pressure (PAOP): With the balloon inflated, pressure at the tip of the catheter reflects the static back pressure of the pulmonary veins. The balloon must not remain inflated for > 30 sec to prevent pulmonary infarction. Normally, PAOP approximates left atrial pressure, which in turn approximates left ventricular end-diastolic pressure (LVEDP). LVEDP reflects left ventricular end-diastolic volume (LVEDV). The LVEDV represents preload, which is the actual target parameter. Many factors cause PAOP to reflect LVEDV inaccurately. These factors include mitral stenosis, high levels of positive end-expiratory pressure (> 10 cm H_2O), and changes in left ventricular compliance (eg, due to MI, pericardial effusion, or increased afterload). Technical difficulties result from excessive balloon inflation, improper catheter position, alveolar pressure exceeding pulmonary venous pressure, or severe pulmonary hypertension (which may make the balloon difficult to wedge).

Elevated PAOP occurs in left-sided heart failure. Decreased PAOP occurs in hypovolemia or decreased preload.

Mixed venous oxygenation: Mixed venous blood comprises blood from the superior and inferior vena cava that has passed through the right heart to the pulmonary artery. The blood may be sampled from the distal port of the PAC, but some catheters have embedded fiberoptic sensors that directly measure O_2 saturation.

[**Table 222-2.** Normal Pressures in the Heart and Great Vessels]

Causes of low mixed venous O_2 content ($SmvO_2$) include anemia, pulmonary disease, carboxyhemoglobin, low cardiac output, and increased tissue metabolic needs. The ratio of SaO_2 to

(SaO_2 - $SmvO_2$) determines the adequacy of O_2 delivery. The ideal ratio is 4:1, whereas 2:1 is the minimum acceptable ratio to maintain aerobic metabolic needs.

Cardiac output: Cardiac output (CO) is measured by intermittent bolus injection of ice water or, in new catheters, continuous warm thermodilution. The cardiac index divides the CO by body surface area to correct for patient size (see Table 222-3).

Other variables can be calculated from CO. They include systemic and pulmonary vascular resistance and right ventricular stroke work (RVSW) and left ventricular stroke work (LVSW).

Complications and precautions: PACs may be difficult to insert. Cardiac arrhythmias are the most common complication. Pulmonary infarction secondary to overinflated or permanently wedged balloons, pulmonary artery perforation, intracardiac perforation, valvular injury, and endocarditis may occur. Rarely, the catheter may curl into a knot within the right ventricle (especially in patients with heart failure, cardiomyopathy, or increased pulmonary pressure).

[**Table 222-3.** Normal Values for Cardiac Index and Related Measurements]

Pulmonary artery rupture occurs in < 0.1% of PAC insertions. This catastrophic complication is often fatal and occurs immediately on wedging the catheter either initially or during a subsequent occlusion pressure check. Thus, many physicians prefer to monitor pulmonary artery diastolic pressures rather than occlusion pressures.

Noninvasive Cardiac Output

Other methods of determining CO, such as thoracic bioimpedance and the esophageal Doppler monitor, are being developed to avoid the complications of PACs. Although these methods are potentially useful, neither is yet as reliable as a PAC.

Thoracic bioimpedance: These systems use topical electrodes on the anterior chest and neck to measure electrical impedance of the thorax. This value varies with beat-to-beat changes in thoracic blood volume and hence can estimate CO. The system is harmless and provides values quickly (within 2 to 5 min); however, the technique is very sensitive to alteration of the electrode contact with the patient. Thoracic bioimpedance is more valuable in recognizing changes in a given patient than in precisely measuring CO.

Esophageal Doppler monitor (EDM): This device is a soft 6-mm catheter that is passed nasopharyngeally into the esophagus and positioned behind the heart. A Doppler flow probe at its tip allows continuous monitoring of CO and stroke volume. Unlike the invasive PAC, the EDM does not cause pneumothorax, arrhythmia, or infection. An EDM may actually be more accurate than a PAC in patients with cardiac valvular lesions, septal defects, arrhythmias, or pulmonary hypertension. However, the EDM may lose its waveform with only a slight positional change and produce dampened, inaccurate readings.

Intracranial Pressure Monitoring

Intracranial pressure (ICP) monitoring is standard for patients with severe closed head injury. These devices are used to optimize cerebral perfusion pressure (mean arterial pressure minus intracranial pressure). Typically, the cerebral perfusion pressure should be kept > 60 mm Hg.

Several types of ICP monitors are available. The most useful method places a catheter through the skull into a cerebral ventricle (ventriculostomy catheter). This device is preferred because the catheter can also drain CSF and hence decrease ICP. However, the ventriculostomy is also the most invasive method, has the highest infection rate, and is the most difficult to place. Occasionally, the ventriculostomy becomes occluded due to severe brain edema.

Other types of intracranial devices include an intraparenchymal monitor and an epidural bolt. Of these,

the intraparenchymal monitor is more commonly used. All ICP devices should usually be changed or removed after 5 to 7 days because infection is a risk.

Other Types of Monitoring

Sublingual capnometry uses a similar correlation between elevated sublingual PCO_2 and systemic hypoperfusion to monitor shock states using a noninvasive sensor placed under the tongue. This device is easier to use than gastric tonometry and responds quickly to perfusion changes with resuscitation.

Tissue spectroscopy uses a noninvasive near infrared (NIR) sensor usually placed on the skin above the target tissue to monitor mitochondrial cytochrome a,a redox states, which reflect tissue perfusion. NIR may help diagnose acute compartment syndromes (eg, in trauma) or ischemia after free tissue transfer and may be helpful in postoperative monitoring of lower-extremity vascular bypass grafts. NIR monitoring of small-bowel pH may be used to gauge the adequacy of resuscitation.

Scoring Systems

Several scoring systems have been developed to grade the severity of illness in critically ill patients. These systems are moderately accurate in predicting individual survival. However, these systems are more valuable for monitoring quality of care and for conducting research studies because they allow comparison of outcomes among groups of critically ill patients with similar illness severity.

The most common system is the 2nd version of the Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score introduced in 1985. It generates a point score ranging from 0 to 71 based on 12 physiologic variables, age, and underlying health (see Table 222-4). The APACHE III system was developed in 1991. This system is more complex, has 17 physiologic variables, and is somewhat less used. There are many other systems, including the 2nd Simplified Acute Physiology Score (SAPS II) and several mortality probability models.

Vascular Access

A number of procedures are used to gain vascular access.

Peripheral Vein Catheterization

Most patients' needs for IV fluid and drugs can be met with a percutaneous peripheral venous catheter. Venous cutdown can be used when percutaneous catheter insertion is not feasible. Typical cutdown sites are the cephalic vein in the arm and the saphenous vein at the ankle.

Common complications (eg, local infection, venous thrombosis, thrombophlebitis, interstitial fluid extravasation) can be reduced by using a meticulous sterile technique during insertion and by replacing or removing the catheters within 72 h.

Central Venous Catheterization

Patients needing secure or long-term vascular access (eg, to receive antibiotics, chemotherapy, or TPN) are best treated with a central venous catheter (CVC). CVCs allow infusion of solutions that are too concentrated or irritating for peripheral veins and allow monitoring of central venous pressure (CVP—see p. 2299).

Procedure: CVCs are inserted using sterile technique and a local anesthetic (eg, 1% lidocaine). The superior vena cava is entered via percutaneous puncture of the subclavian or the internal or external jugular vein or by venous cutdown on the basilic vein. The inferior vena cava may be entered through the common femoral vein percutaneously or by cutdown on the saphenous vein. The choice of site depends on operator preference and patient habitus and ambulatory status. However, femoral venous catheters have a slightly higher rate of complications than those above the waist. Also, during cardiac arrest, fluid and drugs given through a femoral or saphenous vein CVC often fail to circulate above the diaphragm because of the increased intrathoracic pressure generated by CPR. In this case, a subclavian or internal

jugular approach may be preferred.

If possible, the patient's coagulation status and platelet count should be normalized before CVC insertion. Percutaneous femoral lines must be inserted below the inguinal ligament. Otherwise, laceration of the external iliac vein or artery above the inguinal ligament may result in retroperitoneal hemorrhage; external compression of these vessels is nearly impossible. The subclavian vein also is not

[**Table 222-4.** Acute Physiologic Assessment and Chronic Health Evaluation (Apache) II Scoring System*]

compressible with external pressure, and thus hemorrhage can be serious. A cutdown decreases the risk of bleeding-associated complications, particularly if coagulopathy is present.

After a subclavian or internal jugular catheter is inserted, a chest x-ray is taken to locate the catheter tip and to exclude a pneumothorax. To prevent cardiac arrhythmias, clinicians should withdraw catheters in the right atrium or ventricle until the tip is within the superior vena cava.

To reduce the risk of venous thrombosis and catheter sepsis, clinicians should remove CVCs as soon as possible. The skin entry site must be cleansed and inspected daily for local infection; the catheter must be replaced if local or systemic infection occurs. Some clinicians feel it is beneficial to change CVC catheters at regular intervals (eg, every 5 to 7 days) in patients with sepsis who remain febrile; this approach may reduce the risk of bacterial colonization of the catheter.

Complications: CVCs can cause many complications (see Table 222-5). Pneumothorax occurs in 1% of patients after CVC insertion. Atrial or ventricular arrhythmias frequently occur during catheter insertion but are generally self-limited and subside when the guide wire or catheter is withdrawn from within the heart. The incidence of catheter bacterial colonization without systemic infection may be as high as 35%, whereas that of true sepsis is 2 to 8%. Rarely, accidental arterial catheterization requires surgical repair of the artery. Hydrothorax and hydromediastinum may occur when catheters are positioned extravascularly. Catheter damage to the tricuspid valve, bacterial endocarditis, and air and catheter embolism occur rarely.

Arterial Catheterization

The use of automated noninvasive BP devices has diminished the use of arterial catheters simply for pressure monitoring. However, these catheters are beneficial in unstable patients who require minute-to-minute pressure measurement and in those requiring frequent ABG sampling. Indications include refractory shock and respiratory failure. BP is frequently somewhat higher when measured by an arterial catheter than by sphygmomanometry. Initial upstroke, maximum systolic pressure, and pulse pressure increase the more distal the point of measurement, whereas the diastolic and mean arterial pressures decline. Vessel calcification, atherosclerosis, proximal occlusion, and extremity position can all affect the value of arterial catheter measurements.

[**Table 222-5.** Complications Associated with Central Venous Catheters]

Procedure: Arterial catheters are inserted using sterile technique and a local anesthetic (eg, 1% lidocaine). They are typically inserted percutaneously into the radial, femoral, axillary, brachial, dorsalis pedis, and (in children) temporal arteries. The radial artery is most frequently used; insertion into the femoral artery has fewer complications but should be avoided after vascular bypass surgery (due to potential injury to the bypass graft) and in patients with distal vascular insufficiency (to avoid precipitating ischemia). When percutaneous insertion is unsuccessful, a cutdown may be done.

Before radial artery catheterization, Allen's test (digital compression of both ulnar and radial arteries causes palmar blanching followed by hyperemia when either artery is released) can determine whether there is sufficient ulnar collateral flow to perfuse the hand in the event of radial artery occlusion. If reperfusion does not occur within 8 sec of releasing the compressed ulnar artery, arterial catheterization should not be done.

Complications: At all sites, bleeding, infection, thrombosis, and distal embolism may occur. Catheters

should be removed if signs of local or systemic infection are present.

Radial arterial complications include ischemia of the hand and forearm due to thrombosis or embolism, intimal dissection, or spasm at the site of catheterization. The risk of arterial thrombosis is higher in small arteries (explaining the greater incidence in women) and with increased duration of catheterization. Occluded arteries nearly always recanalize after catheter removal.

Femoral arterial complications include atheroembolism during guide wire insertion. The incidence of thrombosis and distal ischemia is much lower than that for radial arterial catheterization.

Axillary arterial complications include hematomas, which are infrequent but may require urgent care because brachial plexus compression can result in permanent peripheral neuropathy. Flushing the axillary arterial catheter may introduce air or a clot. To avoid neurologic sequelae of these emboli, clinicians should select the left axillary artery for catheterization (the left axillary artery branches further distal to the carotid vessels than does the right).

Intraosseous Infusion

Any fluid or substance routinely given IV (including blood products) may be given via a sturdy needle inserted in the medullary cavity of select long bones. Fluids reach the central circulation as quickly as with venous infusion. This technique is used almost exclusively in infants and young children, whose bony cortices are thin and easily penetrated and in whom peripheral and central venous access can be quite difficult, particularly in shock or cardiac arrest. However, this technique can be used in older patients with special devices.

Procedure: A special-purpose intraosseous needle with stylet is used. The preferred insertion sites in children are the proximal tibia and distal femur; both areas are given a sterile preparation and are included in the operative field. For tibial insertion, the needle is placed on the broad, flat anteromedial surface 1 to 2 cm distal to the tibial tubercle. For the femur, the site is 3 cm above the lateral condyle in the midline. For older children, the medial surface of the distal tibia 2 cm above the medial malleolus may be easier.

For all sites, the needle is inserted with a rotary, coring motion. Stabilizing the needle shaft at the skin surface with a gloved fingertip aids control, allowing advancement to be stopped once the cortex is penetrated. On entering the medullary cavity, the stylet is removed and infusion is begun.

Complications: Poor control during insertion may result in the needle exiting the opposite cortex; then, subsequent infusion largely enters the soft tissues, so a site on another bone should be tried. Osteomyelitis may occur but is uncommon (eg, < 2 to 3%). Growth plate damage has not been reported. Other complications include bleeding and compartment syndrome.

Oxygen Desaturation

(Hypoxia)

ICU (and other) patients without respiratory disorders may develop hypoxia (O_2 saturation < 90%) during a hospital stay. Hypoxia in patients with known respiratory conditions is discussed under those disorders.

Etiology

Numerous disorders cause hypoxia (eg, dyspnea, respiratory failure; see Table 222-6); however, acute hypoxia developing in a patient hospitalized with a nonrespiratory illness usually has a more limited set of causes. These causes can be divided into

- Disorders of ventilation

- Disorders of oxygenation

Evaluation

Total fluid volume given during the hospital stay and, in particular, the previous 24 h should be ascertained to identify volume overload. Drugs should be reviewed for sedative administration and dosage. In significant hypoxia (O_2 saturation < 85%), treatment begins simultaneously with evaluation.

History: Very sudden onset dyspnea and hypoxia suggest pulmonary embolus (PE) or pneumothorax (mainly in a patient on positive pressure ventilation). Fever, chills, and productive cough (or increased secretions) suggest pneumonia. A history of cardiopulmonary disease (eg, asthma, COPD, heart failure) may indicate an exacerbation of the disease. Unilateral extremity pain suggests deep venous thrombosis (DVT) and hence possible

[**Table 222-6.** Some Causes of Oxygen Desaturation]

PE. Preceding major trauma or sepsis requiring significant resuscitation suggests acute respiratory distress syndrome. Preceding chest trauma suggests pulmonary contusion.

Physical examination: Patency of the airway and strength and adequacy of respirations should be assessed immediately. For patients on mechanical ventilation, it is important to determine that the endotracheal tube is not obstructed or dislodged. Unilateral decreased breath sounds with clear lung fields suggest pneumothorax or right mainstem bronchus intubation; with crackles and fever, pneumonia is more likely. Distended neck veins with bilateral lung crackles suggest volume overload; distention with clear lungs and tracheal deviation suggests tension pneumothorax. Bilateral lower-extremity edema suggests heart failure, but unilateral edema suggests DVT and hence possible PE. Wheezing represents bronchospasm (typically asthma or allergic reaction, but it occurs rarely with PE or heart failure). Decreased mental status suggests hypoventilation.

Testing: Hypoxia is generally recognized initially by pulse oximetry. Patients should have a chest x-ray, ECG, and ABGs (to confirm hypoxia and evaluate adequacy of ventilation). If diagnosis remains unclear after these tests, testing for PE (see p. 1909) should be considered. Bronchoscopy may be done in intubated patients to rule out (and remove) a tracheobronchial plug. Pulmonary artery catheterization may be needed to rule out heart failure if volume status is unclear.

Treatment

Identified causes are treated as discussed elsewhere in THE MANUAL. If hypoventilation persists, mechanical ventilation via noninvasive positive pressure ventilation or endotracheal intubation is necessary (see p. 2279). Persistent hypoxia requires supplemental O_2.

O_2 therapy: The amount of O_2 given is guided by ABG or pulse oximetry to maintain PaO_2 between 60 and 80 mm Hg (ie, 92 to 100% saturation) without causing O_2 toxicity. This level provides satisfactory tissue O_2 delivery; because the oxyhemoglobin dissociation curve is sigmoidal, increasing PaO_2 to > 80 mm Hg increases O_2 delivery very little and is not necessary. The lowest fractional inspired O_2 (FIO_2) that provides an acceptable PaO_2 should be provided. O_2 toxicity is both concentration- and time-dependent. Sustained elevations in FIO_2 > 60% result in inflammatory changes, alveolar infiltration, and, eventually, pulmonary fibrosis. An FIO_2 > 60% should be avoided unless necessary for survival. An FIO_2 < 60% is well tolerated for long periods.

An FIO_2 < 40% can be given via nasal cannula or simple face mask. A nasal cannula uses an O_2 flow of 1 to 6 L/min. Because 6 L/min is sufficient to fill the nasopharynx, higher flow rates are of no benefit. Simple face masks and nasal cannulas do not deliver a precise FIO_2 because of inconsistent admixture of O_2 with room air from leakage and mouth breathing. However, Venturi-type masks can deliver very accurate O_2 concentrations.

An FIO_2 > 40% requires use of an O_2 mask with a reservoir that is inflated by O_2 from the supply. In the

typical nonrebreather mask, the patient inhales 100% O_2 from the reservoir, but during exhalation, a rubber flap valve diverts exhaled breath to the environment, preventing admixture of CO_2 and water vapor with the inspired O_2. Nonetheless, because of leakage, such masks deliver an FIO_2 of at most 80 to 90%.

Oliguria

Oliguria is urine output < 500 mL in 24 h in an adult or < 0.5 mL/kg/h in an adult or child (< 1 mL/kg/h in neonates).

Etiology

Causes of oliguria are typically divided into 3 categories:

• Prerenal (blood-flow related)

• Renal (intrinsic kidney disorders)

• Postrenal (outlet obstruction)

There are numerous such entities (see p. 2436), but a limited number cause most cases of acute oliguria in hospitalized patients (see Table 222-7).

Evaluation

History: In communicative patients, a marked urge to void suggests outlet obstruction, whereas thirst and no urge to void suggest volume depletion. In obtunded (and presumably catheterized) patients, a sudden decrease in urine flow in a normotensive patient suggests catheter occlusion (eg, caused by a clot or kinking) or displacement, whereas a gradual decrease is more likely due to acute tubular necrosis (ATN) or a prerenal cause.

Recent medical events are helpful; they include review of recent BP readings, surgical procedures, and drug and x-ray contrast administration. Recent surgery or trauma may be consistent with hypovolemia. A severe crush injury, deep electrical burn, or heatstroke suggests rhabdomyolysis.

Physical examination: Vital signs are reviewed, particularly for hypotension, tachycardia, or both (suggesting hypovolemia or sepsis) and fever (suggesting sepsis). Signs of focal infection and cardiac failure should be sought. Palpable bladder distention indicates an outlet obstruction. Dark brown urine suggests myoglobinuria.

Testing: In all catheterized patients (and those with an ileal conduit), patency should be ascertained by irrigation before further testing; this approach may solve the problem. In many of the remaining patients, etiology (eg, shock, sepsis) is clinically apparent. In others, particularly those with multiple disorders, testing is needed to differentiate prerenal from renal (ATN) causes. In patients without a urinary catheter, placement of a catheter should be considered; this will diagnose and treat obstruction and provide continuous monitoring of output.

[**Table 222-7.** Some Causes of Oliguria]

If a central venous or pulmonary artery catheter is in place, volume status (and with a pulmonary artery catheter, cardiac output) can be determined by measuring central venous pressure (see p. 2298) or pulmonary artery occlusion pressure (see p. 2245). However, many physicians would not insert such a line for acute oliguria unless other indications were present. An alternative in the patient without signs of volume overload is to rapidly give a test bolus of IV fluid, 500 mL 0.9% saline (20 mL/kg in children); an increase in output suggests a prerenal cause.

Laboratory tests should be done. Serum electrolytes, BUN, and creatinine are standard; often urine Na and creatinine concentration are also done. Prerenal conditions typically result in a BUN/creatinine ratio > 20, vs ≤ 10 in both normal states and ATN. In prerenal conditions, urine Na is < 20 mEq/L as the kidney attempts to retain maximum Na to preserve intravascular volume. In ATN, urine Na is usually > 40 mEq/L. The fractional Na excretion (FE_{Na}) is a more accurate representation of the kidney's ability to retain Na and is defined as

$$\frac{\text{urine NA/plasma NA}}{\text{urine creatinine/plasma creatinine}} \times 100$$

A ratio < 1 indicates the kidney is able to reabsorb Na, and hence the problem is prerenal. A ratio > 3 indicates a probable renal cause.

Treatment

Identified causes are treated; outflow obstruction is corrected, volume is replaced, cardiac output is normalized. Nephrotoxic drugs are stopped, and another drug is substituted. Hypotension should be avoided to prevent further renal insults. Patients with renal failure that cannot be reversed may require renal replacement therapy (eg, continuous venovenous hemofiltration or hemodialysis).

Agitation, Confusion, and Neuromuscular Blockade

ICU patients are often agitated, confused, and uncomfortable. They can become delirious (ICU delirium). These symptoms are unpleasant for patients and often interfere with care and safety. At worst, they may be life threatening (eg, patients dislodge the endotracheal tube or IV lines).

Etiology

In a critically ill patient, agitation, confusion, or both can result from the original medical condition, from medical complications, or from treatment or the ICU environment (see Table 222-8). It is important to remember that neuromuscular blockade merely masks pain and agitation, it does not prevent it; paralyzed patients may be suffering significantly.

Evaluation

The chart should be reviewed and the patient examined before sedatives are ordered for "agitation."

History: The presenting injury or illness is a prime causative suspect. Nursing notes and discussion with personnel may identify downward trends in BP and urine output (suggesting CNS hypoperfusion) and dysfunctional sleep patterns. Drug administration records are reviewed to identify inadequate or excessive analgesia and sedation.

[**Table 222-8.** Some Causes of Agitation or Confusion in Critical Care Patients]

Past medical history is reviewed for potential causes. Underlying liver disease suggests possible hepatic encephalopathy. Known substance dependency or abuse suggests a withdrawal syndrome.

Awake, coherent patients are asked what is troubling them and are questioned specifically about pain, dyspnea, and previously unreported substance dependency.

Physical examination: O_2 saturation < 90% suggests a hypoxic etiology. Low BP and urine output suggest CNS hypoperfusion. Fever and tachycardia suggest sepsis or delirium tremens. Neck stiffness suggests meningitis, although this finding may be difficult to demonstrate in an agitated patient. Focal findings on neurologic examination suggest stroke, hemorrhage, or increased intracranial pressure (ICP).

The degree of agitation can be quantified using a scale such as the Riker Sedation-Agitation Scale (see Table 222-9) or the Ramsay Sedation Scale. Use of such scales allows better consistency between observers and the identification of trends. Patients who are under neuromuscular blockade are difficult to

evaluate because they may be highly agitated and uncomfortable despite appearing motionless. It is typically necessary to allow paralysis to wear off periodically (eg, daily) so that the patient can be assessed.

Testing: Identified abnormalities (eg, hypoxia, hypotension, fever) should be clarified further with appropriate testing. Head CT need not routinely be done unless focal neurologic findings are present or no other etiology is found. A bispectral index (BIS) monitor may be helpful in determining the level of sedation/agitation of patients under neuromuscular blockade.

Treatment

Underlying conditions (eg, hypoxia, shock, drugs) should be addressed. The environment should be optimized (eg, darkness, quiet, and minimal sleep interruption at night) as much as is compatible with medical care. Clocks, calendars, outside windows, and TV or radio programs also help connect the patient with the world, lessening confusion. Family presence and consistent nursing personnel may be calming.

Drug treatment is dictated by the most vexing symptoms. Pain is treated with analgesics; anxiety and insomnia are treated with sedatives; and psychosis and delirium are treated with small doses of an antipsychotic drug. Intubation may be needed when sedative and analgesic requirements are high enough to jeopardize the airway or respiratory drive. Many drugs are available; generally, short-acting drugs are preferred for patients who need frequent neurologic examination or who are being weaned to extubation.

Analgesia: Pain should be treated with appropriate doses of IV opioids; conscious patients with painful conditions (eg, fractures, surgical incisions) who are unable to communicate should be assumed to have pain and receive analgesics accordingly. Mechanical ventilation is somewhat uncomfortable, and patients generally should receive a combination of opioid and amnestic sedative drugs. Fentanyl is the opioid of choice because of its potency, short duration of action, and minimal cardiovascular effects. A common regimen can be 30 to 100 µg/h of fentanyl; individual requirements are highly variable.

Sedation: Despite analgesia, many patients remain sufficiently agitated as to require sedation. A sedative can also provide

[**Table 222-9.** Riker Sedation-Agitation Scale]

patient comfort at a lower dose of analgesic. Benzodiazepines (eg, lorazepam, midazolam) are most common, but propofol, a sedative-hypnotic drug, may be used. A common regimen for sedation is lorazepam 1 to 2 mg IV q 1 to 2 h or a continuous infusion at 1 to 2 mg/h if the patient is intubated. These drugs pose risks of respiratory depression, hypotension, delirium, and prolonged physiologic effects in some patients. Long-acting benzodiazepines such as diazepam, flurazepam, and chlordiazepoxide should be avoided in the elderly. Antipsychotics with less anticholinergic effect, such as haloperidol 1 to 3 mg IV, may work best when combined with benzodiazepines.

Neuromuscular blockade: For intubated patients, neuromuscular blockade is *not* a substitute for sedation; it only removes visible manifestations of the problem (agitation) without correcting it. However, neuromuscular blockade may be required during tests (eg CT, MRI) or procedures (eg, central line placement) that require patients to be motionless or in patients who cannot be ventilated despite adequate analgesia and sedation. Prolonged neuromuscular blockade should be avoided unless patients have severe lung injury and cannot do the work of breathing safely. Use for > 1 to 2 days may lead to prolonged weakness, particularly when corticosteroids are concomitantly given. Common regimens include vecuronium (continuous infusion as directed by stimulation).

Chapter 223. Cardiac Arrest

Introduction

Cardiac arrest is the terminal event in any fatal disorder. It may also occur suddenly (defined as within 24 h of onset of symptoms in a previously functioning person) and, as such, occurs outside the hospital in about 400,000 people/yr in the US, with a 90% mortality.

Respiratory arrest and cardiac arrest are distinct, but without treatment, one inevitably leads to the other. (See also respiratory failure in Ch. 225, dyspnea on p. 1832, and hypoxia on p. 2250.)

Etiology

In adults, sudden cardiac arrest results primarily from cardiac disease (of all types, but especially coronary artery disease). In a significant percentage of patients, sudden cardiac arrest is the first manifestation of heart disease. Other causes include circulatory shock due to noncardiac disorders (especially pulmonary embolism, GI hemorrhage, or trauma), ventilatory failure, and metabolic disturbance (including drug overdose).

In children, cardiac causes of sudden cardiac arrest are much less common (< 15 to 20%). Instead, predominant causes include trauma, poisoning, and various respiratory disorders (eg, airway obstruction, smoke inhalation, drowning, infection, sudden infant death syndrome).

Pathophysiology

Cardiac arrest causes global ischemia with consequences at the cellular level that adversely affect organ function after resuscitation. The main consequences involve direct cellular damage and edema formation. Edema is particularly harmful in the brain, which has minimal room to expand, and often results in increased intracranial pressure and corresponding decreased cerebral perfusion postresuscitation. A significant proportion of successfully resuscitated patients have short-term or long-term cerebral dysfunction manifested by altered alertness (from mild confusion to coma), seizures, or both.

Decreased ATP production leads to loss of membrane integrity with efflux of K and influx of Na and Ca. Excess Na causes cellular edema. Excess Ca damages mitochondria (depressing ATP production), increases nitric oxide production (leading to formation of damaging free radicals), and, in certain circumstances, activates proteases that further damage cells.

Abnormal ion flux also results in depolarization of neurons, releasing neurotransmitters, some of which are damaging (eg, glutamate activates a specific Ca channel, worsening intracellular Ca overload).

Inflammatory mediators (eg, IL-1B, tumor necrosis factor-α) are elaborated; some of them may cause microvascular thrombosis and loss of vascular integrity with further edema formation. Some mediators trigger apoptosis, resulting in accelerated cell death.

Symptoms and Signs

In critically or terminally ill patients, cardiac arrest is often preceded by a period of clinical deterioration with rapid, shallow breathing, arterial hypotension, and a progressive decrease in mental alertness. In other cases of cardiac arrest, collapse occurs without warning, occasionally accompanied by a brief (< 5 sec) seizure.

Diagnosis

• Clinical evaluation

• Cardiac monitor

• Sometimes testing for cause (eg, echocardiography, chest x-ray, or chest ultrasonography)

Diagnosis is by clinical findings of apnea, pulselessness, and unconsciousness. Arterial pressure is not measurable. Pupils dilate and become unreactive to light after about 1 to 2 min.

A cardiac monitor should be applied; it may indicate ventricular fibrillation (VF), ventricular tachycardia (VT), or asystole. Sometimes a perfusing rhythm (eg, extreme bradycardia) is present; this rhythm may represent true pulseless electrical activity (electromechanical dissociation) or extreme hypotension with failure to detect a pulse.

The patient is evaluated for potentially treatable causes, such as hypoxia, massive volume loss, cardiac tamponade, tension pneumothorax, or massive pulmonary embolus. Unfortunately, many causes are not identified during CPR. Clinical examination, chest ultrasonography, and chest x-ray can detect tension pneumothorax. Cardiac ultrasonography can detect cardiac contractions and recognize cardiac tamponade, extreme hypovolemia (empty heart), right ventricular overload suggesting pulmonary embolism, and focal wall motion abnormalities suggesting MI.

Prognosis

Survival to hospital discharge, particularly neurologically intact survival, is a more meaningful outcome than simply return of spontaneous circulation.

Survival rates vary significantly; favorable factors include

• Witnessed arrest

• In-hospital location (particularly a monitored unit)

• Early and effective bystander-initiated CPR

• Initial rhythm of VF or VT

• Early defibrillation (of VT or VF after initial chest compression)

• Hypothermia (eg, submersion in ice water) preceding onset of cardiac arrest

If many factors are favorable (eg, VF is witnessed in an ICU or emergency department), about 20% of patients survive to hospital discharge. When factors are uniformly unfavorable (eg, patient in asystole after unwitnessed, out-of-hospital arrest), survival is unlikely. Overall, reported survival after out-of-hospital arrest ranges between 1% and 70%; the wide range reflects reporting differences and inclusion criteria as well as differences in system effectiveness. About 8 to 30% of survivors have neurologic dysfunction, and one third return to prearrest status. In-hospital arrest survival is 26%.

Treatment

• CPR (see below)

• When possible, treatment of primary cause

• Postresuscitative care

Rapid intervention is essential.

CPR is an organized, sequential response to cardiac arrest; rapid initiation of chest compressions and early defibrillation of patients who are in VF or VT (more commonly adults) are the keys to success.

In children, who most often have asphyxial causes of cardiac arrest, the presenting rhythm is typically a bradyarrhythmia followed by asystole. However, about 15 to 20% of children (particularly when sudden cardiac arrest has not been preceded by respiratory symptoms) present with VT or VF and thus also

require prompt defibrillation. The incidence of VF as the initial recorded rhythm increases in children > 12 yr.

Primary causes must be promptly treated. If no treatable conditions are present but cardiac motion is detected or pulses are detected by Doppler, severe circulatory shock is identified, and IV fluid (eg, 1 L 0.9% saline, 5% serum albumin, whole blood, or a combination for blood loss) is given. If response to IV fluid is inadequate, most clinicians give one or more vasopressor drugs (eg, norepinephrine, epinephrine, dopamine, vasopressin); however, there is no firm proof that they improve survival.

In addition to treatment of cause, postresuscitative care typically includes methods to optimize O_2 delivery, antiplatelet therapy, and therapeutic hypothermia.

Cardiopulmonary Resuscitation

(For neonatal resuscitation, see p. 2768.)

Cardiopulmonary resuscitation (CPR) is an organized, sequential response to cardiac arrest, including

- Recognition of absent breathing and circulation
- Basic life support with chest compressions and rescue breathing
- Advanced cardiac life support (ACLS) with definitive airway and rhythm control
- Postresuscitative care

Prompt initiation of chest compression and early defibrillation (when indicated) are the keys to success. Speed, efficiency, and proper application of CPR determine successful outcome; the rare exception is profound hypothermia caused by cold water immersion, when successful resuscitation may be accomplished even after prolonged arrest (up to 60 min).

Overview: Guidelines for health care professionals from the American Heart Association are followed (see Fig. 223-1). If a person has collapsed with possible cardiac arrest, a rescuer first establishes unresponsiveness and confirms absence of breathing or the presence of only gasping respirations. Then, the rescuer calls for help. Anyone answering is directed to activate the emergency response system (or appropriate in-hospital resuscitation personnel) and, if possible, obtain a defibrillator. If no one responds, the rescuer first activates the emergency response system and then begins basic life support by giving 30 chest compressions at a rate of 100/min and then opening the airway (lifting the chin and tilting back the forehead) and giving 2 rescue breaths. The cycle of compressions and breaths is continued (see Table 223-1) without interruption; preferably each rescuer is relieved every 2 min. When a defibrillator (manual or automated) becomes available, a person in ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) is given an unsynchronized shock. If the cardiac arrest is witnessed and a defibrillator is on the scene, a person in VF or VT is immediately defibrillated; early defibrillation may promptly convert VF or pulseless VT to a perfusing rhythm. Defibrillation is further discussed on p. 2260.

For children, unless collapse is sudden and witnessed, the first step if no one answers the call for help is to do 5 cycles of CPR before activating the emergency response system.

Airway and Breathing

In a change from previous recommendations, opening the airway is given 2nd priority (see p. 2271) after beginning chest compressions.

Mouth-to-mouth (adults and children) or combined mouth-to-mouth-and-nose (infants) rescue breathing or bag-valve-mask ventilation is begun for asphyxial cardiac arrest. If available, an oropharyngeal airway may be inserted. Cricoid pressure is no longer recommended.

If abdominal distention develops, the airway is rechecked for patency and the amount of air delivered during rescue breathing is reduced. Nasogastric intubation to relieve gastric distention is delayed until suction equipment is available because regurgitation with aspiration of gastric contents may occur during insertion. If marked gastric distention interferes with ventilation and cannot be corrected by the above methods, patients are positioned on their side, the epigastrium is compressed, and the airway is cleared.

When qualified providers are present, an advanced airway (endotracheal tube or supraglottic device) is placed *without interruption of chest compression* as described under Airway Establishment and Control (see p. 2270). A breath is given every 6 to 8 sec (8 to 10 breaths/min) without interrupting chest compression. However, chest compression and defibrillation take precedence over endotracheal intubation. Unless highly experienced providers are available, endotracheal intubation may be delayed in favor of ventilation with bag-valve-mask, laryngeal mask airway, or similar device.

Circulation

Chest compression: In witnessed cardiac arrest, defibrillation, if available immediately, precedes chest compression. In an unresponsive patient whose collapse was unwitnessed, the trained rescuer should immediately begin external (closed chest) cardiac compression, followed by rescue breathing. Chest compressions must be interrupted as little as possible (eg, for intubation, central IV catheter placement, or transport). A compression cycle should consist of 50% compression and 50% release. Mechanical chest compression devices are available; these devices are no more effective than properly executed manual compressions but can minimize effects of performance error and fatigue and can be helpful during patient transport.

Ideally, external cardiac compression produces a palpable pulse with each compression, although cardiac output is only 20 to 30% of normal. However, palpation of pulses during chest compression is difficult, even for experienced clinicians, and often unreliable. End-tidal CO_2 monitoring provides a better estimate of cardiac output during chest compression; patients with inadequate perfusion have little venous return to the lungs and

[**Fig. 223-1.** Adult comprehensive emergency cardiac care.]

[**Table 223-1.** CPR Techniques for Health Care Practitioners]

hence a low end-tidal CO_2. Normal-sized, light-responsive pupils signal adequate brain circulation and oxygenation. Light-responsive but dilated pupils may indicate inadequate cerebral oxygenation, although brain injury may not have occurred. However, persistently dilated, nonreactive pupils do not prove brain injury or death because adrenergic drugs, especially epinephrine and atropine, or cataracts may modify pupil size and reaction. Restoration of spontaneous breathing or eye opening indicates restoration of spontaneous circulation (ROSC).

Open-chest cardiac compression may be effective, but its use is restricted to patients after penetrating chest injuries, shortly after cardiac surgery (ie, within 48 h), in cases of cardiac tamponade, and most especially after cardiac arrest in the operating room when the patient's chest is already open. However, thoracotomy requires training and experience and is best done only within these limited indications.

Complications of chest compression: Laceration of the liver is a rare but potentially serious (sometimes fatal) complication and is usually caused by compressing the abdomen below the sternum. Rupture of the stomach (particularly if the stomach is distended with air) is also a rare complication. Delayed rupture of the spleen is very rare. An occasional complication, however, is regurgitation followed by aspiration of gastric contents, causing life-threatening aspiration pneumonia in resuscitated patients.

Costochondral separation and fractured ribs often cannot be avoided because it is important to compress the chest deeply enough to produce sufficient blood flow. Fractures are quite rare in children because of the flexibility of the chest wall. Bone marrow emboli to the lungs have rarely been reported after external cardiac compression, but there is no clear evidence that they contribute to mortality. Lung injury is rare, but pneumothorax after a penetrating rib fracture may occur. Serious myocardial injury caused by compression is very unlikely, with the possible exception of injury to a preexisting ventricular aneurysm.

Concern for these injuries should not deter the rescuer from doing CPR.

Monitor and IV: ECG monitoring is established to identify the underlying cardiac rhythm. An IV line is started; 2 lines minimize the risk of losing IV access during CPR. Large-bore peripheral lines in the antecubital veins are preferred. In adults, if a peripheral line cannot be established, a subclavian or internal jugular central line can be placed provided it can be done without stopping chest compression (often difficult). Intraosseous and femoral lines (see p. 2250) are the preferred alternatives, especially in children. Femoral vein catheters (preferably long catheters advanced centrally) are practical because CPR does not need to be stopped and they have less potential for lethal complications; however, they may have a lower rate of successful placement because no discrete femoral arterial pulsations are available to guide insertion.

The type and volume of fluids or drugs given depend on the clinical circumstances. Usually, IV 0.9% saline is given slowly (sufficient only to keep an IV line open); vigorous volume replacement (crystalloid and colloid solutions, blood) is required only when arrest results from hypovolemia (see p. 2297).

Defibrillation

The most common rhythm in witnessed adult cardiac arrest is VF; rapid conversion to a perfusing rhythm is essential. Pulseless VT is treated the same as VF.

A precordial thump is advised only when a defibrillator is not available. A forceful precordial thump can rarely convert VF or VT to a functional cardiac rhythm, and there is no evidence of deleterious effect (eg, converting VT to VF) in the cardiac arrest setting. However, it is not recommended for children. One or 2 blows can be delivered to the junction of the middle and lower third of the sternum with a clenched fist held 20 to 25 cm above the chest.

Prompt direct current cardioversion is more effective than antiarrhythmic drugs; however, the success of defibrillation is time dependent, with about a 10% decline in success after each minute of VF (or pulseless VT). Automated external defibrillators (AEDs) allow minimally trained rescuers to treat VT or VF. Their use by first responders (police and fire services) and their prominent availability in public locations has increased the likelihood of resuscitation.

Defibrillating paddles or AED pads are placed between the clavicle and the 2nd intercostal space along the right sternal border and over the 5th or 6th intercostal space at the apex of the heart. Conventional defibrillator paddles are used with conducting paste; pads have conductive gel incorporated into them. Only 1 initial countershock is now advised (the previous recommendation was 3 stacked shocks), after which chest compression is resumed. Energy level for biphasic defibrillators is between 120 and 200 joules (2 joules/kg in children); monophasic defibrillators are set at 360 joules. Postshock rhythm is not checked until after 2 min of chest compression. Subsequent shocks are delivered at the same or higher energy level (maximum 360 joules, 2 to 4 joules/kg in children). Patients remaining in VF or VT receive continued chest compression and ventilation and optional drug therapy as discussed below.

Special Circumstances

In accidental electrical shock, rescuers must be certain that the patient is no longer in contact with the electrical source to avoid shocking themselves. Use of nonmetallic grapples or rods and grounding of the rescuer allows for safe removal of the patient before starting CPR.

In near drowning, rescue breathing may be started in shallow water, although chest compression is not likely to be effectively done until the patient is placed horizontally on a firm surface, such as a surfboard or float.

If cardiac arrest follows traumatic injury, airway opening maneuvers and a brief period of external ventilation after clearing the airway have the highest priority because airway obstruction is the most likely treatable cause of arrest. To minimize cervical spine injury, jaw thrust, but not head tilt and chin lift, is advised. Other survivable causes of traumatic cardiac arrest include cardiac tamponade and tension pneumothorax, for which immediate needle decompression is lifesaving. However, most patients with

traumatic cardiac arrest have severe hypovolemia due to blood loss (for which chest compressions may be ineffective) or nonsurvivable brain injuries.

Drugs for ACLS

Despite widespread and long-standing use, no drug or drug combination has been definitively shown to increase survival to hospital discharge in patients with cardiac arrest. Some drugs do seem to improve the likelihood of ROSC and thus may reasonably be given (for dosing, including pediatric, see Table 223-2). Drug therapy for shock and cardiac arrest continues to be researched.

In a patient with a peripheral IV line, drug administration is followed by a fluid bolus ("wide open" IV in adults; 3 to 5 mL in young children) to flush the drug into the central circulation. In a patient without IV or intraosseous access, atropine and epinephrine, when indicated, may be given via the endotracheal tube at 2 to 2.5 times the IV dose. During administration of a drug via endotracheal tube, compressions should be briefly stopped.

First-line drugs: First-line drugs include

• Epinephrine or vasopressin

Epinephrine has been the main drug used in cardiac arrest, although, as noted previously, its benefit is increasingly challenged. It may be given q 3 to 5 min. Epinephrine has combined α-adrenergic and β-adrenergic effects. The α-adrenergic effects may augment coronary diastolic pressure, thereby increasing subendocardial perfusion during chest compressions. Epinephrine also increases the likelihood of successful defibrillation. However, β-adrenergic effects may be detrimental because they increase O_2 requirements (especially of the heart) and cause vasodilation. Intracardiac injection of epinephrine is not recommended because, in addition to interrupting precordial compression, pneumothorax,

[**Table 223-2.** Drugs for Resuscitation*]

coronary artery laceration, and cardiac tamponade may occur.

A single dose of vasopressin 40 units, which has a duration of activity of 40 min, is an alternative to epinephrine (adults only); it has not been proved more effective than epinephrine.

Amiodarone 300 mg can be given once if defibrillation is unsuccessful after epinephrine or vasopressin, followed by 1 dose of 150 mg. It is also of potential value if VT or VF recurs after successful defibrillation; a lower dose is given over 10 min followed by a continuous infusion. There is no persuasive proof that it increases survival to hospital discharge.

Other drugs: A range of additional drugs may be useful in specific settings.

Atropine sulfate is a vagolytic drug that increases heart rate and conduction through the atrioventricular node. It is given for symptomatic bradyarrhythmias and high-degree atrioventricular nodal block. It is no longer recommended for asystole or pulseless electrical activity.

Ca chloride is recommended for patients with hyperkalemia, hypermagnesemia, hypocalcemia, or Ca channel blocker toxicity. In others, because intracellular Ca is already higher than normal, additional Ca is likely to be detrimental. Because cardiac arrest in patients on renal dialysis is often a result of or accompanied by hyperkalemia, these patients may benefit from a trial of Ca if bedside K determination is unavailable. Caution is necessary because Ca exacerbates digitalis toxicity and can cause cardiac arrest.

Mg sulfate has not been shown to improve outcome in randomized clinical studies. However, it may be helpful in patients with torsades de pointes or known or suspected Mg deficiency (ie, alcoholics, patients with protracted diarrhea).

Procainamide is a 2nd-line drug for treatment of refractory VF or VT. However, procainamide is not recommended for pulseless arrest in children.

Phenytoin may rarely be used to treat VF or VT, but only when VF or VT is due to digitalis toxicity and is refractory to other drugs. A dose of 50 mg/min is given until rhythm improves or the total dose reaches 18 mg/kg.

$NaHCO_3$ (sodium bicarbonate) is no longer recommended unless cardiac arrest is caused by hyperkalemia, hypermagnesemia, or tricyclic antidepressant overdose with complex ventricular arrhythmias. In children, $NaHCO_3$ may be considered when cardiac arrest is prolonged (> 10 min); it is given only if there is good ventilation. When $NaHCO_3$ is used, arterial pH should be monitored before infusion and after each 50-mEq dose (1 to 2 mEq/kg in children).

Lidocaine and bretylium are no longer recommended for management of cardiac arrest.

Dysrhythmia Treatment

VF or pulseless VT is treated with one direct current shock, preferably with biphasic waveform, immediately after witnessed arrest and after 2 min of chest compression in patients with unwitnessed arrest; chest compression is interrupted as little as possible. Recommended energy levels vary: 120 to 200 joules for biphasic waveform and 360 joules for monophasic. If this treatment is unsuccessful, epinephrine 1 mg IV is administered and repeated q 3 to 5 min. Alternatively, vasopressin 40 U IV may be given only once (not in children) although its value is questioned. Cardioversion at the same energy level is attempted 1 min after each drug administration. If VF persists, amiodarone 300 mg IV is given. Then, if VF/VT recurs, 150 mg is given followed by infusion of 1 mg/min q 6 h, then 0.5 mg/min. Current versions of AEDs provide a pediatric cable that effectively reduces the energy delivered to children. (For pediatric energy levels, see Table 223-3; for drug doses, see Table 223-2.)

Asystole can be mimicked by a loose or disconnected monitor lead; thus, monitor connections should be checked and rhythm viewed in an alternative lead. If asystole is confirmed and heart block is suspected, transcutaneous pacing is done and the patient is given epinephrine 1 mg IV repeated q 3 to 5 min and atropine 1 mg IV repeated q 3 to 5 min to a total dose of 0.04 mg/kg. Electrical pacing is not successful in other settings. Pacing and atropine, however, are contraindicated in children with asystole. Defibrillation of apparent asystole (because it "might be fine VF") is discouraged because electrical shocks injure the nonperfused heart.

Pulseless electrical activity is circulatory collapse that occurs despite satisfactory electrical complexes on the ECG. Patients with pulseless electrical activity receive 500- to 1000-mL (20 mL/kg) infusion of 0.9% saline. Epinephrine may be given in amounts of 0.5 to 1.0 mg IV repeated q 3 to 5 min. If the heart rate is < 60/min, atropine 0.5 to 1 mg IV is given. Cardiac tamponade can cause pulseless electrical activity, but this disorder usually occurs in patients after thoracotomy and in patients with known pericardial effusion or major chest trauma. In such settings, immediate pericardiocentesis or thoracotomy is done (see Fig. 216-2 on p. 2206). Tamponade is rarely an occult cause of cardiac arrest but, if suspected, can be confirmed by ultrasonography or, if ultrasonography is unavailable, pericardiocentesis.

Termination of Resuscitation

CPR must be continued until the cardiopulmonary system is stabilized, the patient is pronounced dead, or a lone rescuer is physically unable to continue. If cardiac arrest occurs in hypothermic patients, CPR should be continued until the body is rewarmed to 34° C.

The decision to pronounce death is somewhat subjective, taking into account duration of arrest before treatment, age, prior medical conditions, and other factors but typically is made after failure to establish spontaneous circulation after 30 to 45 min of CPR and ACLS measures.

Postresuscitative Care

Restoration of spontaneous circulation (ROSC) is only an intermediate goal in resuscitation. Only 3 to 8% of patients with ROSC survive to hospital discharge. To maximize the likelihood of a good outcome,

clinicians must manage underlying conditions. In adults, it is particularly important to recognize MI (see p. 2101) and institute reperfusion therapy (preferably percutaneous transluminal coronary angioplasty) promptly. (CAUTION: *Thrombolysis after aggressive CPR sometimes causes cardiac tamponade, and therefore angioplasty is preferred.*)

Postresuscitation laboratory studies include ABG, CBC, and blood chemistries, including electrolytes, glucose, BUN, creatinine, and cardiac markers. (Creatine phosphokinase is usually elevated because of skeletal muscle damage caused by CPR.) Arterial PaO_2 should be kept near normal values (80 to 100 mm Hg). Hct should be maintained at ≥ 30, and glucose at < 200 mg/dL; electrolytes, especially K, should be within the normal range.

BP support: Current recommendations are to maintain a mean arterial pressure (MAP) of > 80 mm Hg in older adults or > 60 mm Hg in younger and previously healthy patients. In patients known to be hypertensive, a reasonable target is systolic BP 30 mm Hg below prearrest level. MAP is best measured with an intra-arterial catheter. Use of a flow-directed pulmonary artery catheter for hemodynamic monitoring has been largely discarded.

BP support includes

• IV 0.9% saline

• Sometimes inotropic or vasopressor drugs

• Rarely intra-aortic balloon counterpulsation

Patients with low MAP and low central venous pressure should have IV fluid challenge with 0.9% saline infused in 250-mL increments.

Although use of inotropic and vasopressor drugs is not proved to enhance long-term survival, older adults with moderately low MAP (70 to 80 mm Hg) and normal or high central

[**Table 223-3.** Guide to Pediatric Resuscitation—Mechanical Measures]

venous pressure may receive an infusion of an inotrope (eg, dobutamine started at 2 to 5 µg/kg/min). Alternatively, amrinone or milrinone is used (see Table 223-2). If this therapy is ineffective, the inotrope and vasoconstrictor dopamine may be considered. Alternatives are epinephrine and the peripheral vasoconstrictors norepinephrine and phenylephrine (see Table 223-2). However, vasoactive drugs should be used at the minimal dose necessary to achieve low-normal MAP because they may increase vascular resistance and decrease organ perfusion, especially in the mesenteric bed. They also increase the workload of the heart at a time when its capability is decreased because of postresuscitation myocardial dysfunction. If MAP remains < 70 mm Hg in patients who may have sustained an MI, intra-aortic balloon counterpulsation should be considered. Patients with normal MAP and high central venous pressure may improve with either inotropic therapy or afterload reduction with nitroprusside or nitroglycerin.

Intra-aortic balloon counterpulsation can assist low-output circulatory states due to left ventricular pump failure that is refractory to drugs. A balloon catheter is introduced via the femoral artery, percutaneously or by arteriotomy, retrograde into the thoracic aorta just distal to the left subclavian artery. The balloon inflates during each diastole, augmenting coronary artery perfusion, and deflates during systole, decreasing afterload. Its primary value is as a temporizing measure when the cause of shock is potentially correctable by surgery or percutaneous intervention (eg, acute MI with major coronary obstruction, acute mitral insufficiency, ventricular septal defect).

Dysrhythmia treatment: Although VF or VT may recur after resuscitation, prophylactic antiarrhythmic drugs do not improve survival and are no longer routinely used. However, patients manifesting such rhythms may be treated with procainamide or amiodarone (see p. 2260).

Postresuscitation rapid supraventricular tachycardias occur frequently because of high levels of β-adrenergic catecholamines (both endogenous and exogenous) during cardiac arrest and resuscitation.

These rhythms should be treated if extreme, prolonged, or associated with hypotension or signs of coronary ischemia. An esmolol IV infusion is given, beginning at 50 µg/kg/min.

Patients who had arrest caused by VF or VT not associated with acute MI are candidates for an implantable cardioverter-defibrillator (ICD). Current ICDs are implanted similarly to pacemakers and have intracardiac leads and sometimes subcutaneous electrodes. They can sense arrhythmias and deliver either cardioversion or cardiac pacing as indicated.

Neurologic support: Between 8% and 30% of adults have CNS dysfunction after resuscitation from cardiac arrest. Hypoxic brain injury is a result of ischemic damage and cerebral edema (see also Pathophysiology on p. 2255). Both damage and recovery may evolve over 48 to 72 h after resuscitation.

Maintenance of oxygenation and cerebral perfusion pressure (avoiding hypotension) may reduce cerebral complications. Both hypoglycemia and hyperglycemia may damage the postischemic brain and should be treated.

Additionally, there is now persuasive evidence of the benefits of inducing mild hypothermia. Surface cooling with ice packs can reduce core body temperature to between 30° and 34° C. Alternative methods of cooling include cardiopulmonary bypass or intravascular cooling devices.

Numerous pharmacologic treatments, including free radical scavengers, antioxidants, glutamate inhibitors, and Ca channel blockers, are of theoretic benefit; many have been successful in animal models, but none have proved effective in human trials.

CPR in Infants and Children

Despite the use of CPR, mortality rates for cardiac arrest are 80 to 97% for infants and children. The mortality rate is almost 25% for respiratory arrest alone. Neurologic outcome is often severely compromised.

About 50 to 65% of children requiring CPR are < 1 yr; of these, most are < 6 mo. About 6% of neonates require resuscitation at delivery (see p. 2768); the incidence increases significantly if birth weight is < 1500 g.

Standardized outcome guidelines should be followed in reporting outcomes of CPR in children; eg, the modified Pittsburgh Outcome Categories Scale reflects cerebral and overall performance (see Table 223-4).

Major Differences Between Pediatric and Adult CPR

Prearrest: *Bradycardia in a distressed child is a sign of impending cardiac arrest* . Neonates, infants, and young children are more likely to develop bradycardia caused by hypoxemia, whereas older children initially tend to have tachycardia. An infant or child with a heart rate < 60/min and signs of poor perfusion that do not rise with ventilatory support should have cardiac compressions (see Fig. 223-2). Bradycardia secondary to heart block is unusual.

[**Table 223-4.** Pediatric Cerebral Performance Category Scale*]

After adequate oxygenation and ventilation, epinephrine is the drug of choice.

BP should be measured with an appropriatesized cuff, but direct invasive arterial BP monitoring is mandatory in severely compromised children.

Because BP varies with age, an easy guideline to remember the lower limits of normal for systolic BP (< 5th percentile) by age is as follows: < 1 mo, 60 mm Hg; 1 mo to 1 yr, 70 mm Hg; > 1 yr, 70 + (2 × age in yr). Thus, in a 5-yr-old child, hypotension would be defined by a BP of < 80 mm Hg (70 + [2 × 5]). Of significant importance is that children maintain BP longer because of stronger compensatory mechanisms (increased heart rate, increased systemic vascular resistance). Once hypotension occurs,

cardiorespiratory arrest may rapidly follow. All effort should be made to start treatment when compensatory signs of shock (eg, increased heart rate, cool extremities, capillary refill > 2 sec, poor peripheral pulses) are present but before hypotension develops.

Equipment and environment: Equipment size, drug dosage, and CPR parameters vary with patient age and weight (see Tables 223-1, 223-2, and 223-3). Size-variable equipment includes defibrillator paddles or electrode pads, masks, ventilation bags, airways, laryngoscope blades, endotracheal tubes, and suction catheters. Weight should be measured rather than guessed; alternatively, commercially

[**Fig. 223-2.** Chest compression.]

available measuring tapes that are calibrated to read standard patient weight based on body length can be used. Some tapes are printed with the recommended drug dose and equipment size for each weight. Dosages should be rounded down; eg, a 2 1/2-yr-old child should receive the dose for a 2-yr-old child.

Susceptibility to heat loss is greater in infants and children because of a large surface area relative to body mass and less subcutaneous tissue. A neutral external thermal environment is crucial during CPR and postresuscitation and may range from 36.5° C in a neonate to 35° C in a child. Hypothermia with core temperature < 35° C makes resuscitation more difficult (distinct from the beneficial effects of postresuscitation hypothermia discussed on p. 2266).

Airway: Upper airway anatomy is different in children. The head is large with a small face, mandible, and external nares, and the neck is relatively short. The tongue is large relative to the mouth, and the larynx lies higher in the neck and is angled more anteriorly. The epiglottis is long, and the narrowest portion of the trachea is inferior to the vocal cords at the cricoid ring, allowing the use of uncuffed endotracheal tubes. In younger children, a straight laryngoscope blade generally allows better visualization of the vocal cords than a curved blade because the larynx is more anterior and the epiglottis is more floppy and redundant.

Rhythm disturbances: In asystole, atropine and pacing are not used.

VF and pulseless VT occur in only about 15 to 20% of cardiac arrests. Vasopressin is not indicated. When cardioversion is used, the absolute energy dose is less than that for adults; waveform can be biphasic (preferred) or monophasic (see Table 223-3). For either waveform, the recommended energy dose is 2 joules/kg for the first shock, increasing to 4 joules/kg for subsequent attempts (if necessary—see p. 2260).

AEDs with adult cables may be used for children as young as 1 yr, but an AED with pediatric cables (maximum biphasic shock of 50 joules) is preferred for children between 1 yr and 8 yr. There is insufficient evidence to recommend for or against the use of AEDs in children < 1 yr.

Chapter 224. Respiratory Arrest

Introduction

Respiratory and cardiac arrest are distinct, but inevitably if untreated, one leads to the other. (See also respiratory failure on p. 2279, dyspnea on p. 1832, and hypoxia on p. 2250).

Interruption of pulmonary gas exchange for > 5 min may irreversibly damage vital organs, especially the brain. Cardiac arrest almost always follows unless respiratory function is immediately restored. However, aggressive ventilation may also have negative hemodynamic consequences, particularly in the periarrest period and in other circumstances when cardiac output is low. In most cases, the ultimate goal is to restore adequate ventilation and oxygenation without further compromising a tentative cardiovascular situation.

Etiology

Respiratory arrest (and impaired respiration that can progress to respiratory arrest) can be caused by

• Airway obstruction

• Decreased respiratory effort

• Respiratory muscle weakness

Airway obstruction: Obstruction may involve the

• Upper airway

• Lower airway

Infants < 3 mo are usually nose breathers and thus may have upper airway obstruction secondary to nasal blockage. At all ages, loss of muscular tone with decreased consciousness may cause upper airway obstruction as the posterior portion of the tongue displaces into the oropharynx. Other causes of upper airway obstruction include blood, mucus, vomitus, or foreign body; spasm or edema of the vocal cords; and pharyngolaryngeal tracheal inflammation (eg, epiglottitis, croup), tumor, or trauma. Patients with congenital developmental disorders often have abnormal upper airways that are more easily obstructed.

Lower airway obstruction may result from aspiration, bronchospasm, airspace filling disorders (eg, pneumonia, pulmonary edema, pulmonary hemorrhage), or drowning.

Decreased respiratory effort: Decreased respiratory effort reflects CNS impairment due to one of the following:

• CNS disorder

• Adverse drug effect

• Metabolic disorder

CNS disorders that affect the brain stem (eg, stroke, infection, tumor) can cause hypoventilation. Disorders that increase intracranial pressure usually cause hyperventilation initially, but hypoventilation may develop if the brain stem is compressed.

Drugs that decrease respiratory effort include opioids and sedative-hypnotics (eg, barbiturates, alcohol; less commonly, benzodiazepines). Usually, an overdose (iatrogenic, intentional, or unintentional) is involved, although a lower dose may decrease effort in patients who are more sensitive to the effects of these drugs (eg, the elderly, those with chronic respiratory insufficiency).

CNS depression due to severe hypoglycemia or hypotension ultimately compromises respiratory effort.

Respiratory muscle weakness: Weakness may be caused by

• Neuromuscular disorders

• Fatigue

Neuromuscular causes include spinal cord injury, neuromuscular diseases (eg, myasthenia gravis, botulism, poliomyelitis, Guillain-Barre syndrome), and neuromuscular blocking drugs.

Respiratory muscle fatigue can occur if patients breathe for extended periods at a minute ventilation exceeding about 70% of their maximum voluntary ventilation (eg, because of severe metabolic acidosis or hypoxemia).

Symptoms and Signs

With respiratory arrest, patients are unconscious or about to become so.

Patients with hypoxemia may be cyanotic, but cyanosis can be masked by anemia or by carbon monoxide or cyanide intoxication. Patients being treated with high-flow O_2 may not be hypoxemic and therefore may not exhibit cyanosis or desaturation until after respiration ceases for several minutes. Conversely, patients with chronic lung disease and polycythemia may exhibit cyanosis without respiratory arrest. If respiratory arrest remains uncorrected, cardiac arrest follows within minutes of onset of hypoxemia, hypercarbia, or both.

Impending respiratory arrest: Before complete respiratory arrest, patients with intact neurologic function may be agitated, confused, and struggling to breathe. Tachycardia and diaphoresis are present; there may be intercostal or sternoclavicular retractions. Patients with CNS impairment or respiratory muscle weakness have feeble, gasping, or irregular respirations and paradoxical breathing movements. Patients with a foreign body in the airway may choke and point to their necks, exhibit inspiratory stridor, or neither. Monitoring end-tidal CO_2 can alert practitioners to impending respiratory arrest in decompensating patients.

Infants, especially if < 3 mo, may develop acute apnea without warning, secondary to overwhelming infection, metabolic disorders, or respiratory fatigue. Asthmatics or patients with other chronic lung diseases may become hypercarbic and fatigued after prolonged periods of respiratory distress and suddenly become obtunded and apneic with little warning, despite adequate oxygen saturation.

Diagnosis

• Clinical evaluation

Respiratory arrest is usually clinically obvious; treatment begins simultaneously with diagnosis. The first consideration is to exclude a foreign body obstructing the airway; if a foreign body is present, resistance to ventilation is marked during mouth-to-mask or bag-valve-mask ventilation. Foreign material may be discovered during laryngoscopy for endotracheal intubation (see p. 2271 for removal).

Treatment

Treatment is clearing the airway, establishing an alternate airway, and providing mechanical ventilation (see p. 2279).

Airway Establishment and Control

Airway management consists of clearing the upper airway, maintaining an open air passage with a mechanical device, and sometimes assisting respirations. There are many indications for airway control

(see
Table 224-1) and many methods of establishing an airway.

[**Table 224-1.** Situations Requiring Airway Control]

Whatever airway management techniques are used, tidal volume should be 6 to 8 cc/kg (significantly less than previously recommended) and ventilatory rate should be 8 to 10 breaths/min (significantly slower than previously recommended to avoid negative hemodynamic consequences).

Clearing and Opening the Upper Airway

To relieve airway obstruction caused by soft tissues of the upper airway and provide optimal position for bag-valve-mask (BVM) ventilation and laryngoscopy, the operator flexes the patient's neck to elevate the head until the external auditory meatus is in the same plane as the sternum and positions the face roughly parallel to the ceiling (see
Fig. 224-1). This position is slightly different from the previously taught head tilt position. The mandible should be displaced upwards by lifting the lower jaw and submandibular soft tissue or by pushing the rami of the mandible upward (see
Fig. 224-2).

[**Fig. 224-1.** Head and neck positioning to open the airway.]

[**Fig. 224-2.** Jaw lift.]

Anatomic restriction, various abnormalities, or considerations caused by trauma (eg, inadvisability of moving a possibly fractured neck) may obviate the operator's ability to employ these maneuvers, but careful attention to optimal positioning can maximize airway patency and improve BVM ventilation and laryngoscopy.

Obstruction by dentures and oropharyngeal foreign material (eg, blood, secretions) may be removed by finger sweep of the oropharynx and suction, taking care not to push the material deeper (more likely in infants and young children, in whom a blind finger sweep is contraindicated). Deeper material can be removed with Magill forceps or by suction.

Heimlich maneuver (subdiaphragmatic abdominal thrusts): The Heimlich maneuver consists of manual thrusts to the upper abdomen or, in the case of pregnant or extremely obese patients, chest thrusts until the airway is clear or the patient becomes unconscious; it is the preferred initial method in the awake, choking patient and in the unconscious patient if the above methods are unsuccessful.

An unconscious adult is rolled into the supine position. The rescuer sits astride the patient above the knees with the heel of a hand in the upper abdominal area below the xiphoid process. To avoid damaging chest structures and the liver, the rescuer should never place the hand on the xiphoid process or lower rib cage. The other hand is placed on top of the first and a firm upward thrust is delivered (see
Fig. 224-3). For chest thrusts, the hand is placed over the sternum similarly to the position used for cardiac compression. With both

[**Fig. 224-3.** Abdominal thrusts with victim lying (conscious or unconscious).]

techniques, 5 quick, firm thrusts are recommended, followed by reevaluation of the airway.

In conscious adults, the rescuer stands behind the patient with arms encircling the patient's midsection. One fist is clenched and placed midway between the umbilicus and xiphoid. The other hand grabs the fist, and a firm inward and upward thrust is delivered by pulling with both arms (see
Fig. 224-4).

In older children, the Heimlich maneuver may be used. However, in children < 20 kg (typically < 5 yr), very moderate pressure should be applied, and the rescuer should kneel at the child's feet rather than astride.

In infants < 1 yr, the Heimlich maneuver should not be done; they should be held in a prone, head-down position, supporting the head with the fingers of one hand, while delivering 5 back blows (see Fig. 224-5). Five chest thrusts should then be delivered with the infant in a head-down position with the infant's back on the rescuer's thigh (supine). This sequence of back blows and chest thrusts is repeated until the airway is cleared.

Airway and Respiratory Devices

If no spontaneous respiration occurs after airway opening and no respiratory devices are available, rescue breathing (mouth-to-mask or mouth-to-barrier device) is started; mouth-to-mouth ventilation is rarely recommended. Exhaled air contains 16 to 18% O_2 and 4 to 5% CO_2, which is adequate to maintain blood O_2 and CO_2 values close to normal. Larger-than-necessary volumes of air may cause gastric distention with associated risk of aspiration.

Bag-valve-mask (BVM) devices: These devices consist of a self-inflating bag (resuscitator bag) with a nonrebreathing valve mechanism and a soft mask that conforms to the tissues of the face; when connected to an O_2 supply, they deliver from 60 to 100% inspired O_2. In the hands of experienced practitioners, a BVM provides adequate temporary ventilation in many situations, allowing time to systematically achieve definitive airway control. However, if BVM ventilation is used for > 5 min, air is typically introduced into the stomach, and an NGT should be inserted to evacuate the accumulated air.

These devices do not maintain airway patency, so patients with soft-tissue relaxation require careful positioning and manual maneuvers (see Figs. 224-1 and 224-2), as well as additional devices to keep the airway open. An oropharyngeal airway or a nasal trumpet is used during BVM ventilation to keep soft tissues of the oropharynx from blocking the airway. These devices cause gagging and the potential for vomiting and aspiration in conscious patients. Devices must be sized appropriately; an oropharyngeal airway should be as long as the distance between the corner of the patient's mouth and the angle of the jaw.

Resuscitator bags are also used with artificial airways, including endotracheal tubes and supraglottic and pharyngeal airways. Pediatric bags have an adjustable pressure relief valve that limits peak airway pressures (usually to 35 to 45 cm H_2O); practitioners must monitor the valve setting to avoid inadvertent hypoventilation.

[**Fig. 224-4.** Abdominal thrusts with victim standing or sitting (conscious).]

[**Fig. 224-5.** Expired air ventilation—child.]

Laryngeal mask airways (LMAs): An LMA or other supraglottic airway can be inserted into the lower oropharynx to prevent airway obstruction by soft tissues and to create an effective channel for ventilation (see Fig. 224-6). As the name implies, these devices seal the laryngeal inlet (rather than the face-mask interface) and thus avoid the difficulty of maintaining an adequate face-mask seal and the risk of displacing the jaw and tongue. LMAs have become the standard rescue ventilation technique for situations in which endotracheal intubation cannot be accomplished, as well as for certain elective anesthesia cases and emergencies. Complications include vomiting and aspiration in patients who have an intact gag reflex, who are receiving excessive ventilation, or both.

There are numerous techniques for LMA insertion. The standard approach is to press the deflated mask against the hard palate (using the long finger of the dominant hand) and rotate it past the base of the tongue until the mask reaches the hypopharynx so that the tip then sits in the upper esophagus. Once in the correct position, the mask is inflated. Inflating the mask with half the recommended volume before insertion stiffens the tip, possibly making insertion easier.

Although an LMA does not isolate the airway from the esophagus as well as an endotracheal tube, it has some advantages over BVM ventilation: It minimizes gastric inflation and provides some protection against passive regurgitation. Newer versions of LMAs have an opening through which a small tube can be

inserted to decompress the stomach.

The efficacy of the airway seal with an LMA, unlike endotracheal tubes, is not directly correlated with the mask inflation pressure. With endotracheal tubes, higher balloon pressure causes a tighter seal; with an LMA, overinflation makes the mask more rigid and *less* able to adapt to the patient's anatomy. If the seal is inadequate, mask pressure should be *lowered* somewhat; if this approach does not work, a larger mask size should be tried.

In emergencies, LMAs should be viewed as bridging devices. Prolonged placement, overinflation of the mask, or both may compress the tongue and cause tongue edema. Also, if noncomatose patients are given muscle relaxants before LMA insertion (eg, for laryngoscopy), they may gag and possibly aspirate when such drugs wear off. Either the device should be removed (assuming ventilation and gag reflexes are adequate), or drugs should be given to eliminate the gag response and provide time for an alternative intubation technique.

Endotracheal tubes: An endotracheal tube is inserted directly into the trachea via the mouth or, less commonly, the nose. Endotracheal tubes have high-volume, low-pressure balloon cuffs to prevent air leakage and minimize the risk of aspiration. Cuffed tubes were traditionally used only in adults and children > 8 yr; however, cuffed tubes are increasingly being used in infants and younger children to limit air leakage (particularly during transport); sometimes cuffs are not inflated or inflated only to the extent needed to prevent obvious leakage.

An endotracheal tube is the definitive method to secure a compromised airway, limit aspiration, and initiate mechanical ventilation in comatose patients, in patients who cannot protect their own airways, and in those who need prolonged mechanical ventilation. It also permits suctioning of the lower respiratory tract. Although drugs can be delivered via an endotracheal tube during cardiac arrest, this practice is discouraged.

Placement typically requires laryngoscopy by a skilled practitioner, but a variety of novel insertion devices that provide other options are becoming available.

Other devices: Another class of rescue ventilation devices is laryngeal tube or twin-lumen airways (eg, Combitube®, King LT®). These devices use 2 balloons to create a seal above and below the larynx and have ventilation ports overlying the laryngeal inlet (which is between the balloons). As with LMAs, prolonged placement and balloon overinflation can cause tongue edema.

Tracheal Intubation

Most patients requiring an artificial airway can be managed with tracheal intubation.

[**Fig. 224-6.** Laryngeal mask airway (LMA).]

Orotracheal intubation, typically done via direct laryngoscopy, is preferred in apneic and critically ill patients because it can usually be done faster than nasotracheal intubation, which is reserved for awake, spontaneously breathing patients or for cases when the mouth must be avoided.

Before intubation: Maneuvers to create a patent airway and to ventilate and oxygenate the patient are always indicated before attempting tracheal intubation. Once a decision to intubate has been made, preparatory measures include

• Correct patient positioning (see Fig. 224-1)

• Ventilation with 100% O_2

• Readying of necessary equipment (including suction devices)

• Sometimes drugs

Ventilation with 100% O_2 denitrogenates healthy patients and significantly prolongs the safe apneic time (effect is less in patients with severe cardiopulmonary disorders).

Strategies to predict difficult laryngoscopy (eg, Mallampati scoring, thyromental distance testing) are of limited value in emergencies. Practitioners should always be prepared to use an alternate technique (eg, LMA, BVM ventilation) if laryngoscopy does not work.

During cardiac arrest, chest compressions should not be halted for intubation attempts. If practitioners cannot intubate while compressions are being done (or during the brief pause that occurs during compressor changes), an alternate airway technique should be used.

Suction should be immediately available with a rigid tonsil-tip suction device to clear secretions and other material from the airway.

Anterior cricoid pressure (Sellick's maneuver) has previously been recommended before and during intubation to prevent passive regurgitation. However, current literature suggests that this maneuver may be less effective than once thought and may compromise laryngeal view during laryngoscopy.

Drugs (see p. 2278), including sedatives, muscle relaxants, and sometimes vagolytics, are typically given to conscious or semiconscious patients before laryngoscopy.

Tube selection and preparation: Most adults can accept a tube with an internal diameter of ≥ 8 mm; these tubes are preferable to smaller ones because they have lower airflow resistance (reducing the work of breathing), facilitate suctioning of secretions, allow passage of a bronchoscope, and may aid in liberation from mechanical ventilation.

For infants and children ≥ 1 yr, uncuffed tube size is calculated by (patient's age + 16)/4; thus, a 4-yr-old should have a (4 + 16)/4 = 5 mm endotracheal tube. The tube size suggested by this formula should be reduced by 0.5 (1 tube size) if a cuffed tube is to be used. Reference charts (see Table 223-3) or devices such as the Broselow Tape or Pedi-Wheel can rapidly identify appropriate-sized laryngoscope blades and endotracheal tubes for infants and children.

For adults (and sometimes in children), a rigid stylet should be placed in the tube, taking care to stop the stylet 1 to 2 cm before the distal end of the endotracheal tube, so that the tube tip remains soft. The stylet should then be used to make the tube straight to the beginning of the distal cuff; from that point, the tube is bent upward about 35° to form a hockey stick shape. This straight-to-cuff shape improves tube delivery and avoids blocking the operator's view of the cords during tube passage. Routinely filling the distal ET tube cuff with air to check the balloon is not required; if this technique is used, care must be taken to remove all the air before tube insertion.

Insertion technique: Successful intubation on the first attempt is important. Repeated laryngoscopy (≥ 3 attempts) is associated with much higher rates of significant hypoxemia, aspiration, and cardiac arrest. In addition to correct positioning, several other general principles are critical for success:

• Visualizing the epiglottis

• Visualizing the posterior laryngeal structures (ideally, the vocal cords)

• Not passing the tube unless tracheal insertion is ensured

The laryngoscope is held in the left hand, and the blade is inserted into the mouth and used as a retractor to displace the mandible and tongue up and away from the laryngoscopist, revealing the posterior pharynx. Avoiding contact with the incisors and not placing undue pressure on laryngeal structures are important.

The importance of identifying the epiglottis cannot be overstated. Identifying the epiglottis allows the operator to recognize critical airway landmarks and correctly position the laryngoscope blade. The epiglottis may rest against the posterior pharyngeal wall, where it blends in with the other pink mucus

membranes or gets lost in the pool of secretions that invariably exists in the cardiac arrest patient's airway.

Once the epiglottis is found, the operator may pick it up with the tip of the blade (the typical straight blade approach) or advance the tip of the blade into the vallecula to indirectly lift the epiglottis up and out of the line of sight (the typical curved blade approach). Success with the curved blade depends on the proper positioning of the blade tip in the vallecula and the direction of the lifting force (see Fig. 224-7). Lifting the epiglottis by either technique reveals the posterior laryngeal structures (arytenoid cartilages, interarytenoid notch), glottis, and vocal cords. If the tip of the blade is too deep, laryngeal landmarks may be entirely bypassed, and the dark, round hole of the esophagus may be mistaken for the glottis opening.

If identifying structures is difficult, manipulating the larynx with the right hand placed on the anterior neck (allowing the right and left hands to work together) may optimize the laryngeal view (see Fig. 224-7). Another technique involves lifting the head higher (lifting at the occiput, not atlanto-occipital extension), which distracts the jaw and improves the line of sight. Head elevation is inadvisable in patients with potential cervical spine injury and is difficult in the morbidly obese (who must be placed in a ramped or head-elevated position beforehand).

[**Fig. 224-7.** Bimanual laryngoscopy.]

In an optimal view, the vocal cords are clearly seen. If the vocal cords are not seen, at a minimum, the posterior laryngeal landmarks must be viewed and the tip of the tube must be seen passing above the interarytenoid notch and posterior cartilages. Operators must clearly identify laryngeal landmarks to avoid potentially fatal esophageal intubation. If operators are not confident that the tube is going into the trachea, the tube should not be inserted.

Once an optimal view has been achieved, the right hand inserts the tube through the larynx into the trachea (if operators have been applying anterior laryngeal pressure with the right hand, an assistant should continue applying this pressure). If the tube does not pass easily, a 90° clockwise twist of the tube may help it pass more smoothly over the anterior tracheal rings. Before withdrawing the laryngoscope, operators should confirm that the tube is passing between the cords. Appropriate tube depth is usually 21 to 23 cm in adults and 3 times the endotracheal tube size in children (for a 4.0-mm endotracheal tube, 12 cm; for a 5.5-mm endotracheal tube, 16.5 cm). In adults, the tube, if inadvertently advanced, typically migrates into the right mainstem bronchus.

Alternative intubation devices: A number of devices and techniques are increasingly used for intubation after failed laryngoscopy or as a primary means of intubation. Devices include

• Video laryngoscopes

• Mirror laryngoscopes

• LMAs with a passage that allows tracheal intubation

• Fiberoptic scopes and optical stylets

• Tube introducers

Each device has its own subtleties; practitioners who are skilled in standard laryngoscopic intubation techniques should not assume they can use one of these devices (especially after use of muscle relaxants) without becoming thoroughly familiarized with it.

Video and mirror laryngoscopes enable practitioners to look around the curvature of the tongue and usually provide excellent laryngeal views. However, the tube requires an exaggerated bend angle to go around the tongue and thus may be more difficult to manipulate and insert.

To pass an endotracheal tube through an LMA, practitioners must understand how to optimally position

the mask over the laryngeal inlet; there are sometimes mechanical difficulties passing the endotracheal tube.

Flexible fiberoptic scopes and optical stylets are very maneuverable and can be used in patients with abnormal anatomy. However, practice is required to recognize laryngeal landmarks from a fiberoptic perspective. Compared with video and mirror laryngoscopes, fiberoptic scopes are more difficult to master and are more susceptible to problems with blood and secretions; also, they do not separate and divide tissue but instead must be moved through open channels.

Tube introducers (commonly called gum elastic bougies) are semirigid stylets that can be used when laryngeal visualization is suboptimal (eg, the epiglottis is visible, but the laryngeal opening is not). In such cases, the introducer is passed along the undersurface of the epiglottis; from this point, it is likely to enter the trachea. Tracheal entry is suggested by the tactile feedback, noted as the tip bounces over the tracheal rings. An endotracheal tube is then advanced over the introducer.

Postinsertion: The stylet is removed and the balloon cuff is inflated with air using a 10-mL syringe; a manometer is used to verify that balloon pressure is < 30 cm H_2O. Properly sized endotracheal tubes may need considerably < 10 mL of air to create the correct pressure.

After balloon inflation, tube placement should be checked using a variety of methods, including

• Inspection and auscultation

• CO_2 detection

• Esophageal detector devices

• Sometimes chest x-ray

When a tube is correctly placed, manual ventilation should produce symmetric chest rise, good breath sounds over both lungs, and no gurgling over the upper abdomen.

Exhaled air should contain CO_2 and gastric air should not; detecting CO_2 with a colori-metric end-tidal CO_2 device or waveform capnography confirms tracheal placement. However, in prolonged cardiac arrest (ie, with little or no metabolic activity), CO_2 may not be detectable even with correct tube placement. In such cases, an esophageal detector device may be used. These devices use an inflatable bulb or a large syringe to apply negative pressure to the endotracheal tube. The flexible esophagus collapses, and little or no air flows into the device; in contrast, the rigid trachea does not collapse, and the resultant airflow confirms tracheal placement.

In the absence of cardiac arrest, tube placement is typically also confirmed with a chest x-ray.

After correct placement is confirmed, the tube should be secured using a commercially available device or adhesive tape. Adapters connect the endotracheal tube to a resuscitator bag, T-piece supplying humidity and O_2, or a mechanical ventilator.

Endotracheal tubes can be displaced, particularly in chaotic resuscitation situations, so tube position should be rechecked frequently. If breath sounds are absent on the left, right mainstem bronchus intubation is probably more likely than a left-sided tension pneumothorax, but both should be considered.

Nasotracheal intubation: If patients are spontaneously breathing, this technique can be used in certain emergency situations—eg, when patients have severe oral or cervical disorders (eg, injuries, edema, limitation of motion) that make laryngoscopy difficult. Historically, nasal intubation was also used when muscle relaxants were unavailable or forbidden (eg, prehospital settings, certain emergency departments) and when patients with tachypnea, hyperpnea, and upright positioning (eg, those with heart failure) might literally inhale a tube. However, availability of noninvasive means of ventilation (eg, bilevel positive airway pressure [BiPAP]), improved access to and training in pharmacologic adjuncts to intubation, and newer

airway devices have markedly decreased the use of nasal intubation. Additional considerations are problems with nasal intubation, including sinusitis (universal after 3 days), and the fact that tubes large enough to permit bronchoscopy (eg, ≥ 8 mm) can rarely be inserted nasotracheally.

When nasotracheal intubation is done, a vasoconstrictor (eg, phenylephrine) and topical anesthetic (eg, benzocaine, lidocaine) must be applied to the nasal mucosa and the larynx to prevent bleeding and to blunt protective reflexes. Some patients may also require IV sedatives, opioids, or dissociative drugs. After the nasal mucosa is prepared, a soft nasal trumpet should be inserted to ensure adequate patency of the selected nasal passage and to serve as a conduit for topical drugs to the pharynx and larynx. The trumpet may be placed using a plain or anesthetic (eg, lidocaine) lubricant. The nasal trumpet is removed after the pharyngeal mucosa has been sprayed. The nasotracheal tube is then inserted to about 14 cm depth (just above the laryngeal inlet in most adults); at this point, air movement should be audible. As the patient breathes in, opening the vocal cords, the tube is promptly passed into the trachea. More flexible endotracheal tubes with a controllable tip improve likelihood of success. Some practitioners soften tubes by placing them in warm water to lessen the risk of bleeding and make insertion easier. A small commercially available whistle can also be attached to the proximal tube connector to accentuate the noise of air movement when the tube is in the correct position above the larynx and in the trachea.

Surgical Airway

If the upper airway is obstructed because of a foreign body or massive trauma or if ventilation cannot be accomplished by other means, surgical entry into the trachea is required. Historically, a surgical airway was also the response to failed intubation. However, surgical airways require on average about 100 sec from initial incision to ventilation; LMAs and other devices provide a faster means of rescue ventilation, and very few patients require an emergency surgical airway.

Cricothyrotomy: Cricothyrotomy (see Fig. 224-8) is typically used for emergency surgical access because it is faster and simpler than tracheostomy.

Unlike positioning for laryngoscopy or ventilation, the correct position for cricothyrotomy involves extending the neck and arching the shoulders backward. After sterile preparation, the larynx is grasped with the nondominant hand while a blade held in the dominant hand is used to incise the skin, subcutaneous tissue, and cricothyroid membrane. A tracheal hook helps keep the space open and prevent retraction of the trachea while a small endotracheal tube (6.0 mm internal diameter [ID]) or small tracheotomy tube (cuffed 4.0 Shiley preferred) is advanced through the surgical site into the trachea.

Complications include hemorrhage, subcutaneous emphysema, pneumomediastinum, and pneumothorax. Various commercial products allow rapid surgical access to the

[**Fig. 224-8.** Emergency cricothyrotomy.]

cricothyroid space and provide a tube that allows adequate oxygenation and ventilation.

Tracheostomy: Tracheostomy is a more complex procedure because the trachea rings are very close together and part of at least one ring usually must be removed to allow tube placement. Tracheostomy is preferably done in an operating room by a surgeon. In emergencies, the procedure has a higher rate of complications than cricothyrotomy and offers no advantage. However, it is the preferred procedure for patients requiring long-term ventilation.

Percutaneous tracheostomy is an attractive alternative for critically ill patients who cannot be moved to the operating room. This bedside technique uses skin puncture and dilators to insert a tracheostomy tube. Fiberoptic assistance (within the trachea) is usually used to prevent puncture of the membranous (posterior) trachea and esophagus.

Complications of Tracheal Intubation

Complications include

• Direct trauma

• Esophageal intubation

• Tracheal erosion or stenosis

Laryngoscopy can damage lips, teeth, tongue, and supraglottic and subglottic areas.

Tube placement in the esophagus, if unrecognized, causes failure to ventilate and potentially death or hypoxic injury. Insufflating a tube in the stomach causes regurgitation, which can result in aspiration, compromise subsequent BVM ventilation, and obscure visualization in subsequent intubation attempts.

Any translaryngeal tube injures the vocal cords somewhat; sometimes ulceration, ischemia, and prolonged cord paralysis occur. Subglottic stenosis can occur later (usually 3 to 4 wk).

Rarely, tracheostomy insertion causes hemorrhage, thyroid damage, pneumothorax, recurrent laryngeal nerve paralysis, injury to major vessels, or late tracheal stenosis at the insertion site.

Erosion of the trachea is uncommon. It results more commonly from excessively high cuff pressure. Rarely, hemorrhage from major vessels (eg, innominate artery), fistulas (especially tracheoesophageal), and tracheal stenosis occur. Using high-volume, low-pressure cuffs with tubes of appropriate size and measuring cuff pressure frequently (every 8 h) to maintain it at < 30 cm H_2O decrease the risk of ischemic pressure necrosis, but patients in shock, with low cardiac output, or with sepsis remain especially vulnerable.

Drugs to Aid Intubation

Pulseless and apneic or severely obtunded patients can (and should) be intubated without pharmacologic assistance. Other patients are given sedating and paralytic drugs to minimize discomfort and facilitate intubation (termed rapid sequence intubation).

Pretreatment: Pretreatment typically includes

• 100% O_2

• Lidocaine

• Sometimes atropine, a neuromuscular blocker, or both

If time permits, patients should be placed on 100% O_2 for 3 to 5 min; this measure may maintain satisfactory oxygenation in previously healthy patients for up to 8 min. However, O_2 demand and safe apnea times are very dependent on pulse rate, pulmonary function, RBC count, and numerous other metabolic factors.

Laryngoscopy causes a sympathetic-mediated pressor response with an increase in heart rate, BP, and possibly intracranial pressure. To blunt this response, when time permits, some practitioners give lidocaine 1.5 mg/kg IV 1 to 2 min before sedation and paralysis.

Children and adolescents often have a vagal response (marked bradycardia) in response to intubation and are given atropine 0.02 mg/kg IV (minimum: 0.1 mg in infants, 0.5 mg in children and adolescents) at the same time.

Some physicians include a small dose of a neuromuscular blocker (NMB), such as vecuronium 0.01 mg/kg IV, in patients > 4 yr to prevent muscle fasciculations caused by full doses of succinylcholine. Fasciculations may result in muscle pain on awakening and cause transient hyperkalemia; however, the actual benefit of such pretreatment is unclear.

Sedation and analgesia: Laryngoscopy and intubation are uncomfortable; in conscious patients, a short-acting IV drug with sedative or combined sedative and analgesic properties is mandatory.

Etomidate 0.3 mg/kg, a nonbarbiturate hypnotic, may be the preferred drug. Fentanyl 5 µg/kg (2 to 5 µg/kg in children; NOTE: this dose is higher than the analgesic dose) also works well and causes no cardiovascular depression. Fentanyl is an opioid and thus has analgesic as well as sedative properties. However, at higher doses, chest wall rigidity may occur. Ketamine 1 to 2 mg/kg is a dissociative anesthetic with cardiostimulatory properties. It is generally safe but may cause hallucinations or bizarre behavior on awakening. Thiopental 3 to 4 mg/kg and methohexital 1 to 2 mg/kg are effective but tend to cause hypotension and are used less often.

Paralysis: Skeletal muscle relaxation with an IV NMB markedly facilitates intubation.

Succinylcholine (1.5 mg/kg IV, 2.0 mg/kg for infants), a depolarizing NMB, has the most rapid onset (30 sec to 1 min) and shortest duration (3 to 5 min). It should be avoided in patients with burns, muscle crush injuries > 1 to 2 days old, spinal cord injury, neuromuscular disease, renal failure, or possibly penetrating eye injury. About 1/15,000 children (and fewer adults) have a genetic susceptibility to malignant hyperthermia (see p. 3266) from succinylcholine. Succinylcholine should always be given with atropine in children because pronounced bradycardia may occur.

Alternative nondepolarizing NMBs have longer duration of action (> 30 min) but also have slower onset unless used in high doses that prolong paralysis significantly. Drugs include atracurium 0.5 mg/kg, mivacurium 0.15 mg/kg, rocuronium 1.0 mg/kg, and vecuronium 0.1 to 0.2 mg/kg injected over 60 sec.

Topical anesthesia: Intubation of an awake patient (typically not done in children) requires anesthesia of the nose and pharynx. A commercial aerosol preparation of benzocaine, tetracaine, butyl aminobenzoate (butamben), and benzalkonium is commonly used. Alternatively, 4% lidocaine can be nebulized and inhaled via face mask.

Chapter 225. Respiratory Failure and Mechanical Ventilation

Introduction

Respiratory failure is a life-threatening impairment of oxygenation or CO_2 elimination. Respiratory failure may occur because of impaired gas exchange, decreased ventilation, or both. Common manifestations include dyspnea, use of accessory muscles of respiration, tachypnea, tachycardia, diaphoresis, cyanosis, altered consciousness, and, without treatment, eventually obtundation, respiratory arrest, and death. Diagnosis is clinical, supplemented by ABGs and chest x-ray. Treatment is usually in an ICU and involves correction of the underlying cause, supplemental O_2, control of secretions, and ventilatory assistance if needed.

The respiratory system oxygenates and eliminates CO_2 from venous blood. Thus, a useful classification of respiratory failure is whether the principal abnormality is inadequate oxygenation or inadequate CO_2 elimination (which means inadequate ventilation), although many disorders affect both. Although temporizing measures exist, respiratory failure frequently necessitates mechanical ventilation.

Overview of Mechanical Ventilation

Mechanical ventilation can be noninvasive, involving various types of face masks, or invasive, involving endotracheal intubation. Selection and use of appropriate techniques require an understanding of respiratory mechanics.

Indications: There are numerous indications for endotracheal intubation and mechanical ventilation (see Table 224-1 on p. 2270), but in general, mechanical ventilation should be considered when there are clinical or laboratory signs that the patient cannot maintain an airway or adequate oxygenation or ventilation. Concerning findings include respiratory rate > 30/min, inability to maintain arterial O_2 saturation > 90% with fractional inspired O_2 (FIO_2) > 0.60, and $PaCO_2$ > 50 mm Hg with pH < 7.25. The decision to initiate mechanical ventilation should be based on clinical judgment that considers the entire clinical situation and should not be delayed until the patient is in extremis.

Respiratory Mechanics

Normal inspiration generates negative intrapleural pressure, which creates a pressure gradient between the atmosphere and the alveoli, resulting in air inflow. In mechanical ventilation, the pressure gradient results from increased (positive) pressure of the air source.

Peak airway pressure is measured at the airway opening (Pao) and is routinely displayed by mechanical ventilators. It represents the total pressure needed to push a volume of gas into the lung and is composed of pressures resulting from inspiratory flow resistance (resistive pressure), the elastic recoil of the lung and chest wall (elastic pressure), and the alveolar pressure present at the beginning of the breath (positive end-expiratory pressure [PEEP]—see also Fig. 225-1). Thus

Peak airway pressure = resistive pressure + elastic pressure + PEEP

Resistive pressure is the product of circuit resistance and airflow. In the mechanically ventilated patient, resistance to airflow occurs in the ventilator circuit, the endotracheal tube, and, most importantly, the patient's airways. NOTE: Even when these factors are constant, an increase in airflow increases resistive pressure.

Elastic pressure is the product of the elastic recoil of the lungs and chest wall (elastance) and the volume of gas delivered. For a given volume, elastic pressure is increased by increased lung stiffness (as in pulmonary fibrosis) or restricted excursion of the chest wall or diaphragm (eg, in tense ascites or massive obesity). Because elastance is the inverse of compliance, high elastance is the same as low compliance.

End-expiratory pressure in the alveoli is normally the same as atmospheric pressure. However, when the alveoli fail to empty completely because of airway obstruction, airflow limitation, or shortened expiratory time, end-expiratory pressure may be positive relative to the atmosphere. This pressure is called intrinsic PEEP or autoPEEP to differentiate it from externally applied (therapeutic) PEEP, which is created by adjusting the mechanical ventilator or by placing a tight-fitting mask that applies positive pressure throughout the respiratory cycle.

Any elevation in peak airway pressure (eg, > 25 cm H_2O) should prompt measurement of the end-inspiratory pressure (plateau pressure) by an end-inspiratory hold maneuver to determine the relative contributions of resistive and elastic pressures. The maneuver keeps the exhalation valve closed for an additional 0.3 to 0.5 sec after inspiration, delaying exhalation. During this time, airway pressure falls from its peak value as airflow ceases. The resulting end-inspiratory pressure represents the elastic pressure once PEEP is subtracted (assuming the patient is not making active inspiratory or expiratory muscle contractions at the time of measurement). The difference between peak and plateau pressure is the resistive pressure.

Elevated resistive pressure (eg, > 10 cm H_2O) suggests that the endotracheal tube has been kinked or plugged with secretions or that an intraluminal mass, increased intraluminal secretions, or bronchospasm is present. An increase in elastic pressure (eg, > 10 cm H_2O) suggests decreased lung compliance due to edema, fibrosis, or lobar atelectasis; large pleural effusions, pneumothorax or fibrothorax; extrapulmonary restriction as may result from circumferential burns or other chest wall deformity, ascites, pregnancy, or massive obesity; or a tidal volume too large for the amount of lung being ventilated (eg, a normal tidal volume being delivered to a single lung because the endotracheal tube is malpositioned).

Intrinsic PEEP can be measured in the passive patient through an end-expiratory hold maneuver. Immediately before a breath, the expiratory port is closed for 2 sec. Flow ceases, eliminating resistive pressure; the resulting pressure reflects alveolar pressure at the end of expiration (intrinsic PEEP). A nonquantitative method of identifying intrinsic PEEP is to inspect the expiratory flow tracing. If expiratory flow continues until the next breath or the patient's chest fails to come to rest before the next breath, intrinsic PEEP is present. The consequences of elevated intrinsic PEEP include increased inspiratory work of breathing and decreased venous return, which may result in decreased cardiac output and hypotension.

[Fig. 225-1. Components of airway pressure during mechanical ventilation, illustrated by an inspiratory-hold maneuver.]

The demonstration of intrinsic PEEP should prompt a search for causes of airflow obstruction (eg, airway secretions, bronchospasm); however, a high minute ventilation (> 20 L/min) alone can result in intrinsic PEEP in a patient with no airflow obstruction. If the cause is airflow limitation, intrinsic PEEP can be reduced by shortening inspiratory time (ie, increasing inspiratory flow) or reducing the respiratory rate, thereby allowing a greater fraction of the respiratory cycle to be spent in exhalation.

Means and Modes of Mechanical Ventilation

Mechanical ventilators are typically volume or pressure cycled; some newer models combine features of both. Because pressures and volumes are directly linked by the pressure-volume curve, any given volume will correspond to a specific pressure, and vice versa, regardless of whether the ventilator is pressure or volume cycled.

Adjustable ventilator settings differ with mode but include respiratory rate, tidal volume, trigger sensitivity, flow rate, waveform, and inspiratory/expiratory (I/E) ratio.

Volume-cycled ventilation: In this mode, which includes assist-control (A/C) and synchronized intermittent mandatory ventilation (SIMV), the ventilator delivers a set tidal volume. The resultant airway pressure is not fixed but varies with the resistance and elastance of the respiratory system and with the flow rate selected.

A/C ventilation is the simplest and most effective means of providing full mechanical ventilation. In this mode, each inspiratory effort beyond the set sensitivity threshold triggers delivery of the fixed tidal volume. If the patient does not trigger the ventilator frequently enough, the ventilator initiates a breath, ensuring the desired minimum respiratory rate.

SIMV also delivers breaths at a set rate and volume that is synchronized to the patient's efforts. In contrast to A/C, however, patient efforts above the set respiratory rate are unassisted, although the intake valve opens to allow the breath. This mode remains popular, despite the fact that it neither provides full ventilator support as does A/C nor facilitates liberating the patient from mechanical ventilation.

Pressure-cycled ventilation: This form of mechanical ventilation includes pressure control ventilation (PCV), pressure support ventilation (PSV), and several noninvasive modalities applied via a tight-fitting face mask. In all of these modalities, the ventilator delivers a set inspiratory pressure. Hence, tidal volume varies depending on the resistance and elastance of the respiratory system. In this mode, changes in respiratory system mechanics can result in unrecognized changes in minute ventilation. Because it limits the distending pressure of the lungs, this mode can theoretically benefit patients with acute lung injury/acute respiratory distress syndrome (ALI/ARDS); however, no clear clinical advantage over A/C has been shown.

Pressure control ventilation is similar to A/C; each inspiratory effort beyond the set sensitivity threshold delivers full pressure support maintained for a fixed inspiratory time. A minimum respiratory rate is maintained.

In **pressure support ventilation,** a minimum rate is not set; all breaths are triggered by the patient. Pressure is typically cut off when back-pressure causes flow to drop below a certain point. Thus, a longer or deeper inspiratory effort by the patient results in a larger tidal volume. This mode is commonly used to liberate patients from mechanical ventilation by letting them assume more of the work of breathing. However, no studies indicate that this approach is more successful.

Noninvasive positive pressure ventilation (NIPPV): NIPPV is the delivery of positive pressure ventilation via a tight-fitting mask that covers the nose or both the nose and mouth. Because of its use in spontaneously breathing patients, it is primarily applied as a form of PSV, although volume control can be used.

NIPPV can be given as continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP). In CPAP, constant pressure is maintained throughout the respiratory cycle with no additional inspiratory support. With BiPAP, the physician sets both the expiratory positive airway pressure (EPAP) and the inspiratory positive airway pressure (IPAP), with respirations triggered by the patient. Because the airway is unprotected, aspiration is possible, so patients must have adequate mentation and airway protective reflexes and no imminent indication for surgery or transport off the floor for prolonged procedures. NIPPV should be avoided in patients who are hemodynamically unstable and in those with evidence of impaired gastric emptying, as occurs with ileus, bowel obstruction, or pregnancy. In such circumstances, swallowing large quantities of air may result in vomiting and life-threatening aspiration. Indications for conversion to endotracheal intubation and conventional mechanical ventilation include the development of shock or frequent arrhythmias, myocardial ischemia, and transport to a cardiac catheterization laboratory or surgical suite where control of the airway and full ventilatory support are desired. Obtunded patients and patients with copious secretions are not good candidates. Also, IPAP must be set below esophageal opening pressure (20 cm H_2O) to avoid gastric insufflation.

NIPPV can be used in the outpatient setting. For example, CPAP is often used for patients with obstructive sleep apnea (see p. 1903), whereas BiPAP can be used for those with concomitant central sleep apnea (see p. 1907) and obstructive sleep apnea or for chronic ventilation in patients with progressive neuromuscular diseases.

Ventilator settings: Ventilator settings are tailored to the underlying condition, but the basic principles are as follows.

Tidal volume and respiratory rate set the minute ventilation. Too high a volume risks overinflation; too low a volume risks atelectasis. Too high a rate risks hyperventilation and respiratory alkalosis along with inadequate expiratory time and autoPEEP; too low a rate risks inadequate minute ventilation and respiratory acidosis. A tidal volume of 8 to 10 mL/kg ideal body weight (see p. 2287) is usually appropriate, although some patients with normal lung mechanics (particularly those with neuromuscular disease) benefit from tidal volumes on the high end of this range to prevent atelectasis, whereas patients with ALI/ARDS or acute exacerbations of COPD or asthma may require lower volumes (see p. 2286). Ideal body weight (IBW) rather than actual body weight is used to determine the appropriate tidal volume for patients with lung disease and receiving mechanical ventilation:

Males: IBW (kg) =
50 + 2.3 (height in inches - 60)
or 50 + 0.91 (height in cm - 152.4)
Females: IBW (kg) =
45.5 + 2.3 (height in inches - 60)
or 45.5 + 0.91 (height in cm - 152.4)

Sensitivity adjusts the level of negative pressure required to trigger the ventilator. A typical setting is -2 cm H_2O. Too high a setting causes weak patients to be unable to trigger a breath. Too low a setting may lead to overventilation by causing the machine to auto-cycle. Patients with high levels of autoPEEP may have difficulty inhaling deeply enough to achieve a sufficiently negative intra-airway pressure.

The ratio of time spent in inhalation versus that spent in exhalation (I:E ratio) can be adjusted in some modes of ventilation. A normal setting for patients with normal mechanics is 1:3. Patients with asthma or COPD exacerbations should have ratios of 1:4 or even more to limit the degree of autoPEEP.

The inspiratory flow rate can be adjusted in some modes of ventilation (ie, either the flow rate or the I:E ratio can be adjusted, not both). The inspiratory flow should generally be set at about 60 L/min but can be increased up to 120 L/min for patients with airflow limitation to facilitate having more time in exhalation, thereby limiting autoPEEP.

FIO_2 is initially set at 1.0 and is subsequently decreased to the lowest level necessary to maintain adequate oxygenation.

PEEP can be applied in any ventilator mode. PEEP increases end-expired lung volume and reduces airspace closure at the end of expiration. Most patients undergoing mechanical ventilation may benefit from the application of PEEP at 5 cm H_2O to limit the atelectasis that frequently accompanies endotracheal intubation, sedation, paralysis, and/or supine positioning. Higher levels of PEEP improve oxygenation in disorders such as cardiogenic pulmonary edema and ARDS. PEEP permits use of lower levels of FIO_2 while preserving adequate arterial oxygenation. This effect may be important in limiting the lung injury that may result from prolonged exposure to a high FIO_2 (≥ 0.6). PEEP increases intrathoracic pressure and thus may impede venous return, provoking hypotension in a hypovolemic patient, and may overdistend portions of the lung, thereby causing ventilator-associated lung injury (VALI). By contrast, if PEEP is too low, it may result in cyclic airspace opening and closing, which in turn may also cause VALI from the resultant repetitive shear forces.

Patient positioning: Mechanical ventilation is typically done with the patient in the semiupright position. However, in patients with ALI/ARDS, prone positioning may result in better oxygenation primarily by creating more uniform ventilation. Uniform ventilation reduces the amount of lung that has no ventilation (ie, the amount of shunt), which is generally greatest in the dorsal and caudal lung regions, while having minimal effects on perfusion distribution.

Although many investigators advocate a trial of prone positioning in patients with ALI/ARDS who require high levels of PEEP (eg, > 12 cm H_2O) and FIO_2 (eg, > 0.6), trials have not shown any improvement in mortality with this strategy. Prone positioning is contraindicated in patients with spinal instability or increased intracranial pressure. This position also requires concerted effort by the ICU staff to avoid

complications, such as dislodgement of the endotracheal tube or intravascular lines.

Sedation and comfort: Although some patients tolerate mechanical ventilation via endotracheal tube without sedatives, most require continuous IV administration of sedatives (eg, propofol, lorazepam, midazolam) and analgesics (eg, morphine, fentanyl) to minimize stress and anxiety. These drugs can also reduce energy expenditure to some extent, thereby reducing CO_2 production and O_2 consumption. Doses should be titrated to the desired effect, guided by standard sedation/analgesia scoring systems. Patients undergoing mechanical ventilation for ALI/ARDS typically require higher levels of sedation and analgesia. The use of propofol for longer than 24 to 48 h requires periodic monitoring of serum triglyceride levels.

Neuromuscular blocking agents are now rarely used in patients undergoing mechanical ventilation because of the risk of prolonged neuromuscular weakness and the need for continuous heavy sedation. Exceptions include for failure to tolerate some of the more sophisticated and complicated modes of mechanical ventilation and for prevention of shivering when cooling is used after cardiac arrest.

Complications and safeguards: Complications can be divided into those resulting from endotracheal intubation, from mechanical ventilation itself, or from prolonged immobility and inability to eat normally.

The presence of an endotracheal tube causes risk of sinusitis (which is rarely of clinical importance), ventilator-associated pneumonia (see p. 1929), tracheal stenosis, vocal cord injury, and rarely tracheal-esophageal or trachealvascular fistula. Purulent tracheal aspirate in a febrile patient who has an elevated WBC count > 48 h after ventilation has begun suggests ventilator-associated pneumonia.

Complications of ongoing mechanical ventilation itself include pneumothorax, O_2 toxicity, hypotension, and VALI.

If acute hypotension develops in a mechanically ventilated patient, particularly when it is accompanied by tachycardia and/or a sudden increase in peak inspiratory pressure, tension pneumothorax must always be considered; patients with such findings should immediately have a chest examination and a chest x-ray (or immediate treatment if examination is confirmatory). More commonly, however, hypotension is a result of sympathetic lysis caused by sedatives or opioids used to facilitate intubation and ventilation. Hypotension can also be caused by decreased venous return due to high intrathoracic pressure in patients receiving high levels of PEEP or in those with high levels of intrinsic PEEP due to asthma or COPD. If there are no physical findings suggesting tension pneumothorax and if ventilation-related causes of hypotension are a possible etiology, pending a portable chest x-ray, the patient may be disconnected from the ventilator and gently bagged manually at 2 to 3 breaths/min with 100% O_2 while fluids are infused (eg, 500 to 1000 mL of 0.9% saline in adults, 20 mL/kg in children). An immediate improvement suggests a ventilation-related cause, and ventilator settings should be adjusted accordingly.

Relative immobility increases the risk of venous thromboembolic disease, skin breakdown, and atelectasis.

Most hospitals have standardized protocols to reduce complications. Elevating the head of the bed to > 30° decreases risk of ventilator-associated pneumonia, and routine turning of the patient every 2 h decreases the risk of skin breakdown. All patients receiving mechanical ventilation should receive deep venous thrombosis prophylaxis, either heparin 5000 units sc bid to tid or low molecular weight heparin or, if heparin is contraindicated, sequential compression devices. To prevent GI bleeding, patients should receive an H_2 blocker (eg, famotidine 20 mg enterally or IV bid) or sucralfate (1 g enterally qid). Proton pump inhibitors should be reserved for patients with a preexisting indication or active bleeding. Routine nutritional evaluations are mandatory, and enteral tube feedings should be initiated if ongoing mechanical ventilation is anticipated.

The most effective way to reduce complications of mechanical ventilation is to limit its duration. Daily "sedation vacations" and spontaneous breathing trials help determine the earliest point at which the patient may be liberated from mechanical support.

Acute Hypoxemic Respiratory Failure

Acute hypoxemic respiratory failure (AHRF) is severe arterial hypoxemia that is refractory to supplemental O_2. It is caused by intrapulmonary shunting of blood secondary to airspace filling or collapse. Findings include dyspnea and tachypnea. Diagnosis is by ABGs and chest x-ray. Treatment usually requires mechanical ventilation.

Etiology

Airspace filling in AHRF may result from

- Elevated alveolar capillary hydrostatic pressure, as occurs in left ventricular failure or hypervolemia
- Increased alveolar capillary permeability, as occurs in any of the conditions predisposing to acute lung injury/acute respiratory distress syndrome (ALI/ARDS)
- Blood, as seen in diffuse alveolar hemorrhage

Pathophysiology

ALI/ARDS: ALI resulting in more severe hypoxemia is known as ARDS. However, differentiation between these 2 forms (see Table 225-1) is arbitrary given that Pao_2 correlates poorly with lung pathology and clinical course.

In ALI/ARDS, pulmonary or systemic inflammation leads to release of cytokines and other proinflammatory molecules. The cytokines activate alveolar macrophages and recruit neutrophils to the lungs, which in turn release leukotrienes, oxidants, platelet-activating factor, and proteases. These substances damage capillary endothelium and alveolar epithelium, disrupting the barriers between capillaries and airspaces. Edema fluid, protein, and cellular debris flood the airspaces and interstitium, causing disruption of surfactant, airspace collapse, ventilation-perfusion mismatch, shunting, and pulmonary hypertension. The injury is distributed heterogeneously but mainly affects dependent lung zones.

Causes of ALI/ARDS (see Table 225-2) may involve direct lung injury (eg, pneumonia, acid aspiration) or indirect lung injury (eg, sepsis, pancreatitis, massive blood transfusion, nonthoracic trauma). Sepsis and pneumonia account for about 60% of cases.

Refractory hypoxemia: In both types of AHRF, flooded airspaces allow no inspired gas to enter, so the blood perfusing those alveoli remains at the mixed venous O_2 content no matter how high the fractional inspired O_2 (FIO_2). This effect ensures constant admixture of deoxygenated blood into the pulmonary vein and hence arterial hypoxemia. In contrast, hypoxemia that results from ventilating alveoli that have less ventilation than perfusion (ie, low ventilation-to-perfusion ratios as occurs in asthma or COPD and, to some extent, in ARDS/ALI) is readily corrected by supplemental O_2.

[**Table 225-1.** Consensus Definition of ALI/ARDS]

[**Table 225-2.** Causes of ALI/ARDS]

Symptoms and Signs

Acute hypoxemia (see also p. 2250) may cause dyspnea, restlessness, and anxiety. Signs include confusion or alteration of consciousness, cyanosis, tachypnea, tachycardia, and diaphoresis. Cardiac arrhythmia and coma can result. Airway flooding or closure causes crackles, detected during chest auscultation; the crackles are typically diffuse but sometimes worse at the lung bases. Jugular venous distention occurs with high levels of PEEP or severe right ventricular failure.

Diagnosis

• Chest x-ray and ABGs

• Clinical definition (see Table 225-1)

Hypoxemia is usually first recognized using pulse oximetry. Patients with low O_2 saturation should have a chest x-ray and ABGs. Symptomatic patients should be treated with supplemental O_2 while awaiting test results.

If supplemental O_2 does not improve the O_2 saturation to > 90%, right-to-left shunting of blood should be suspected. An obvious alveolar infiltrate on chest x-ray implicates alveolar flooding as the cause, rather than an intracardiac shunt. However, at the onset of illness, hypoxemia is often present before changes are seen on x-ray.

Once AHRF is diagnosed, the cause must be determined, considering both pulmonary and extrapulmonary causes. Sometimes a known ongoing disorder (eg, acute MI, pancreatitis, sepsis) is an obvious cause. In other cases, history is suggestive; pneumonia should be suspected in an immunocompromised patient, and alveolar hemorrhage is suspected after bone marrow transplant or in a patient with a connective tissue disease. Frequently, however, critically ill patients have received a large volume of IV fluids for resuscitation, and high-pressure AHRF (eg, caused by ventricular failure or fluid overload) resulting from treatment must be distinguished from an underlying low-pressure AHRF (eg, caused by sepsis or pneumonia).

High-pressure pulmonary edema is suggested by a 3rd heart sound, jugular venous distention, and peripheral edema on examination and by the presence of diffuse central infiltrates, cardiomegaly, and an abnormally wide vascular pedicle on chest x-ray. The diffuse, bilateral infiltrates of ALI/ARDS are generally more peripheral. Focal infiltrates are typically caused by lobar pneumonia, atelectasis, or lung contusion. Although echocardiography may show left ventricular dysfunction, implying a cardiac origin, this finding is not specific because sepsis can also reduce myocardial contractility.

When ALI/ARDS is diagnosed but the cause is not obvious (eg, trauma, sepsis, severe pulmonary infection, pancreatitis), a review of drugs and recent diagnostic tests, procedures, and treatments may suggest an unrecognized cause, such as use of a radiographic contrast agent, air embolism, or transfusion. When no predisposing cause can be uncovered, some experts recommend doing bronchoscopy with bronchoalveolar lavage to exclude alveolar hemorrhage and eosinophilic pneumonia and, if this procedure is not revealing, a lung biopsy to exclude other disorders (eg, extrinsic allergic alveolitis, acute interstitial pneumonitis).

Prognosis

Prognosis is highly variable and depends on a variety of factors, including etiology of respiratory failure, severity of disease, age, and chronic health status. In particular, mortality in ALI/ARDS was very high (40 to 60%) but has declined in recent years to 25 to 40%, probably because of improvements in mechanical ventilation and in treatment of sepsis. Most often, death is not caused by respiratory dysfunction but by sepsis and multiorgan failure. Persistence of neutrophils and high cytokine levels in bronchoalveolar lavage fluid predict a poor prognosis. Mortality otherwise increases with age, presence of sepsis, and severity of preexisting organ insufficiency or coexisting organ dysfunction. Pulmonary function returns to close to normal in 6 to 12 mo in most ALI/ARDS patients who survive; however, patients with a protracted clinical course or severe disease may have residual pulmonary symptoms, and many have persistent neuromuscular weakness.

Treatment

• Mechanical ventilation if saturation is < 90% on high-flow O_2

Underlying conditions must be addressed as discussed elsewhere in THE MANUAL. AHRF is initially treated with high flows of 70 to 100% O_2 by a nonrebreather face mask. If O_2 saturation > 90% is not obtained, mechanical ventilation probably should be instituted. Specific management varies by condition.

Mechanical ventilation in cardiogenic pulmonary edema: Mechanical ventilation benefits the failing left ventricle in several ways. Positive inspiratory pressure reduces left and right ventricular preload and left ventricular afterload and unloads the respiratory muscles, reducing the work of breathing. Reducing the work of breathing may allow redistribution of a limited cardiac output away from overworked respiratory muscles. Expiratory pressure (expiratory positive airway pressure [EPAP] or positive end-expiratory pressure [PEEP]) redistributes pulmonary edema from alveoli to the interstitium, allowing more alveoli to participate in gas exchange.

Noninvasive positive pressure ventilation (NIPPV) is useful in averting endotracheal intubation in many patients because drug therapy often leads to rapid improvement. Typical settings are inspiratory positive airway pressure (IPAP) of 10 to 15 cm H_2O and EPAP of 5 to 8 cm H_2O.

Conventional mechanical ventilation can use several ventilator modes. Most often, assist-control (A/C) is used in the acute setting, when full ventilatory support is desired. Initial settings are tidal volume of 6 mL/kg ideal body weight (see Sidebar 225-1), respiratory rate of 25/min, FIO_2 of 1.0, and PEEP of 5 to 8 cm H_2O. PEEP may then be titrated upward in 2.5-cm H_2O increments while the FIO_2 is decreased to nontoxic levels. Pressure support ventilation can also be used (with similar levels of PEEP). The initial pressure delivered should be sufficient to fully rest the respiratory muscles as judged by subjective patient assessment, respiratory rate, and accessory muscle use. Typically, a pressure support level of 10 to 20 cm H_2O over PEEP is required.

Mechanical ventilation in ALI/ARDS: Nearly all patients require mechanical ventilation (see Sidebar 225-1), which, in addition to improving oxygenation, reduces O_2 demand by resting respiratory muscles. Targets include

- Plateau transpulmonary pressures < 30 cm H_2O (estimated from plateau alveolar pressures and a consideration of factors that potentially decrease chest wall and abdominal compliance)
- Tidal volume 6 mL/kg predicted body weight to minimize further lung injury
- FIO_2 as low as is allowed to maintain adequate SaO_2 to minimize possible O_2 toxicity

NIPPV is occasionally useful with ALI/ARDS. However, compared with treatment of cardiogenic pulmonary edema, higher levels of support for a longer duration are often required, and EPAP of 8 to 12 cm H_2O is often necessary to maintain adequate oxygenation. Achieving this expiratory pressure requires inspiratory pressures > 18 to 20 cm H_2O, which are poorly tolerated; maintaining an adequate seal becomes difficult, the mask becomes more uncomfortable, and skin necrosis and gastric insufflation may occur. Also, NIPPV-treated patients who subsequently need intubation have generally progressed to a more advanced condition than if they had been intubated earlier; thus, critical desaturation is possible at the time of intubation. Intensive monitoring and careful selection of patients (see p. 2282) are required.

Conventional mechanical ventilation in ALI/ARDS previously focused on normalizing ABG values. It is now clear that ventilating with lower tidal volumes reduces mortality. Accordingly, in most patients, tidal volume should be set at 6 mL/kg ideal body weight (see Sidebar 225-1). This necessitates an increase in respiratory rate, even up to 35/min, to produce sufficient alveolar ventilation to allow for adequate CO_2 removal. On occasion, however, respiratory acidosis develops, some degree of which is accepted for the greater good of limiting ventilator-associated lung injury and is generally well tolerated, particularly when pH is ≥ 7.15. If pH drops below 7.15, bicarbonate infusion may be helpful. Because hypercapnia may cause dyspnea and cause the patient to breathe in a fashion that is not coordinated with the ventilator, analgesics (fentanyl or morphine) and sedatives may be needed (eg, propofol initiated at 5 µg/kg/min and increasing to effect up to 50 µg/kg/min; because of the risk of hypertriglyceridemia, triglyceride levels should be checked every 48 h). Sedation is preferred to neuromuscular blockade because blockade still

requires sedation and may cause residual weakness.

Sidebar 225-1 Initial Ventilator Management in ALI/ARDS

Generally, the following approach is recommended for ventilator management in ALI/ARDS:

- Assist-control mode is used initially with a tidal volume 6 mL/kg ideal body weight, respiratory rate 25/min, flow rate 60 L/min, FIO_2 1.0, and PEEP 15 cm H_2O.
- Once O_2 saturation is > 90%, FIO_2 is decreased.
- Then, PEEP is decreased in 2.5-cm H_2O increments as tolerated to find the least PEEP associated with an arterial O_2 saturation of 90% on an FIO_2 of ≤ 0.6.
- The respiratory rate is increased up to 35/min to achieve a pH of > 7.15 or until the expiratory flow tracing shows end-expiratory flow.

Ideal body weight (IBW) rather than actual body weight is used to determine the appropriate tidal volume for patients with lung disease receiving mechanical ventilation:

Males: IBW (kg) =
50 + 2.3 (height in inches - 60)
or 50 + 0.91 (height in cm - 152.4)
Females: IBW (kg) =
45.5 + 2.3 (height in inches - 60)
or 45.5 + 0.91 (height in cm - 152.4)

PEEP improves oxygenation in ALI/ARDS by increasing the volume of aerated lung through alveolar recruitment, permitting the use of a lower FIO_2. The optimal level of PEEP and the way to identify it have been debated. Many clinicians simply use the least amount of PEEP that results in an adequate arterial O_2 saturation on a nontoxic FIO_2. In most patients, this level is a PEEP of 8 to 15 cm H_2O, although occasionally, patients with severe ARDS require levels > 20 cm H_2O. In these cases, close attention must be paid to other means of optimizing O_2 delivery and minimizing O_2 consumption (see p. 2283).

The best indicator of alveolar overdistention is measurement of a plateau pressure through an end-inspiratory hold maneuver (see p. 2286); it should be checked every 4 h and after each change in PEEP or tidal volume. The target plateau pressure is < 30 cm H_2O. If the plateau pressure exceeds this value and there is no problem with the chest wall that could be contributing (eg, ascites, pleural effusion, acute abdomen, chest trauma), the physician should reduce the tidal volume in 0.5- to 1.0-mL/kg increments as tolerated to a minimum of 4 mL/kg, raising the respiratory rate to compensate for the reduction in minute ventilation and inspecting the ventilator waveform display to ensure that full exhalation occurs. The respiratory rate may often be raised as high as 35/min before overt gas trapping due to incomplete exhalation results. If plateau pressure is < 25 cm H_2O and tidal volume is < 6 mL/kg, tidal volume may be increased to 6 mL/kg or until plateau pressure is > 25 cm H_2O. Some investigators believe pressure control ventilation protects the lungs better, although supportive data are lacking and it is the peak pressure rather than the plateau pressure that is being controlled.

Prone positioning (see p. 2283) improves oxygenation in some patients by allowing recruitment of nonventilating lung regions. However, there is no evidence of improved survival.

Optimal fluid management of patients with ALI/ARDS balances the requirement for an adequate circulating volume to preserve end-organ perfusion with the goal of lowering preload and thereby limiting transudation of fluid in the lungs. Recently, a large multicenter trial has shown that a conservative

approach to fluid management, in which less fluid is given, shortens the duration of mechanical ventilation and ICU length of stay when compared with a more liberal strategy. However, there was no difference in survival between the 2 approaches, and use of a pulmonary artery catheter also did not improve outcome. Patients not in shock are candidates for such an approach but should be monitored closely for evidence of decreased end-organ perfusion, such as hypotension, oliguria, thready pulses, or cool extremities (see p. 2292).

A definitive pharmacologic treatment for ALI/ARDS that reduces morbidity and mortality remains elusive. Inhaled nitric oxide, surfactant replacement, and many other agents directed at modulating the inflammatory response have been studied and found not to reduce morbidity or mortality. Some small studies suggest that systemic corticosteroids may be beneficial in late-stage ALI/ARDS, but a larger, prospective randomized trial found no reduction in mortality. Corticosteroids may be deleterious when given early in the course of the condition.

Ventilatory Failure

Ventilatory failure is a rise in $PaCO_2$ (hypercapnia) that occurs when the respiratory load can no longer be supported by the strength or activity of the system. The most common causes are acute exacerbations of asthma and COPD, overdoses of drugs that suppress ventilatory drive, and conditions that cause respiratory muscle weakness (eg, Guillain-Barre syndrome, myasthenia gravis, botulism). Findings include dyspnea, tachypnea, and confusion. Death can result. Diagnosis is by ABGs and patient observation; chest x-ray and clinical evaluation may help delineate cause. Treatment varies by condition but often includes mechanical ventilation.

Pathophysiology

Hypercapnia occurs when alveolar ventilation either falls or fails to rise adequately in response to increased CO_2 production. A fall in alveolar ventilation results from a decrease in minute ventilation or an increase in dead space ventilation.

Minute ventilation decreases when there is an imbalance between the load on the respiratory system (including resistive loads, lung and chest wall elastic loads, and minute ventilation loads) and neuromuscular competence for an effective inspiratory effort (see Fig. 225-2 for causes).

Physiologic dead space is the part of the respiratory tree that does not participate in gas exchange. It includes the anatomic dead space (oropharynx, trachea, and airways) and alveolar dead space (ie, alveoli that are ventilated but not perfused). The physiologic dead space is normally about 30 to 40% of tidal volume but increases to 50% in intubated patients and to > 70% in massive pulmonary embolism, severe emphysema, and status asthmaticus. Thus, for any given minute ventilation, the greater the dead space, the poorer the CO_2 elimination.

Increased CO_2 production, as occurs with fever, sepsis, trauma, burns, hyperthyroidism, and malignant hyperthermia, is not a primary cause of ventilatory failure because patients should increase their ventilation to compensate. Ventilatory failure cause by these problems results only when the ability to compensate is compromised.

Hypercapnia lowers arterial pH (respiratory acidosis). Severe acidemia (pH < 7.2) contributes to pulmonary arteriolar vasoconstriction, systemic vascular dilation, reduced myocardial contractility, hyperkalemia, hypotension, and cardiac irritability, with the potential for life-threatening arrhythmias. Acute hypercapnia also causes cerebral vasodilation and increased intracranial pressure, a major problem in patients with acute head injury. Over time, tissue buffering and renal compensation can largely correct the acidemia. However, sudden increases in $PaCO_2$ can occur faster than compensatory changes ($PaCO_2$ rises 3 to 6 mm Hg/min in a totally apneic patient).

Symptoms and Signs

The predominant symptom is dyspnea. Signs include vigorous use of accessory ventilatory muscles, tachypnea, tachycardia, diaphoresis, anxiety, declining tidal volume, irregular or gasping breathing patterns, and paradoxical abdominal motion.

CNS manifestations range from subtle personality changes to marked confusion, obtundation, or coma. Chronic hypercapnia is better tolerated than acute and has fewer symptoms.

Diagnosis

• ABGs

• Chest x-ray

• Tests to determine etiology

Ventilatory failure should be suspected in patients with respiratory distress, visible ventilatory fatigue or cyanosis, or changes in sensorium and in those with disorders causing neuromuscular weakness. Tachypnea is also

[Fig. 225-2. The balance between load (resistive, elastic, and minute ventilation) and neuromuscular competence (drive, transmission, and muscle strength) determines the ability to sustain alveolar ventilation.]

a concern; respiratory rates > 28 to 30/min cannot be sustained for very long, particularly in elderly or weakened patients.

If ventilatory failure is suspected, ABG analysis, continuous pulse oximetry, and a chest x-ray should be done. Respiratory acidosis on the ABG (eg, pH < 7.35 and PCO_2 > 50) confirms the diagnosis. Patients with chronic ventilatory failure often have quite elevated PCO_2 (eg, 60 to 90 mm Hg) at baseline, typically with a pH that is only slightly acidemic. In such patients, the degree of acidemia rather than the PCO_2 must serve as the primary marker for acute hypoventilation.

Because ABGs can be normal in patients with incipient ventilatory failure, certain bedside pulmonary function tests can help predict ventilatory failure, particularly in patients with neuromuscular weakness who may succumb to ventilatory failure without exhibiting respiratory distress. Vital capacity < 10 to 15 mL/kg and a maximum negative inspiratory force of ≤ 15 cm H_2O suggest imminent ventilatory failure.

Once ventilatory failure is diagnosed, the cause must be identified. Sometimes a known ongoing disorder (eg, coma, acute asthma, COPD exacerbation, myxedema, myasthenia gravis, botulism) is an obvious cause. In other cases, history is suggestive; sudden onset of tachypnea and hypotension after surgery suggests pulmonary embolism, and focal neurologic findings suggest a CNS or neuromuscular cause. Neuromuscular competence may be assessed through measurement of inspiratory muscle strength (negative inspiratory force and positive expiratory force), neuromuscular transmission (nerve conduction tests and electromyography), and investigations into causes of diminished drive (toxicology screens, brain imaging, sleep studies, and thyroid function tests).

Treatment

• Treatment of cause

• Often positive pressure ventilation

Treatment aims to correct the imbalance between the strength of the respiratory system and its load and varies with etiology. Obvious precipitants (eg, bronchospasm, mucus plugging, foreign bodies) should be corrected if possible.

The 2 most common causes are acute exacerbation of asthma (ie, status asthmaticus) and COPD.

Respiratory failure due to COPD is termed acute-on-chronic respiratory failure (ACRF).

Status asthmaticus (SA): Patients should be treated in an ICU by personnel skilled in airway management.

Noninvasive positive pressure ventilation (NIPPV) can immediately reduce the work of breathing and may forestall endotracheal intubation until drug therapy can take effect. In contrast to patients with COPD, who often welcome NIPPV, the mask often increases the perception of dyspnea in asthmatic patients, so introduction must be done carefully, perhaps starting with titration of expiratory positive airway pressure (EPAP) alone (because one of the major functions of inspiratory positive airway pressure [IPAP] is to increase tidal volume, and in these patients, end-expiratory lung volume approaches total lung capacity). After an explanation of its benefit, patients hold the mask against their face while modest amounts of pressure are applied (continuous positive airway pressure [CPAP] 3 to 5 cm H_2O). Once tolerated, the mask is strapped in place while pressures are increased to patient comfort and reduced work of breathing as assessed by respiratory rate and accessory muscle use. Final settings are typically IPAP 10 to 15 cm H_2O and EPAP 5 to 8 cm H_2O. Patients should be selected carefully (see p. 2282).

Conventional mechanical ventilation via endotracheal intubation is indicated for impending respiratory failure as indicated clinically by obtundation, monosyllabic speech, slumped posture, and shallow breathing. ABGs showing worsening hypercapnia are also an indication, although blood-gas confirmation is not required and should not replace the physician's judgment. Oral intubation is preferred over nasal because a larger endotracheal tube, which decreases airway resistance and permits easier suctioning, can be used.

Hypotension and pneumothorax occasionally occur after intubation for SA (see also p. 2283). These complications and their corresponding mortality have declined significantly because of a ventilator strategy that emphasizes limiting dynamic hyperinflation over achieving eucapnia. In SA, ventilation sufficient to achieve a normal pH typically causes severe hyperinflation. To avoid hyperinflation, initial ventilator settings include a tidal volume of 5 to 7 mL/kg and a respiratory rate of 10 to 18/min. Inspiratory flows may need to be quite high (eg, 70 to 120 L/min) with a square wave pattern to facilitate maximum time in exhalation. Dangerous dynamic hyperinflation is unlikely so long as the measured plateau pressure is < 30 to 35 cm H_2O and intrinsic positive end-expiratory pressure (PEEP) is < 15 cm H_2O (although these pressures may be difficult to measure because of inspiratory and expiratory respiratory muscle activity). Plateau pressure > 35 cm H_2O is managed by reducing the tidal volume (assuming that clinical evaluation does not indicate that the high pressures are the result of decreased compliance of the chest wall or abdomen) or the respiratory rate.

Although it is possible to reduce peak airway pressure by reducing peak flow rate or by changing the waveform to a descending profile, it should *not* be done. Although high flow rates require a high pressure to overcome the high airway resistance of SA, this pressure is dissipated across robust, cartilage-containing airways. Lower flow rates (eg, < 60 L/min) reduce time available for exhalation, thereby increasing the end-expiratory volume (and the resultant intrinsic PEEP) and allowing a greater inspiratory volume during the next breath.

Using low tidal volumes often results in hypercapnia, which is permitted for the greater good of reducing dynamic hyperinflation. An arterial pH > 7.15 is generally well tolerated but often requires large doses of sedatives and opioids. Neuromuscular blockers should be avoided after the peri-intubation period because use of these agents in combination with corticosteroids can cause a severe and occasionally irreversible myopathy, particularly after 24 h of combined use. Patient agitation should be managed with sedation rather than paralysis, but ideally ventilation can be adjusted to patients' needs so as to reduce the need for sedation.

Most patients with SA improve to the point of liberation from mechanical ventilation within 2 to 5 days, although a minority experience protracted severe airflow obstruction. The general approach to liberation is discussed on p. 2291.

ACRF: In patients with ACRF caused by COPD, the O_2 cost of breathing is several times that of patients

without underlying lung disease. This increased respiratory load occurs in the setting of barely adequate neuromuscular competence, so patients easily become too tired to maintain ventilation. These patients are vulnerable to respiratory failure from seemingly trivial insults, and recovery requires systematic identification and correction of these precipitants (see also p. 1889). To restore the balance between neuromuscular competence and load, clinicians reduce airflow obstruction and dynamic hyperinflation with bronchodilators and corticosteroids and treat infection with antibiotics. Low serum levels of K, phosphorus, and Mg may exacerbate muscle weakness, frustrating recovery, and must be identified and treated.

NIPPV is the preferred initial treatment for many patients with ACRF, resulting in decreased rates of ventilator-associated pneumonia, length of stay, and mortality compared with endotracheal intubation. Perhaps 75% of patients managed with NIPPV do not require endotracheal intubation. Advantages include the ease of application and removal; once initial stabilization has occurred, NIPPV may be stopped temporarily to allow oral intake in selected patients. Trials of unassisted breathing are easily done, and NIPPV can be reapplied as indicated.

Typical settings are IPAP of 10 to 15 cm H_2O and EPAP of 5 to 8 cm H_2O, titrated to the work of breathing as assessed by patient report, respiratory rate and tidal volume, and accessory muscle use. The same concerns regarding the potential effect of excessive IPAP on total lung capacity as discussed above exist in these patients as well. Deterioration (and need for endotracheal intubation) is best assessed clinically; ABGs may be misleading. Although worsening hypercapnia typically indicates treatment failure, patients differ markedly in tolerance of hypercapnia. Some with $PaCO_2$ > 100 mm Hg are alert and conversant on NIPPV, whereas others require intubation at much lower levels.

Conventional mechanical ventilation in ACRF aims to minimize dynamic hyperinflation and counter the adverse effects of intrinsic PEEP while resting the fatigued respiratory muscles. Initial recommended settings are assist-control (A/C) with a tidal volume of 5 to 7 mL/kg and a respiratory rate of 20 to 24/min, although some patients need lower initial rates to limit intrinsic PEEP. This intrinsic PEEP represents an inspiratory threshold load that must be overcome by the patient to trigger the ventilator, further increasing the work of breathing and preventing full rest on the ventilator. To counterbalance the effect of intrinsic PEEP, external PEEP should be applied to a level ≤ 85% of intrinsic PEEP (typical setting 5 to 10 cm H_2O). This application decreases the inspiratory work of breathing to maximize the time for expiration without increasing dynamic hyperinflation. High inspiratory flow rates should be used to maximize the time for expiration. These settings minimize the risk of alkalemia that follows overly vigorous initial ventilation. Hypotension may also occur immediately after intubation (see p. 2283).

Most patients require full ventilatory support for 24 to 48 h before spontaneous breathing trials are considered. It has not been determined whether this duration of treatment is needed to rest the respiratory muscles or to allow hyperinflation to diminish, thereby increasing respiratory muscle strength. The patient often sleeps heavily during this time and, in contrast to patients with asthma, typically requires little sedation. Adequate rest is often not achieved unless sufficient attention is paid to ongoing patient effort. This effort may manifest as accessory muscle use, inappropriately low airway pressures at the onset or throughout inspiration, or frequent failures to trigger the ventilator, indicating high intrinsic PEEP, weakness, or both.

Other Types of Respiratory Failure

Perioperative respiratory failure is usually caused by atelectasis. Effective means of preventing or treating atelectasis include incentive spirometry, ensuring adequate analgesia for chest and abdominal incisions, upright positioning, and early mobilization. Atelectasis caused by abdominal distention should be alleviated according to the cause (eg, nasogastric suction for excessive intraluminal air, paracentesis to evacuate tense ascites).

Hypoperfusion, regardless of cause, may result in respiratory failure through inadequate delivery of O_2 to respiratory muscles coupled with excess respiratory muscle load (eg, acidosis, sepsis). Mechanical ventilation is useful for diverting blood flow from overworked respiratory muscles to critical organs such as the brain, kidney, and gut.

Liberation From Mechanical Ventilation

The discontinuation of ventilatory support is best achieved not by gradually reducing the level of ventilatory support (weaning) but by systematically identifying and eliminating the precipitants of respiratory failure. Once this goal has been achieved, the ventilator is no longer necessary. However, if precipitants are still present or recovery is incomplete, reducing needed ventilatory support is more likely to delay recovery. It is now clear that daily spontaneous breathing trials on a T-piece reduce the duration of mechanical ventilation compared with gradual reduction of the respiratory rate using synchronized intermittent mandatory ventilation and, in some studies, compared with pressure support trials.

Once the patient is no longer in shock, has an adequate arterial saturation on a fractional inspired O_2 (FIO_2) ≤ 0.5 with a positive end-expiratory pressure (PEEP) ≤ 7.5 cm H_2O and does not have an obviously unsustainable respiratory load (eg, minute ventilation > 20 L/min), a daily spontaneous breathing trial is done using a T-piece or continuous positive airway pressure (CPAP) of 5 cm H_2O. Patients capable of sustaining spontaneous breathing generally breathe slowly and deeply, instead of rapidly and shallowly. This observation has been formalized as the rapid shallow breathing (RSB) index, determined by dividing the patient's unassisted respiratory rate (in breaths/min) by the tidal volume (in L). A value < 105 suggests that spontaneous breathing is likely to be successful, although a single isolated measurement is not perfectly predictive of success. Recently, the decision of whether to extubate a patient after a spontaneous breathing trial has shifted away from the use of the RSB index and has relied more on clinical assessment during the course of the trial, supplemented by measuring ABGs. Patients who fare well during a brief 1- to 2-h spontaneous breathing trial and who have favorable ABGs are good candidates for extubation. The decision to extubate is a separate one from the decision to stop ventilatory support and requires evaluation of the patient's mentation and airway protective reflexes, as well as the patency of the airway.

Although sedatives and opioids are essential for ensuring comfort, rest, and synchrony with the ventilator, their use may prolong mechanical ventilation. Such drugs may accumulate and cause protracted sedation, frustrating attempts to do spontaneous breathing trials even when the cause of respiratory failure has been corrected. The level of sedation should be continually assessed, and progressive sedative withdrawal should be begun as soon as possible. Formal protocols can be used, or simple daily interruption can be carried out. The infusion is stopped until the patient is either awake and following commands or needs re-sedation for agitation, breathing asynchronously with the ventilator, or other physiologic derangements. If sedation is still needed, it is restarted at half the previous dose and titrated as necessary. Several studies have shown that the mean duration of mechanical ventilation is reduced in institutions that use either daily "sedation vacations" or other sedation protocols, as well as daily spontaneous breathing trials.

Chapter 226. Shock and Fluid Resuscitation

Introduction

(See also Ch. 227.)

The fundamental defect in shock is reduced perfusion of vital tissues. Definitive treatment restores adequate tissue perfusion, usually by giving IV fluids.

Shock

Shock is a state of organ hypoperfusion with resultant cellular dysfunction and death. Mechanisms may involve decreased circulating volume, decreased cardiac output, and vasodilation, sometimes with shunting of blood to bypass capillary exchange beds. Symptoms include altered mental status, tachycardia, hypotension, and oliguria. Diagnosis is clinical, including BP measurement. Treatment is with IV fluids, correction of the underlying disorder, and sometimes vasopressors.

Pathophysiology

The fundamental defect in shock is reduced perfusion of vital tissues. Once perfusion declines so that O_2 is inadequate for aerobic metabolism, cells shift to anaerobic metabolism with increased production of CO_2 and accumulation of lactic acid. Cellular function declines, and if shock persists, irreversible cell damage and death occur.

During shock, both the inflammatory and clotting cascades may be triggered in areas of hypoperfusion. Hypoxic vascular endothelial cells activate WBCs, which bind to the endothelium and release directly damaging substances (eg, reactive O_2 species, proteolytic enzymes) and inflammatory mediators (eg, cytokines, leukotrienes, tumor necrosis factor [TNF]). Some of these mediators bind to cell surface receptors and activate nuclear factor kappa B (NFκB), which leads to production of additional cytokines and nitric oxide (NO), a potent vasodilator. Septic shock (see p. 2299) may be more proinflammatory than other forms because of the actions of bacterial toxins, especially endotoxin.

Vasodilation of capacitance vessels leads to pooling of blood and hypotension because of "relative" hypovolemia (ie, too much volume to be filled by the existing amount of blood). Localized vasodilation may shunt blood past the capillary exchange beds, causing focal hypoperfusion despite normal cardiac output and BP. Additionally, excess NO is converted to peroxynitrite, a free radical that damages mitochondria and decreases ATP production.

Blood flow to microvessels including capillaries is reduced even though large-vessel blood flow is preserved in settings of septic shock. Mechanical microvascular obstruction may, at least in part, account for such limiting of substrate delivery. Leukocytes and platelets adhere to the endothelium, and the clotting system is activated with fibrin deposition.

Multiple mediators, along with endothelial cell dysfunction, markedly increase microvascular permeability, allowing fluid and sometimes plasma proteins to escape into the interstitial space. In the GI tract, increased permeability possibly allows translocation of the enteric bacteria from the lumen to the bloodstream, potentially leading to sepsis or metastatic infection.

Neutrophil apoptosis may be inhibited, enhancing the release of inflammatory mediators. In other cells, apoptosis may be augmented, increasing cell death and thus worsening organ function.

BP is not always low in the early stages of shock (although hypotension eventually occurs if shock is not reversed). Similarly, not all patients with "low" BP have shock. The degree and consequences of hypotension vary with the adequacy of physiologic compensation and the patient's underlying diseases. Thus, a modest degree of hypotension that is well tolerated by a young, relatively healthy person might result in severe cerebral, cardiac, or renal dysfunction in a patient with significant arteriosclerosis.

Compensation: Initially, when O_2 delivery (DO_2) is decreased, tissues compensate by extracting a greater percentage of delivered O_2. Current guidelines provide for interventions that will maintain mixed-venous O_2 saturation above 30%. Additionally, low arterial pressure triggers an adrenergic response with sympathetic-mediated vasoconstriction and often increased heart rate. Initially, vasoconstriction is selective, shunting blood to the heart and brain. Circulating β-adrenergic amines (epinephrine, norepinephrine) also increase cardiac contractility and trigger release of corticosteroids from the adrenal gland, renin from the kidney, and glucose from the liver. Increased glucose may overwhelm ailing mitochondria, causing further lactate production.

Reperfusion: Reperfusion of ischemic cells can cause further injury. As substrate is reintroduced, neutrophil activity may increase, increasing production of damaging superoxide and hydroxyl radicals. After blood flow is restored, inflammatory mediators may be circulated to other organs.

Multiple organ dysfunction syndrome (MODS): The combination of direct and reperfusion injury may cause MODS—the progressive dysfunction of ≥ 2 organs consequent to life-threatening illness or injury. MODS can follow any type of shock but is most common when infection is involved; organ failure is one of the defining features of septic shock (see p. 2299). MODS also occurs in > 10% of patients with severe traumatic injury and is the primary cause of death in those surviving > 24 h.

Any organ system can be affected, but the most frequent target organ is the lung, in which increased membrane permeability leads to flooding of alveoli due to capillary leaks. Progressive hypoxia may be increasingly resistant to supplemental O_2 therapy. This condition is termed acute lung injury or, if severe, acute respiratory distress syndrome (ARDS—see p. 2284).

The kidneys are injured when renal perfusion is critically reduced, leading to acute tubular necrosis and renal insufficiency manifested by oliguria and progressive rise in serum creatinine.

In the heart, reduced coronary perfusion and mediators (including TNF and IL-1) may depress contractility, worsen myocardial compliance, and down-regulate β-receptors. These factors decrease cardiac output, further worsening both myocardial and systemic perfusion and causing a vicious circle often culminating in death.

In the GI tract, ileus and submucosal hemorrhage can develop. Liver hypoperfusion can cause focal or extensive hepatocellular necrosis, transaminase elevation, and decreased production of clotting factors.

Etiology and Classification

There are several mechanisms of organ hypoperfusion and shock. Shock may be due to a low circulating volume (hypovolemic shock), vasodilation (distributive shock), a primary decrease in cardiac output (both cardiogenic and obstructive shock), or a combination.

Hypovolemic shock: Hypovolemic shock is caused by a critical decrease in intravascular volume. Diminished venous return (preload) results in decreased ventricular filling and reduced stroke volume. Unless compensated for by increased heart rate, cardiac output decreases.

A common cause is bleeding (hemorrhagic shock), typically due to trauma, surgical interventions, peptic ulcer, esophageal varices, or aortic aneurysm. Bleeding may be overt (eg, hematemesis, melena) or concealed (eg, ruptured ectopic pregnancy).

Hypovolemic shock may also follow increased losses of body fluids other than blood (see Table 226-1).

Hypovolemic shock may be due to inadequate fluid intake (with or without increased fluid loss). Water may be unavailable, neurologic disability may impair the thirst mechanism, or physical disability may impair access.

[**Table 226-1.** Hypovolemic Shock Caused by Body Fluid Loss]

In hospitalized patients, hypovolemia can be compounded if early signs of circulatory insufficiency are incorrectly ascribed to heart failure and fluids are withheld or diuretics are given.

Distributive shock: Distributive shock results from a relative inadequacy of intravascular volume caused by arterial or venous vasodilation; circulating blood volume is normal. In some cases, cardiac output (and DO_2) is high, but increased blood flow through arteriovenous shunts bypasses capillary beds, causing cellular hypoperfusion (demonstrated by decreased O_2 consumption). In other situations, blood pools in venous capacitance beds and cardiac output falls.

Distributive shock may be caused by anaphylaxis (anaphylactic shock—see p. 1120); bacterial infection with endotoxin release (septic shock—see p. 2299); severe injury to the brain or spinal cord (neurogenic shock); and ingestion of certain drugs or poisons, such as nitrates, opioids, and adrenergic blockers. Anaphylactic shock and septic shock often have a component of hypovolemia as well.

Cardiogenic and obstructive shock: Cardiogenic shock is a relative or absolute reduction in cardiac output due to a primary cardiac disorder. Mechanical factors that interfere with filling or emptying of the heart or great vessels explain obstructive shock. Causes are listed in Table 226-2.

Symptoms and Signs

Lethargy, confusion, and somnolence are common. The hands and feet are pale, cool, clammy, and often cyanotic, as are the earlobes, nose, and nail beds. Capillary filling time is prolonged, and except in distributive shock, the skin appears grayish or dusky and moist. Overt diaphoresis may occur. Peripheral pulses are weak and typically rapid; often, only femoral or carotid pulses are palpable. Tachypnea and hyperventilation may be present. BP tends to be low (< 90 mm Hg systolic) or unobtainable; direct measurement by intra-arterial catheter, if done, often gives higher and more accurate values. Urine output is low.

Distributive shock produces similar symptoms, except the skin may appear warm or flushed, especially during sepsis. The pulse may be bounding rather than weak. In septic shock, fever, usually preceded by chills, is generally present. Some patients with anaphylactic shock have urticaria or wheezing.

Numerous other symptoms (eg, chest pain, dyspnea, abdominal pain) may be due to the underlying disease or secondary organ failure.

[**Table 226-2.** Mechanisms of Cardiogenic and Obstructive Shock]

Diagnosis

Diagnosis is mostly clinical, based on evidence of insufficient tissue perfusion (obtundation, oliguria, peripheral cyanosis) and signs of compensatory mechanisms (tachycardia, tachypnea, diaphoresis). Specific criteria include obtundation, heart rate > 100, respiratory rate > 22, hypotension (systolic BP < 90 mm Hg) or a 30-mm Hg fall in baseline BP, and urine output < 0.5 mL/kg/h. Laboratory findings that support the diagnosis include lactate > 3 mmol/L, base deficit < -5 mEq/L, and $PaCO_2$ < 32 mm Hg. However, none of these findings alone is diagnostic, and each is evaluated in the overall clinical context, including physical signs. Recently, measurement of sublingual PCO_2 has been introduced as a noninvasive and rapid measurement of the severity of shock.

Diagnosis of cause: Recognizing the cause of shock is more important than categorizing the type. Often, the cause is obvious or can be recognized quickly by history and physical examination, aided by simple testing.

Chest pain (with or without dyspnea) suggests MI, aortic dissection, or pulmonary embolism. A systolic murmur may indicate ventricular septal rupture or mitral insufficiency due to acute MI. A diastolic murmur

may indicate aortic regurgitation due to aortic dissection involving the aortic root. Cardiac tamponade is suggested by jugular venous distention, muffled heart sounds, and a paradoxical pulse. Pulmonary embolism severe enough to produce shock typically produces decreased O_2 saturation and occurs more often in special settings, including prolonged bed rest and after a surgical procedure. Tests include ECG, troponin I, chest x-ray, ABG measurements, lung scan, helical CT, and echocardiography.

Abdominal or back pain or a tender abdomen suggests pancreatitis, ruptured abdominal aortic aneurysm, peritonitis, and, in women of childbearing age, ruptured ectopic pregnancy. A pulsatile midline mass suggests ruptured abdominal aortic aneurysm. A tender adnexal mass suggests ectopic pregnancy. Testing typically includes abdominal CT (if the patient is unstable, bedside ultrasound can be helpful), CBC, amylase, lipase, and, for women of childbearing age, urine pregnancy test.

Fever, chills, and focal signs of infection suggest septic shock, particularly in immunocompromised patients. Isolated fever, contingent on history and clinical settings, may point to heatstroke. Tests include chest x-ray; urinalysis; CBC; and cultures of wounds, blood, urine, and other relevant body fluids.

In a few patients, the cause is occult. Patients with no focal symptoms or signs indicative of cause should have ECG, cardiac enzymes, chest x-ray, and ABGs. If results of these tests are normal, the most likely causes include drug overdose, occult infection (including toxic shock), and obstructive shock.

Ancillary testing: If not already obtained, ECG, chest x-ray, CBC, serum electrolytes, BUN, creatinine, PT, PTT, liver function tests, and fibrinogen and fibrin split products are done to monitor patient status and serve as a baseline. If the patient's volume status is difficult to determine, monitoring of central venous pressure (CVP) or pulmonary artery occlusion pressure (PAOP) may be useful. CVP < 5 mm Hg (< 7 cm H_2O) or PAOP < 8 mm Hg may indicate hypovolemia, although CVP may be greater in hypovolemic patients with preexisting pulmonary hypertension.

Prognosis and Treatment

Untreated shock is usually fatal. Even with treatment, mortality from cardiogenic shock after MI and from septic shock is high (60 to 65%). Prognosis depends on the cause, preexisting or complicating illness, time between onset and diagnosis, and promptness and adequacy of therapy.

General management: First aid involves keeping the patient warm. Hemorrhage is controlled, airway and ventilation are checked, and respiratory assistance is given if necessary. Nothing is given by mouth, and the patient's head is turned to one side to avoid aspiration if emesis occurs.

Treatment begins simultaneously with evaluation. Supplemental O_2 by face mask is provided. If shock is severe or if ventilation is inadequate, airway intubation with mechanical ventilation is necessary. Two large (16- to 18-gauge) IV catheters are inserted into separate peripheral veins. A central venous line or an intraosseous needle, especially in children, provides an alternative when peripheral veins cannot promptly be accessed (see also p. 2250).

Typically, 1 L (or 20 mL/kg in children) of 0.9% saline is infused over 15 min. In major hemorrhage, Ringer's lactate is commonly used. Unless clinical parameters return to normal, the infusion is repeated. Smaller volumes (eg, 250 to 500 mL) are used for patients with signs of high right-sided pressure (eg, distention of neck veins) or acute MI. A fluid challenge should probably not be done in a patient with signs of pulmonary edema. Further fluid therapy is based on the underlying condition and may require monitoring of CVP or PAOP.

Patients in shock are critically ill and should be admitted to an ICU. Monitoring includes ECG; systolic, diastolic, and mean BP, preferably by intra-arterial catheter; respiratory rate and depth; pulse oximetry; urine flow by indwelling bladder catheter; body temperature; and clinical status, including sensorium (eg, Glasgow Coma Scale—see
Table 174-4 on p. 1661), pulse volume, skin temperature, and color. Measurement of CVP, PAOP, and thermodilution cardiac output using a balloon-tipped pulmonary arterial catheter may be helpful for diagnosis and initial management of patients with shock of uncertain or mixed etiology or with severe

shock, especially when accompanied by oliguria or pulmonary edema. Echocardiography (bedside or transesophageal) is a less invasive alternative. Serial measurements of ABGs, Hct, electrolytes, serum creatinine, and blood lactate are obtained. Sublingual CO_2 measurement (see p. 2247), if available, is a noninvasive monitor of visceral perfusion. A well-designed flow sheet is helpful.

Because tissue hypoperfusion makes intramuscular absorption unreliable, all parenteral drugs are given IV. Opioids generally are avoided because they may cause vasodilation, but severe pain may be treated with morphine 1 to 4 mg IV given over 2 min and repeated q 10 to 15 min if necessary. Although cerebral hypoperfusion may cause anxiety, sedatives or tranquilizers are not routinely given.

After initial resuscitation, specific treatment is directed at the underlying condition. Additional supportive care is guided by the type of shock.

Hemorrhagic shock: In hemorrhagic shock, surgical control of bleeding is primary. Vigorous volume replacement (see also p. 2297) accompanies rather than precedes surgical control. Blood transfusion is used for hemorrhagic shock unresponsive to 2 L (or 40 mL/kg in children) of crystalloid. Failure to respond usually indicates insufficient volume administration or unrecognized ongoing hemorrhage. Vasopressor agents are not indicated for treatment of hemorrhagic shock unless cardiogenic, obstructive, or distributive causes are also present.

Distributive shock: Distributive shock with profound hypotension after initial fluid replacement with 0.9% saline may be treated with inotropic or vasopressor agents (eg, dopamine, norepinephrine—see Table 226-3). Patients with septic shock also receive at least two broad-spectrum antibiotics (see p. 2302). Patients with anaphylactic shock unresponsive to fluid challenge (especially if accompanied by bronchoconstriction) receive epinephrine 0.05 to 0.1 mg IV, followed by epinephrine infusion of 5 mg in 500 mL 5% D/W at 10 mL/h or 0.02 µg/kg/min (see also p. 1121).

Cardiogenic shock: In cardiogenic shock, structural disorders (eg, valvular dysfunction, septal rupture) are repaired surgically. Coronary thrombosis is treated either by percutaneous interventions (angioplasty, stenting), coronary artery bypass surgery, or thrombolysis (see also Ch. 210). Tachydysrhythmia (eg, rapid atrial fibrillation, ventricular tachycardia) is slowed by cardioversion or with drugs. Bradycardia is treated with a transcutaneous or transvenous pacemaker; atropine 0.5 mg IV up to 4 doses q 5 min may be given pending pacemaker placement. Isoproterenol (2 mg/500 mL 5% D/W at 1 to 4 µg/min [0.25 to 1 mL/min]) is occasionally useful if atropine is ineffective, but it is not advised in patients with myocardial ischemia due to coronary artery disease.

Shock after acute MI is treated with volume expansion if PAOP is low or normal; 15 to 18 mm Hg is considered optimal. If a pulmonary artery catheter is not in place, cautious volume infusion (250- to 500-mL bolus of 0.9% saline) may be tried while auscultating the chest frequently for signs of fluid overload. Shock after right ventricular MI usually responds partially to volume expansion; however, vasopressor agents may be needed.

If hypotension is moderate (eg, mean arterial pressure [MAP] 70 to 90 mm Hg), dobutamine infusion may be used to improve cardiac output and reduce left ventricular filling pressure. Tachycardia and arrhythmias occasionally occur during dobutamine administration, particularly at higher doses, necessitating dose reduction. Vasodilators (eg, nitroprusside, nitroglycerin), which increase venous capacitance or lower systemic vascular resistance, reduce the workload on the damaged myocardium and may increase cardiac output in patients without severe hypotension. Combination therapy (eg, dopamine or dobutamine with nitroprusside or nitroglycerin) may be particularly useful but requires close ECG and pulmonary and systemic hemodynamic monitoring.

For more serious hypotension (MAP < 70 mm Hg), norepinephrine or dopamine may be given, with a target systolic pressure of 80 to 90 mm Hg (and not > 110 mm Hg). Intra-aortic balloon counterpulsation is valuable for temporarily reversing shock in patients with acute MI. This procedure should be considered as a bridge to permit cardiac catheterization and coronary angiography before possible surgical intervention in patients with acute MI complicated by ventricular septal rupture or severe acute mitral regurgitation who require vasopressor support for > 30 min.

In obstructive shock, cardiac tamponade requires immediate pericardiocentesis, which can be done at the bedside. Tension pneumothorax should be immediately decompressed with a catheter inserted into the 2nd intercostal space, midclavicular line. Massive pulmonary embolism resulting in shock is treated with thrombolysis or surgical embolectomy.

Intravenous Fluid Resuscitation

Almost all circulatory shock states require large-volume IV fluid replacement, as does severe intravascular volume depletion (eg, due to diarrhea or heatstroke). Intravascular volume deficiency is acutely compensated for by vasoconstriction, followed over hours by migration of fluid from the extravascular compartment to the intravascular compartment, maintaining circulating volume at the expense of total body water. However, this compensation is overwhelmed after major losses. See Ch. 97 for maintenance fluid requirement discussion, and see Ch. 278 for mild dehydration discussion.

Fluids

Choice of resuscitation fluid depends on the cause of the deficit.

Hemorrhage: Loss of RBCs diminishes O_2-carrying capacity. However, the body increases cardiac output to maintain O_2 delivery (DO_2) and increases O_2 extraction. These factors provide a safety margin of about 9 times the resting O_2 requirement. Thus, non-O_2-carrying fluids (eg, crystalloid or colloid solutions) may be used to restore intravascular volume in mild to moderate blood loss.

[**Table 226-3.** Inotropic and Vasoactive Catecholamines]

However, once Hb declines to < 7 g/dL, in the absence of cardiac or cerebral vascular disease, O_2-carrying capacity must be restored by infusion of blood (or in the future by blood substitutes). Patients with coronary or cerebral vascular disease require blood for Hb < 10 g/dL.

Crystalloid solutions for intravascular volume replenishment are typically isotonic (eg, 0.9% saline or Ringer's lactate [RL]). H_2O freely travels outside the vasculature, so as little as 10% of isotonic fluid remains in the intravascular space. With hypotonic fluid (eg, 0.45% saline), even less remains in the vasculature, and thus, this fluid is not used for resuscitation. Both 0.9% saline and RL are equally effective; RL may be preferred in hemorrhagic shock because it somewhat minimizes acidosis. However, the Ca in RL may interfere with concurrently infused drugs and may trigger clotting in transfused blood unless the ratio of blood:RL is > 2:1. For patients with acute brain injury and hemorrhagic shock, 0.9% saline is preferred. Hypertonic saline (7.5%) is also an effective crystalloid; it shifts more volume from the extravascular space and therefore requires lower absolute volume, which has practical advantages in a prehospital setting.

Colloid solutions (eg, hydroxyethyl starch, albumin, dextrans) are also effective for volume replacement during major hemorrhage. Despite theoretical benefits over crystalloid, no differences in survival have been proved. Albumin is the colloid of choice, although it may have a negative inotropic effect. Both dextrans and hydroxyethyl starch may adversely affect coagulation when > 1.5 L is given.

Blood typically is given as packed RBCs, which should be cross-matched, but in an urgent situation, 1 to 2 units of type O Rh-negative blood are an acceptable alternative. When > 1 to 2 units are transfused (eg, in major trauma), blood is warmed to 37°C. Patients receiving > 8 to 10 units may require replacement of clotting factors with infusion of fresh frozen plasma or cryoprecipitate and platelet transfusion (see also p. 1039).

Blood substitutes are O_2-carrying fluids that can be Hb-based or perfluorocarbons. Hb-based fluids may contain free Hb that is liposome-encapsulated or modified (eg, by surface modification or cross-linking with other molecules) to limit renal excretion and toxicity. Because the antigen-bearing RBC membrane is not present, these substances do not require cross-matching. They can also be stored > 1 yr, providing a more stable source than banked blood. Perfluorocarbons are IV carbon-fluorine emulsions that carry large amounts of O_2. However, they have not been proved to increase survival and cannot be

given in amounts sufficient to compensate for critical RBC losses.

Nonhemorrhagic hypovolemia: Isotonic crystalloid solutions are typically given for intravascular repletion during shock and hypovolemia. Colloid solutions are generally not used. Patients with dehydration and adequate circulatory volume typically have a free water deficit, and hypotonic solutions (eg, D5 0.45% saline) are used.

Route and Rate of Fluid Administration

Standard, large (eg, 14- to 16-gauge) peripheral IV catheters are adequate for most fluid resuscitation. With an infusion pump, they typically allow infusion of 1 L of crystalloid in 10 to 15 min and 1 unit of packed RBCs in 20 min. For patients at risk of exsanguination, a large (eg, 8.5 French) central venous catheter provides more rapid infusion rates; a pressure infusion device can infuse 1 unit of packed RBCs in < 5 min.

Patients in shock typically require and tolerate infusion at the maximum rate. Adults are given 1 L of crystalloid (20 mL/kg in children) or, in hemorrhagic shock, 5 to 10 mL/kg of colloid or packed RBCs, and the patient is reassessed. An exception is a patient with cardiogenic shock who typically does not require large volume infusion.

Patients with intravascular volume depletion without shock can receive infusion at a controlled rate, typically 500 mL/h. Children should have fluid deficit calculated (see p. 2807) and replacement given over 24 h (one half in the first 8 h).

End Point and Monitoring

The actual end point of fluid therapy in shock is normalization of DO_2. However, this parameter is not often measured directly. Surrogate end points include clinical indicators of end-organ perfusion and measurements of preload.

Adequate end-organ perfusion is best indicated by urine output of > 0.5 to 1 mL/kg/h. Heart rate, mental status, and capillary refill may be affected by the underlying disease process and are less reliable markers. Because of compensatory vasoconstriction, mean arterial pressure (MAP) is only a rough guideline; organ hypoperfusion may be present despite apparently normal values. An elevated arterial blood lactate level reflects hypoperfusion; however, levels do not decline for several hours after successful resuscitation. Sublingual tissue CO_2 level responds more rapidly (eg, within minutes) and may be a more useful indicator.

Central venous pressure: Because urine output does not provide a minute-to-minute indication, measures of preload may be helpful in guiding fluid resuscitation for critically ill patients. Central venous pressure (CVP) is the mean pressure in the superior vena cava, reflecting right ventricular end-diastolic pressure or preload. Normal CVP ranges from 2 to 7 mm Hg (3 to 9 cm H_2O). A sick or injured patient with a CVP < 3 mm Hg is presumed to be volume depleted and may be given fluids with relative safety. When the CVP is within the normal range, volume depletion cannot be excluded, and the response to 100- to 200-mL fluid boluses should be assessed; a modest increase in CVP in response to fluid generally indicates hypovolemia. An increase of > 3 to 5 mm Hg in response to a 100-mL fluid bolus suggests limited cardiac reserve. A CVP > 12 to 15 mm Hg casts doubt on hypovolemia as the sole etiology of hypoperfusion, and fluid administration risks fluid overload.

Because CVP may be unreliable in assessing volume status or left ventricular function, pulmonary artery catheterization (see p. 2244) may be considered for diagnosis or for more precise titration of fluid therapy if there is no cardiovascular improvement after initial therapy. Care must be taken when interpreting filling pressures in patients during mechanical ventilation, particularly when positive end-expiratory pressure (PEEP) levels exceeding 10 cm H_2O are being used or during respiratory distress when pleural pressures fluctuate widely. Measurements are made at the end of expiration, and the transducer is referenced to atrial zero levels (mid chest) and carefully calibrated.

Traumatic hemorrhagic shock: These patients may require a slightly different approach. Experimental and clinical evidence indicates that internal hemorrhage (eg, due to visceral or vascular laceration or crush) may be worsened by resuscitation to normal or supranormal MAP. Some physicians advocate an MAP of 60 to 80 mm Hg as the resuscitation end point in such patients pending surgical control of bleeding.

After blood loss is controlled, Hct is used to guide the need for further transfusion. A target Hct of 23 to 28% is suggested to minimize the use of blood products. Patients who may have difficulty tolerating moderate anemia (eg, those with coronary or cerebral artery disease) are kept above 30%. A higher Hct does not improve outcome and, by causing increased blood viscosity, may impair perfusion of capillary beds.

Complications

Overly rapid infusion of any type of fluid may precipitate pulmonary edema.

Hemodilution from crystalloid infusion is not of itself injurious, although Hct must be monitored to note whether threshold values for transfusion are met.

RBC transfusion has a low risk of directly transmitting infection, but in critically ill patients, it seems to cause a slightly higher rate of hospital-acquired infection. This risk may be minimized by using blood < 12 days old; such RBCs are more plastic and less likely to cause sludging in the microvasculature. For other complications of massive transfusion, see p. 1040.

Chapter 227. Sepsis and Septic Shock

Introduction

(See also Ch. 226.)

Sepsis, severe sepsis, and septic shock are inflammatory states resulting from the systemic response to bacterial infection. In severe sepsis and septic shock, there is critical reduction in tissue perfusion. Common causes include gram-negative organisms, staphylococci, and meningococci. Symptoms often begin with shaking chills and include fever, hypotension, oliguria, and confusion. Acute failure of multiple organs, including the lungs, kidneys, and liver, can occur. Treatment is aggressive fluid resuscitation, antibiotics, surgical excision of infected or necrotic tissues and drainage of pus, supportive care, and sometimes intensive control of blood glucose and administration of corticosteroids and activated protein C.

A spectrum of severity exists (see Table 227-1).

Sepsis is infection accompanied by an acute inflammatory reaction with systemic manifestations associated with release into the bloodstream of numerous endogenous mediators of inflammation. Acute pancreatitis and major trauma, including burns, may manifest with signs of sepsis. The inflammatory reaction typically manifests with ≥ 2 of the following:

• Temperature > 38°C or < 36°C

• Heart rate > 90 beats/min

• Respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mm Hg

• WBC count > 12,000 cells/μL or < 4,000 cells/μL or > 10% immature forms

However, these criteria are now viewed as suggestive but not sufficiently precise to be diagnostic.

Severe sepsis is sepsis accompanied by signs of failure of at least one organ. Cardiovascular failure is typically manifested by hypotension, respiratory failure by hypoxemia, renal failure by oliguria, and hematologic failure by coagulopathy.

Septic shock is severe sepsis with organ hypoperfusion and hypotension that are poorly responsive to initial fluid resuscitation.

Etiology

Most cases of septic shock are caused by hospital-acquired gram-negative bacilli or gram-positive cocci and often occur in immunocompromised patients and patients with chronic and debilitating diseases. Rarely, it is caused by *Candida* or other fungi. A unique form of shock caused by staphylococcal and streptococcal toxins is called toxic shock (see p. 1235).

Septic shock occurs more often in neonates (see p. 2832), patients > 35 yr, and pregnant women. Predisposing factors include diabetes mellitus; cirrhosis; leukopenia, especially that associated with cancer or treatment with cytotoxic drugs; invasive devices, including endotracheal tubes, vascular or urinary catheters, drainage tubes, and other foreign materials; and prior treatment with antibiotics or corticosteroids. Common causative sites of infection include the lungs and the urinary, biliary, and GI tracts.

Pathophysiology

The pathogenesis of septic shock is not completely understood. An inflammatory stimulus (eg, a bacterial

toxin) triggers production of proinflammatory mediators, including tumor necrosis factor and IL-1. These cytokines cause neutrophil-endothelial cell adhesion, activate the clotting mechanism, and generate microthrombi. They also release numerous other mediators, including leukotrienes, lipoxygenase, histamine, bradykinin, serotonin, and IL-2. They are opposed by anti-inflammatory mediators, such as IL-4 and IL-10, resulting in a negative feedback mechanism.

Initially, arteries and arterioles dilate, decreasing peripheral arterial resistance; cardiac output typically increases. This stage has been referred to as warm shock. Later, cardiac output may decrease, BP falls (with or without an increase in peripheral resistance), and typical features of shock appear.

Even in the stage of increased cardiac output, vasoactive mediators cause blood flow to bypass capillary exchange vessels (a distributive defect). Poor capillary flow from this shunting along with capillary obstruction by microthrombi decreases delivery of O_2 and impairs removal of CO_2 and waste products. Decreased perfusion causes dysfunction and sometimes failure of one or more organs, including the kidneys, lungs, liver, brain, and heart.

Coagulopathy may develop because of intravascular coagulation with consumption of major clotting factors, excessive fibrinolysis in reaction thereto, and more often a combination of both.

Symptoms and Signs

With sepsis, the patient typically has fever, tachycardia, and tachypnea; BP remains

[**Table 227-1.** Sepsis in the United States]

normal. Other signs of the causative infection are generally present. As severe sepsis or septic shock develops, the first sign may be confusion or decreased alertness. BP generally falls, yet the skin is paradoxically warm. Oliguria (< 0.5 mL/kg/h) is likely to be present. Later, extremities become cool and pale, with peripheral cyanosis and mottling. Organ failure causes additional symptoms and signs specific to the organ involved.

Diagnosis

Sepsis is suspected when a patient with a known infection develops systemic signs of inflammation or organ dysfunction. Similarly, a patient with otherwise unexplained signs of systemic inflammation should be evaluated for infection by history, physical examination, and tests, including urinalysis and urine culture (particularly in patients who have indwelling catheters), serial blood cultures, and cultures of other suspect body fluids. Blood levels of procalcitonin and C-reactive protein are elevated in severe sepsis and may facilitate diagnosis, but they are not specific. Ultimately, diagnosis is clinical.

Other causes of shock (eg, hypovolemia, MI) should be sought via history, physical examination, ECG, and serum cardiac markers. Even without MI, hypoperfusion may result in ECG findings of ischemia including non-specific ST-T wave abnormalities, T-wave inversions, and supraventricular and ventricular arrhythmias.

CBC, ABGs, chest x-ray, serum electrolytes, lactate levels or sublingual PCO_2, and liver function are monitored. At the onset of septic shock, the WBC count may initially decrease to < 4000/µL, and PMNs may be as low as 20%. However, this situation reverses within 1 to 4 h, and a significant increase in both the total WBC count to > 15,000/µL and PMNs to > 80% (with predominantly juvenile forms) usually occurs. A sharp decrease in platelet count to ≤ 50,000/µL is often present early.

Hyperventilation with respiratory alkalosis (low $PaCO_2$ and increased arterial pH) occurs early, in part as compensation for lactic acidemia. Serum HCO_3 is usually low, and serum and blood lactate levels increase. As shock progresses, metabolic acidosis worsens, and blood pH decreases. Early respiratory failure leads to hypoxemia with PaO_2 < 70 mm Hg. Diffuse infiltrates may appear on the chest x-ray (see Respiratory Arrest on p. 2269). BUN and creatinine usually increase progressively as a result of renal insufficiency. Bilirubin and transaminases may rise, although overt hepatic failure is uncommon.

Up to 50% of patients with severe sepsis develop relative adrenal insufficiency (ie, normal or slightly elevated baseline cortisol levels that do not increase significantly in response to further stress or exogenous ACTH). Adrenal function may be tested by measuring serum cortisol at 8 AM; a level < 5 mg/dL is inadequate. Alternatively, cortisol can be measured before and after injection of 250 µg of synthetic ACTH; a rise of < 9 µg/dL is considered insufficient. However, most physicians simply give replacement doses of corticosteroids without testing.

Hemodynamic measurements with a central venous or pulmonary artery catheter can be used when the specific type of shock is unclear or when large fluid volumes (eg, > 4 to 5 L 0.9% saline over 6 to 8 h) are needed. Unlike in hypovolemic shock, cardiac output in septic shock is more likely to be normal or increased, and peripheral resistance is decreased. Neither central venous pressure (CVP) nor pulmonary artery occlusive pressure (PAOP) is likely to be abnormal, unlike in hypovolemic, obstructive, or cardiogenic shock (see p. 2294). Echocardiography (including transesophageal echocardiography) is a useful alternative for evaluating cardiac performance.

Prognosis

Overall mortality in patients with septic shock is decreasing and now averages 40% (range 10 to 90%, depending on patient characteristics). Poor outcomes often follow failure to institute early aggressive therapy (eg, within 6 h of suspected diagnosis). Once severe lactic acidosis with decompensated metabolic acidosis becomes established, especially in conjunction with multiorgan failure, septic shock is likely to be irreversible and fatal.

Treatment

- Fluid resuscitation with 0.9% normal saline
- O_2
- Broad-spectrum antibiotics (modified by culture results)
- Drainage of abscesses and excision of necrotic tissue
- Normalization of blood glucose levels
- Replacement-dose corticosteroids

Patients with septic shock should be treated in an ICU. The following should be monitored frequently (see also p. 2244): systemic pressure; CVP, PAOP, or both; pulse oximetry; ABGs; blood glucose, lactate, and electrolyte levels; renal function, and possibly sublingual PCO_2. Urine output, a good indicator of renal perfusion, should be measured, usually with an indwelling catheter.

Fluid resuscitation with 0.9% saline should be given until CVP reaches 8 mm Hg (10 cm H_2O) or PAOP reaches 12 to 15 mm Hg. Oliguria with hypotension is not a contraindication to vigorous fluid resuscitation. The quantity of fluid required often far exceeds the normal blood volume and may reach 10 L over 4 to 12 h. PAOP or echocardiography can identify limitations in left ventricular function and incipient pulmonary edema due to fluid overload.

If a patient with septic shock remains hypotensive after CVP or PAOP has been raised to target levels, dopamine may be given to increase mean BP to at least 60 mm Hg. If dopamine dose exceeds 20 µg/kg/min, another vasopressor, typically norepinephrine, may be added. However, vasoconstriction caused by higher doses of dopamine and norepinephrine poses risks of organ hypoperfusion and acidosis, and these drugs have not been shown to improve survival.

O_2 is given by mask or nasal prongs. Tracheal intubation and mechanical ventilation may be needed subsequently for respiratory failure (see p. 2279).

Parenteral antibiotics should be given after specimens of blood, body fluids, and wound sites have been taken for Gram stain and culture. Very prompt empiric therapy, started immediately after suspecting sepsis, is essential and may be lifesaving. Antibiotic selection requires an educated guess based on the suspected source, clinical setting, knowledge or suspicion of causative organisms and of sensitivity patterns common to that specific inpatient unit, and previous culture results.

One regimen for septic shock of unknown cause is gentamicin or tobramycin 5.1 mg/kg IV once/day plus a 3rd-generation cephalosporin (cefotaxime 2 g q 6 to 8 h or ceftriaxone 2 g once/day or, if *Pseudomonas* is suspected, ceftazidime 2 g IV q 8 h). Alternatively, ceftazidime plus a fluoroquinolone (eg, ciprofloxacin) may be used. Monotherapy with maximal therapeutic doses of ceftazidime (2 g IV q 8 h) or imipenem (1 g IV q 6 h) may be effective but is not recommended.

Vancomycin must be added if resistant staphylococci or enterococci are suspected. If there is an abdominal source, a drug effective against anaerobes (eg, metronidazole) should be included. When culture and sensitivity results are available, the antibiotic regimen is changed accordingly. Antibiotics are continued for at least 5 days after shock resolves and evidence of infection subsides.

Abscesses must be drained, and necrotic tissues (eg, infarcted bowel, gangrenous gall-bladder, abscessed uterus) must be surgically excised. The patient's condition will continue to deteriorate despite antibiotic therapy unless septic foci are eliminated.

Normalization of blood glucose improves outcome in critically ill patients, even those not known to be diabetic. A continuous IV insulin infusion (crystalline zinc 1 to 4 U/h) is titrated to maintain glucose between 80 to 110 mg/dL (4.4 to 6.1 mmol/L). This approach necessitates frequent (eg, q 1 to 4 h) glucose measurement.

Corticosteroid therapy seems beneficial. Treatment is with replacement doses rather than pharmacologic doses. One regimen consists of hydrocortisone 50 mg IV q 6 h (or 100 mg q 8 h) plus fludrocortisone 50 µg po once/day during hemodynamic instability and for 3 days thereafter.

Activated protein C (drotrecogin alfa), a recombinant drug with fibrinolytic and anti-inflammatory activity, seems beneficial for severe sepsis and septic shock if it is begun early; benefit has been shown only in patients with significant risk of death as defined by an APACHE II score of > 25 (see Table 222-4 on p. 2248). Dosage is 24 µg/kg/h by continuous IV infusion for 96 h. Bleeding is the most common complication; thus, contraindications include hemorrhagic stroke within 3 mo, spinal or intracranial surgery within 2 mo, acute trauma with a risk of bleeding, and intracranial neoplasm. Risk-benefit assessment is required in other patients with increased risk of serious bleeding (eg, with thrombocytopenia or recent GI bleeding, receiving concurrent heparin, or with recent aspirin or other anticoagulant use).

Other emerging therapies for severe sepsis include cooling for hyperthermia and early treatment of renal failure (eg, with continuous venovenous hemofiltration).

Trials of monoclonal antibodies to the lipid A fraction of endotoxin, antileukotrienes, and antibodies to tumor necrosis factor have been unsuccessful.