Use of vasopressors and inotropes

INTRODUCTION — Vasopressors are a powerful class of drugs that induce vasoconstriction and thereby elevate mean arterial pressure (MAP). Vasopressors differ from inotropes, which increase cardiac contractility; however, many drugs have both vasopressor and inotropic effects. Although many vasopressors have been used since the 1940s, few controlled clinical trials have directly compared these agents or documented improved outcomes due to their use. Thus, the manner in which these agents are commonly used largely reflects expert opinion, animal data, and the use of surrogate end points such as tissue oxygenation as a proxy for decreased morbidity and mortality.

Basic adrenergic receptor physiology and the principles, complications, and controversies surrounding use of vasopressors and inotropes for treatment of shock are presented here. Issues related to the differential diagnosis of shock and the use of vasopressors in patients with septic shock are discussed separately. (See "General evaluation and differential diagnosis of shock in adults" and see "Management of severe sepsis and septic shock in adults").

RECEPTOR PHYSIOLOGY — The main categories of adrenergic receptors relevant to vasopressor activity are the alpha-1, beta-1, and beta-2 adrenergic receptors, as well as the dopamine receptors.

Alpha adrenergic — Activation of alpha-1 adrenergic receptors, located in vascular walls, induces significant vasoconstriction. Alpha-1 adrenergic receptors are also present in the heart and can increase the duration of contraction without increased chronotropy. However, clinical significance of this phenomenon is unclear.

Beta adrenergic — Beta-1 adrenergic receptors are most common in the heart, and mediate increases in inotropy and chronotropy with minimal vasoconstriction. Stimulation of beta-2 adrenergic receptors in blood vessels induces vasodilation.

Dopamine — Dopamine receptors are present in the renal, splanchnic (mesenteric), coronary, and cerebral vascular beds; stimulation of these receptors leads to vasodilation. A second subtype of dopamine receptors causes vasoconstriction by inducing norepinephrine release.

PRINCIPLES — Hypotension may result from hypovolemia (eg, exsanguination), pump failure (eg, severe medically refractory heart failure or shock complicating myocardial infarction), or a pathologic maldistribution of blood flow (eg, septic shock, anaphylaxis). (See "General evaluation and differential diagnosis of shock in adults" and see "Inotropic agents in heart failure due to systolic dysfunction").

Vasopressors are indicated for a decrease of >30 mmHg from baseline systolic blood pressure, or a mean arterial pressure <60 mmHg when either condition results in end-organ dysfunction due to hypoperfusion. Hypovolemia should be corrected prior to the institution of vasopressor therapy. (See "Treatment of severe hypovolemia or hypovolemic shock in adults").

The rational use of vasopressors and inotropes is guided by three fundamental concepts:

- One drug, many receptors — A given drug often has multiple effects because of actions upon more than one receptor. As an example, dobutamine increases cardiac output by beta-1 adrenergic receptor activation; however, it also acts upon
beta-2 adrenergic receptors and thus induces vasodilation and can cause hypotension.

- **Dose-response curve** — Many agents have dose-response curves, such that the primary adrenergic receptor subtype activated by the drug is dose-dependent. As an example, dopamine stimulates beta-1 adrenergic receptors at doses of 2 to 10 mcg/kg per minute, and alpha adrenergic receptors when doses exceed 10 mcg/kg per minute.

- **Direct versus reflex actions** — A given agent can affect MAP both by direct actions on adrenergic receptors and by reflex actions triggered by the pharmacologic response. Norepinephrine-induced beta-1 adrenergic stimulation alone normally would cause tachycardia. However, the elevated MAP from norepinephrine's alpha-adrenergic receptor-induced vasoconstriction results in a reflex decrease in heart rate. The net result may be a stable or slightly reduced heart rate when the drug is used.

**PRACTICAL ISSUES** — Use of vasopressors and inotropic agents requires attention to a number of issues:

**Volume resuscitation** — Repletion of adequate intravascular volume, when time permits, is crucial prior to the initiation of vasopressors. As an example, most patients with septic shock require at least 2 liters of intravenous fluid in order for vasopressors to be maximally effective [6]. Vasopressors will be ineffective or only partially effective in the setting of coexistent hypovolemia. Fluids may be withheld in patients with significant pulmonary edema due to the acute respiratory distress syndrome (ARDS) or congestive heart failure (CHF). In patients with a pulmonary artery catheter, pulmonary capillary wedge pressures (PCWP) of 18 to 24 mmHg are recommended for cardiogenic shock [7], and 12 to 14 mmHg for septic or hypovolemic shock [8]. (See "Swan-Ganz catheterization: Interpretation of tracings").

**Selection and titration** — Choice of an initial agent should be based upon the suspected underlying etiology of shock (eg, dobutamine in cases of cardiac failure without significant hypotension). The dose should be titrated up to achieve effective blood pressure or end-organ perfusion as evidenced by such criteria as urine output or mentation. If maximal doses of a first agent are inadequate, then a second drug should be added to the first. In situations where this is ineffective, such as refractory septic shock, anecdotal reports describe adding a third agent, although no controlled trials have demonstrated the utility of this approach.

**Tachyphylaxis** — Responsiveness to these drugs can decrease over time due to tachyphylaxis. Doses must be constantly titrated to adjust for this phenomenon and for changes in the patient's clinical condition [9,10].

**Hemodynamic effects** — MAP is influenced by systemic vascular resistance (SVR) and cardiac output (CO). In situations such as cardiogenic shock, elevating SVR increases afterload and the work of an already failing heart, thus potentially lowering CO. Some authors recommend keeping the SVR approximately 700 to 1000 dynes x sec/cm5 to avoid excessive afterload and to minimize complications from profound vasoconstriction [11]. However, there is no consensus regarding an ideal target cardiac index (CI). Studies that have attempted to maintain a supraphysiologic CI of >4.0 to 4.5 L/minute per m2 have not shown consistent benefit [12,13]. (See "ATS guidelines: Tissue hypoxia: How to detect; how to correct; how to prevent").
Subcutaneous delivery — Critically ill patients often receive subcutaneously injected medications, including heparin and insulin. The bioavailability of these medications can be reduced during treatment with vasopressors due to cutaneous vasoconstriction. This was demonstrated in a study that monitored plasma factor Xa levels in three groups of hospitalized patients following the initiation of prophylactic low molecular weight heparin [14]. Patients who required vasopressor support (dopamine >10 µg/kg per minute, norepinephrine >0.25 µg/kg per minute, or phenylephrine >2 µg/kg per minute) had decreased factor Xa activity when compared with ICU patients who did not require vasopressors or with routine postoperative controls.

The authors suggested that such patients might need higher doses of LMW heparin, or a different mode of administration of the drug, to attain adequate thrombosis prophylaxis. However, the clinical significance of the decrease in plasma factor Xa levels in patients receiving vasopressors was not addressed.

Frequent reevaluation — Critically ill patients may undergo a second hemodynamic insult which necessitates a change in vasopressor or inotrope management. The dosage of a given agent should not simply be increased because of persistent or worsening hypotension without reconsideration of the patient's clinical situation and the appropriateness of the current strategy.

ADRENERGIC AGENTS — Adrenergic agents, such as phenylephrine, norepinephrine, dopamine, and dobutamine, are the most commonly used vasopressor and inotropic drugs in critically ill patients. These agents manifest different receptor selectivity and clinical effects (show table 1).

Phenylephrine — Phenylephrine (Neosynephrine®) has purely alpha-adrenergic agonist activity and therefore results in vasoconstriction with minimal cardiac inotropy or chronotropy. MAP is augmented by raising SVR [15]. The drug is useful in the setting of hypotension with an SVR <700 dynes x sec/cm5 (eg, hyperdynamic sepsis, neurologic disorders, anesthesia-induced hypotension).

Although SVR elevation increases cardiac afterload, most studies document that CO is either maintained or actually increased among patients without preexisting cardiac dysfunction [4,16]. The drug is contraindicated if the SVR is >1200 dynes x sec/cm5.

Norepinephrine — Norepinephrine (Levophed®) acts on both alpha-1 and beta-1 adrenergic receptors, thus producing potent vasoconstriction as well as a less pronounced increase in cardiac output [5]. A reflex bradycardia usually occurs in response to the increased MAP, such that the mild chronotropic effect is canceled out and the heart rate remains unchanged or even decreases slightly.

Norepinephrine is used most commonly to treat septic shock. (See "Management of severe sepsis and septic shock in adults").

Epinephrine — Epinephrine (Adrenalin®) has potent beta-1 adrenergic receptor activity and moderate beta-2 and alpha-1 adrenergic receptor effects. Clinically, low doses of epinephrine increase CO because of the beta-1 adrenergic receptor inotropic and chronotropic effects, while the alpha adrenergic receptor-induced vasoconstriction is often offset by the beta-2 adrenergic receptor vasodilation. The result is an increased CO, with decreased SVR and variable effects on the MAP [3]. Beta-1 adrenergic receptor stimulation may provoke dysrhythmias. The degree of splanchnic vasoconstriction appears to be greater with epinephrine than with equipotent doses of norepinephrine or dopamine in patients with severe shock [17].
However, the alpha-adrenergic receptor effect predominates at higher epinephrine doses, producing increased SVR in addition to an increased CO. Epinephrine is most often used for the treatment of anaphylaxis, as a second line agent in septic shock, and for management of hypotension following coronary artery bypass grafting.

**Ephedrine** — Similar to epinephrine, ephedrine acts primarily on alpha- and beta-adrenergic receptors with less potency. It also has an effect by leading to release of endogenous norepinephrine. Ephedrine is rarely used except in the setting of post-anesthesia-induced hypotension.

**Dopamine** — Dopamine (Intropin®) has a variety of effects depending upon the dose range administered:

- At doses of 1 to 2 mcg/kg per minute, dopamine acts predominantly on dopamine-1 receptors in the renal, mesenteric, cerebral, and coronary beds, resulting in selective vasodilation. Some reports suggest that dopamine increases urine output by augmenting renal blood flow and glomerular filtration rate, and natriuresis by inhibiting aldosterone and renal tubular sodium transport [18-20]. These effects may be blunt by haloperidol and other butyrophenones [20]. However, the clinical significance of these phenomena is unclear, and some patients may develop hypotension at these low doses [21]. (See "Renal actions of dopamine").

- At 5 to 10 mcg/kg per minute, dopamine also stimulates beta-1 adrenergic receptors and increases cardiac output, predominantly by increasing stroke volume with variable effects on heart rate [22]. Doses between 2 and 5 mcg/kg per minute have variable effects on hemodynamics in individual patients: vasodilation is often balanced by increased stroke volume, producing little net effect upon systemic blood pressure. Some mild alpha adrenergic receptor activation increases SVR, and the sum of these effects is an increase in MAP.

- At doses >10 mcg/kg per minute, the predominant effect of dopamine is to stimulate alpha-adrenergic receptors and produce vasoconstriction with an increased SVR [22,23]. However, the overall alpha-adrenergic receptor effect of dopamine is weaker than that of norepinephrine, and the beta-1 adrenergic receptor stimulation of dopamine at doses >2 mcg/kg per minute can result in dose-limiting dysrhythmias.

In practical terms, the dose-dependent effects of dopamine mean that increasing the dose of the drug is akin to switching vasopressors. Conversely, simply increasing the dose of dopamine without being cognizant of the different receptor populations activated can cause untoward results.

The usual dose range for dopamine is 2 to 20 mcg/kg per minute, although doses as high as 130 mcg/kg per minute have been employed [24]. Dopamine is most often used in hypotension due to sepsis or cardiac failure, where it should be started at 2 mcg/kg per minute and then titrated to a desired physiologic effect rather than a predicted pharmacologic range. Such titration is necessary because weight-based administration of dopamine can achieve quite different serum drug concentrations in different individuals [25].

**Dobutamine** — Dobutamine (Dobutrex®) is not a vasopressor but rather is an inotrope that causes vasodilation. Dobutamine's predominant beta-1 adrenergic receptor effect increases inotropy and chronotropy and reduces left ventricular filling pressure. In patients with heart failure this results in a reduction in cardiac sympathetic activity [26]. However, minimal alpha- and beta-2 adrenergic receptor effects result in overall vasodilation, complemented by reflex vasodilation to the
increased CO. The net effect is increased CO, with decreased SVR with or without a small reduction in blood pressure.

**Dobutamine** is most frequently used in severe, medically refractory heart failure and cardiogenic shock and should not be routinely used in sepsis because of the risk of hypotension. Dobutamine does not selectively vasodilate the renal vascular bed, as does **dopamine** at low doses. (See "Inotropic agents in heart failure due to systolic dysfunction").

**Isoproterenol** — **Isoproterenol** (Isuprel®) also is primarily an inotropic and chronotropic agent rather than a vasopressor. It acts upon beta-1 adrenergic receptors and, unlike **dobutamine**, has a prominent chronotropic effect. The drug's high affinity for the beta-2 adrenergic receptor causes vasodilation and a decrease in MAP. Therefore, its utility in hypotensive patients is limited to situations in which hypotension results from bradycardia.

**NONADRENERGIC AGENTS** — A number of agents produce vasoconstriction or inotropy through nonadrenergic mechanisms, including phosphodiesterase inhibitors, and **nitric oxide** synthase inhibitors.

**Vasopressin** — **Vasopressin** is an antidiuretic hormone (ADH) analogue usually used in the management of diabetes insipidus and esophageal variceal bleeding. However, nonrandomized, open label case series have suggested that it also may be useful in the treatment of refractory septic shock, particularly as a second pressor agent [27-34].

Although **vasopressin** is a weak pressor in normal subjects, a small randomized controlled clinical trial found that the addition of vasopressin (infused at a fixed rate of 0.04 U/min) to norepinephrine was more effective in reversing late vasodilatory shock than norepinephrine alone [33]. Similar results were noted when norepinephrine and vasopressin were compared in a blinded study of 23 patients with severe septic shock [34]. The use of vasopressin was associated with a decreased requirement for other vasopressors, higher urine output, and improved creatinine clearance.

**Terlipressin** — The hemodynamic effects of terlipressin, an ADH analogue with a serum half-life of six hours used in the management of variceal hemorrhage, have also been assessed in patients with sepsis [35,36]. In several small open label trials, terlipressin has been reported to improve the hemodynamic profile and decrease (or eliminate) the requirement for catecholamine vasopressors in patients with sepsis [37-40]. However, randomized clinical trials demonstrating a clear benefit are lacking, and rebound hypotension appears to be common following withdrawal. In addition, terlipressin is not available for clinical use in the United States.

The precise role of **vasopressin** and terlipressin for the treatment of vasodilatory shock remains to be defined [41,42]. Potential complications of ADH analogs in this setting include coronary and mesenteric ischemia, hyponatremia, pulmonary vasoconstriction, and skin necrosis from peripheral infusion [43-46].

**PDE inhibitors** — Phosphodiesterase (PDE) inhibitors, such as **amrinone** and **milrinone**, are nonadrenergic drugs with inotropic and vasodilatory actions. In many ways, their effects are similar to those of **dobutamine** but with a lower incidence of dysrhythmias. PDE inhibitors most often are used to treat patients with impaired cardiac function and medically refractory heart failure, but their vasodilatory properties limit their use in hypotensive patients [22]. (See "Inotropic agents in heart failure due to systolic dysfunction").
NOS inhibitors — Nitric oxide overproduction appears to play a major role in vasodilation induced by sepsis. (See "Pathophysiology of sepsis"). Studies of nitric oxide synthase (NOS) inhibitors such as N-monomethyl-L-arginine (L-NMMA) in sepsis demonstrate a dose-dependent increase in SVR [47]. However, CI and HR decrease, even when patients are treated concomitantly with norepinephrine or epinephrine. The increase in SVR tends to be offset by the drop in CI, such that MAP is only minimally augmented. The clinical utility of this class of drugs remains unproven.

COMPLICATIONS — Vasopressors and inotropic agents have the potential to cause a number of significant complications including hypoperfusion, dysrhythmias, myocardial ischemia, local effects, and hyperglycemia. In addition, a number of drug interactions exists.

- Hypoperfusion — Excessive vasoconstriction in response to hypotension and vasopressors can produce inadequate perfusion of the extremities, mesenteric organs, or kidneys. Excessive vasoconstriction with inadequate perfusion, usually with an SVR >1300 dynes x sec/cm5, commonly occurs in the setting of inadequate cardiac output or inadequate volume resuscitation.

  The initial findings are dusky skin changes at the tips of the fingers and/or toes, which may progress to frank necrosis with autoamputation of the digits. Compromise of the renal vascular bed may produce renal insufficiency and oliguria, while patients with underlying peripheral arterial disease may develop acute limb ischemia.

  Inadequate mesenteric perfusion increases the risk of gastritis, shock liver, intestinal ischemia, or translocation of gut flora with resultant bacteremia. Despite these concerns, maintenance of MAP with vasopressors appears more effective in maintaining renal and mesenteric blood flow than allowing the MAP to drop, and maintenance of MAP with vasopressors may be life-saving despite evidence of localized hypoperfusion [15,48].

- Dysrhythmias — Many vasopressors and inotropes exert powerful chronotropic effects via stimulation of beta-1 adrenergic receptors. This increases the risk of sinus tachycardia (most common), atrial fibrillation (potentially with increased A-V conduction and therefore an increased ventricular response), reentrant atrioventricular node tachycardia, or ventricular tachyarrhythmias. Often these dysrhythmias limit the maximal dose and necessitate switching to another agent with less prominent beta-1 effects. Adequate volume loading can minimize the frequency or severity of these dysrhythmias.

- Myocardial ischemia — The chronotropic and inotropic effects of beta-adrenergic receptor stimulation can increase myocardial oxygen consumption. While there is usually coronary vasodilation in response to vasopressors [49], perfusion may still be inadequate to accommodate the increased myocardial oxygen demand. Daily electrocardiograms on patients treated with vasopressors or inotropes may screen for occult ischemia, and excessive tachycardia should be avoided because of impaired diastolic filling of the coronary arteries.

- Local effects — Peripheral extravasation of vasopressors into the surrounding connective tissue can lead to excessive local vasoconstriction with subsequent skin necrosis. To avoid this complication, vasopressors should be administered via a central vein whenever possible. If infiltration occurs, local treatment with phentolamine (5 to 10 mg in 10 mL of normal saline) injected subcutaneously can minimize local vasoconstriction [50].
• Hyperglycemia — Hyperglycemia may occur due to the inhibition of insulin secretion. The magnitude of hyperglycemia generally is minor and is more pronounced with norepinephrine and epinephrine than dopamine [19]. Monitoring of blood glucose while on vasopressors can prevent complications of untreated hyperglycemia.

• Unique drug interactions and contraindications — Several conditions or medications require avoidance of specific agents. For example, patients with pheochromocytoma are at risk of excessive autonomic stimulation from adrenergic vasopressors, dobutamine is contraindicated in the setting of idiopathic hypertrophic subaortic stenosis, and patients receiving monoamine oxidase inhibitors are extremely sensitive to vasopressors, and require much lower doses.

CONTROVERSIES — Several controversies exist regarding the use of vasopressors and inotropic agents in critically ill patients; most stem from the relative paucity of large-scale studies comparing similar patient populations treated with different regimens. The development of clear definitions for the systemic inflammatory response syndrome, sepsis, and septic shock is a step forward toward comparative trials among standardized patient populations. (See "Sepsis and the systemic inflammatory response syndrome: Definitions, epidemiology, and prognosis").

"Renal dose" dopamine — Dopamine selectively increases renal blood flow when administered to normal volunteers at 1 to 3 mcg/kg per minute [51,52]. Animal studies also suggest that low-dose dopamine in the setting of vasopressor-dependent sepsis helps preserve renal blood flow [53]. (See "Renal actions of dopamine"). However, a beneficial effect of low or "renal dose" dopamine is less proven in human patients with sepsis or other critical illness. Critically ill patients who do not have evidence of renal insufficiency or decreased urine output will develop a diuresis in response to dopamine at 2 to 3 mcg/kg per minute, with variable effects on creatinine clearance, but the benefit of this diuresis is questionable [9,21]. The intervention is not entirely benign because hypotension and tachycardia may ensue. One small study demonstrated that the addition of low dose dopamine to patients receiving other vasopressors increases splanchnic blood flow but does not alter other indices of mesenteric perfusion, such as gastric intramucosal pH (pHi) [54]. At present, there are no data to support the routine use of low dose dopamine to prevent or treat acute renal failure or mesenteric ischemia. In general, the most effective means of protecting the kidneys in the setting of septic shock appears to be the maintenance of MAP >60 mmHg while attempting to avoid excessive vasoconstriction (ie, the SVR should not exceed 1300 dynes x sec/cm5) [6,11,55,56].

Optimal dosage — Several studies have suggested improved tissue perfusion when higher doses of norepinephrine (up to 350 mcg/min) are used [11,56]. However, no survival benefit of high-dose norepinephrine has been conclusively proven.

Supranormal cardiac index — Elevation of the cardiac index with inotropic agents to supranormal values (ie, >4.5 L/minute per m2) potentially increases oxygen delivery to peripheral tissues. In theory, increased oxygen delivery may prevent tissue hypoxia and improve outcomes, and initial studies appeared to support this hypothesis [57-59]. However, later larger trials showed that goal-oriented hemodynamic therapy to increase either cardiac index to >4.5 L/min per m2 or oxygen delivery to >600 to 650 mL/min per m2 with volume expansion or dobutamine resulted in either no improvement, or worsened morbidity or mortality.
Therefore, the routine administration of vasopressors or inotropes to improve cardiac output or oxygen delivery to supranormal levels is not advocated. (See "ATS Guidelines: Tissue hypoxia: How to detect; how to correct; how to prevent").

**Choice of agent in septic shock** — No study has demonstrated a survival benefit due to one vasopressor compared to another. Thus, the choice of vasopressor in septic shock must be based on theoretical considerations.

The Surviving Sepsis Campaign recommends norepinephrine or dopamine as the first-choice vasopressor agent [61]. However, phenylephrine, a pure alpha-adrenergic agonist, may be particularly useful when tachycardia or arrhythmias preclude the use of agents with beta-adrenergic activity. (See "Management of severe sepsis and septic shock in adults", section on Vasopressors).

We believe that the most appropriate vasopressor choice depends on whether the patient has hyperdynamic or hypodynamic septic shock:

- **Hyperdynamic shock** — Patients with hyperdynamic septic shock (hypotension, low SVR, and high CI) tend to have warm extremities ("warm sepsis"). Agents with prominent alpha vasoconstrictor effects (eg, norepinephrine and phenylephrine) are most effective in this setting, increasing MAP by increasing the SVR [11-13,62-66]. The published experience with norepinephrine is more extensive than with phenylephrine [15,16,67,68]. Supporting this approach, a double-blind trial randomly assigned 32 patients with hyperdynamic septic shock to receive dopamine (3 to 25 mcg/kg per minute) or norepinephrine (35 to 350 mcg/min) [11]. Patients who received norepinephrine were more likely to achieve an adequate hemodynamic response (31 versus 93 percent). Also, more than 90 percent of the dopamine failures responded to norepinephrine.

- **Hypodynamic shock** — Patients with hypodynamic septic shock (hypotension, low SVR, and low CI) manifest hypoperfusion of the extremities ("cold sepsis"). Dopamine may be preferable in patients with hypodynamic sepsis because it can increase the MAP with minimal increase of the SVR. As a result, myocardial oxygen consumption is minimized [62]. Given the potential for dopamine to fail as a single agent, however, one must be prepared to rapidly add or substitute a second agent such as norepinephrine.

Of concern, retrospective analysis of data collected from 462 patients with septic shock during a prospective cohort study found a higher ICU mortality among the patients who received dopamine (odds ratio 2.05, 95% CI 1.25-3.37) [69]. However, the study was severely limited by its retrospective analysis and its design, which permitted most patients to receive multiple vasoactive agents and many to receive dopamine only in "renal" dosing. These observational data need to be confirmed by a controlled trials before a change of clinical practice is warranted.

Epinephrine is not routinely used as an initial, single agent in septic shock because it has been shown to impair splanchnic blood flow and tissue perfusion [70,71]. Although the addition of dobutamine might blunt these effects, epinephrine remains a third-line agent [72].

**SUMMARY AND RECOMMENDATIONS**

- Vasopressors are a powerful class of drugs that induce vasoconstriction and elevate mean arterial pressure. (See "Introduction" above).
Alpha-1, beta-1, and beta-2 adrenergic receptors induce vasoconstriction, inotropy plus chronotropy, and vasodilation, respectively. One subtype of dopamine receptor induces norepinephrine release with subsequent vasoconstriction, although many dopamine receptors induce vasodilation. (See "Receptor physiology" above).

Vaspressors are indicated for a mean arterial pressure <60 mmHg, or a decrease of systolic blood pressure that exceeds 30 mmHg from baseline, when either condition results in end-organ dysfunction due to hypoperfusion. (See "Principles" above).

We recommend that hypovolemia be corrected prior to the institution of vasopressor therapy for maximum efficacy. Patients should be reevaluated frequently once vasopressor therapy has been initiated. Common issues that arise include tachyphylaxis, which may require dose titration, and additional hemodynamic insults, which should be recognized and managed. (See "Practical Issues" above).

We suggest norepinephrine or phenylephrine as the first-line agent for patients with hyperdynamic septic shock. Vasopressin may be of benefit if these agents are inadequate. We suggest dopamine as the first-line agent for patients with hypodynamic septic shock; however, patients should be closely monitored for lack of response and the need for a second agent. Epinephrine is the preferred agent for most patients with anaphylactic shock and dopamine is the preferred agent for patients with cardiogenic shock. (See "Adrenergic Agents" above, see "Nonadrenergic agents" above, and see "Choice of agent in septic shock" above).

Complications of vasopressor therapy include hypoperfusion (particularly affecting the extremities, mesentery or kidneys), dysrhythmias, myocardial ischemia, peripheral extravasation with skin necrosis, and hyperglycemia. (See "Complications" above).

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