hydroxyethyl groups (0.5, 0.62, 0.7). Thus the first-generation high-molecular-weight HES Hetastarch has a concentration of 6%, a mean molecular weight of 450 kDa and a molar substitution of 0.7, whereas Elohaes, for example, has a mean molecular weight of 200 kDa and a molar substitution of 0.62. The half-life of these HES solutions is between 12 and 24 hours, whilst that of the low-molecular-weight solutions (e.g. Pentaspan) is 4–6 hours. Elimination of HES occurs primarily via the kidneys following hydrolysis by amylase.

HES are stored in the reticuloendothelial system, apparently without causing functional impairment, but skin deposits have been associated with persistent pruritus (Morgan and Berridge, 2000). This pruritus can be generalized or localized, can have a delayed onset of up to several weeks and may be precipitated by warmth or mechanical irritation. It is frequently persistent, lasting months or even years, and is usually refractory to treatment. HES, especially the higher-molecular-weight fractions, reduce factor VIII activity and inhibit platelet aggregation; although these anticoagulant properties are rarely implicated in clinical bleeding, many therefore recommend limiting the volume of HES administered. Preparations with a low molecular weight and low degree of substitution may be safer in this regard. Finally, there is some evidence from animal models to suggest that HES are more effective in avoiding or reducing increased capillary permeability (‘plugging the capillaries’) than other preparations. On the other hand in a recent study of patients with severe sepsis or septic shock the use of Elohaes as opposed to gelatin was an independent risk factor for the development of acute renal failure, although the mechanism is unknown (Schortgen et al., 2001). Moreover in a recent randomised controlled trial the use of a low molecular weight starch to resuscitate patients with severe sepsis was associated with a higher rate of acute renal failure and renal replacement therapy than was Ringer’s lactate (Brunkhorst et al., 2008). In patients undergoing abdominal aortic aneurysm surgery, perioperative lung function was better in those receiving HES compared to those given Gelofusine (Rittoo et al., 2004). Anaphylactic reactions are less common than with the gelatins.

**Inotropic and vasoactive agents**

If the signs of shock persist despite adequate volume replacement, and perfusion of vital organs is jeopardized, inotropic or vasoactive agents may be administered to improve cardiac output and blood pressure. Vasopressor therapy may also be required to maintain perfusion in those with life-threatening hypotension, even when volume replacement is incomplete. It is also important at this stage to identify and if possible correct any of the various associated abnormalities that can impair cardiac performance and vascular responsiveness. These include:

- hypoxaemia;
- hypocalcaemia;
- the effects of some drugs (e.g. ß-blockers, angiotensin-converting enzyme (ACE) inhibitors, antiarrhythmics and sedatives).

**Correction of metabolic acidosis**

Conventionally, extreme acidosis is said to depress myocardial contractility and limit the response to vasopressor agents, although there is little evidence to support this contention. Moreover, attempted correction of acidosis with intravenous sodium bicarbonate may be detrimental. Additional carbon dioxide is generated and, as carbon dioxide but not bicarbonate readily diffuses across the cell membrane, intracellular and, in some cases, extracellular, pH may be paradoxically further reduced. Other potential disadvantages of bicarbonate therapy include sodium overload, hyperosmolality, a left shift of the oxyhaemoglobin dissociation curve and hypokalaemia. Also ionized calcium levels may be reduced and, in combination with the fall in intracellular pH, may contribute to impaired myocardial performance.

In a prospective, randomized, controlled, cross-over clinical study both sodium bicarbonate and sodium chloride produced slight increases in PAOP and cardiac output, while MAP was unchanged. Sodium bicarbonate significantly increased pH and plasma bicarbonate but, unlike sodium chloride, decreased ionized calcium and increased both $P_{CO_2}$ and end-tidal carbon dioxide. The response to infused catecholamines was unaffected (Cooper et al., 1990). In general, therefore, treatment of lactic acidosis should concentrate on correcting the cause. In the absence of hard data, some believe that acidosis may be most safely controlled by hyperventilation; others suggest that administration of bicarbonate may be indicated as a temporizing measure, and to provide a margin of safety, in those with severe persistent metabolic acidosis ($pH < 7.15$). Bicarbonate therapy is still considered to be useful in renal tubular acidosis and in acidosis due to gastrointestinal losses of bicarbonate.

**Choice of inotropic/vasoactive agent**

The rational selection of an appropriate pressor agent depends on a thorough understanding of the cardiovascular effects of the available drugs (Table 5.8), combined with an accurate assessment of the haemodynamic disturbance. The effects of a particular agent in an individual patient are unpredictable and the response must therefore be closely monitored so that the regimen can be altered appropriately if necessary. In many cases this requires measurement of cardiac output, monitoring of venous oxygen saturation and calculation of derived variables (see Chapter 4). In some patients, inodilators are administered to redistribute blood flow (e.g. dopexamine to improve splanchnic perfusion) and, in others, inotropic support can be usefully combined with the administration of a vasodilator (see below). All inotropic agents should be given via a large central vein. Although it is recognized that ß-agonists have anti-inflammatory properties, mediated by reduced degradation of NFκB and increased intracellular concentrations of cyclic adenosine monophosphate, the clinical importance of the immune-modulating activities of adrenergic agents remains uncertain.
ADRENALINE (EPINEPHRINE)

Adrenaline stimulates both α- and β-receptors but, at low doses, β effects seem to predominate. This produces a tachycardia with an increase in stroke volume and cardiac index; peripheral resistance may fall. As the dose is increased, α-mediated vasoconstriction develops. If this is associated with an increase in perfusion pressure, urine output may improve.

Particularly at higher doses and in severe septic shock, however, adrenaline can cause excessive vasoconstriction, with potentially worrying reductions in splanchnic flow and associated falls in gastric mucosal pH, indicative of gut mucosal ischaemia (De Backer et al., 2003; Levy et al., 1997a; Meier-Hellmann et al., 1997). Renal blood flow may fall with adrenaline and prolonged high-dose administration can cause peripheral gangrene. Adrenaline may also precipitate tachyarrhythmias. Lactic acidosis is a common complication of adrenaline administration (Day et al., 1996) and is probably explained by β₂-mediated accelerated glycolysis, often combined with other causes of increased lactate production and, in many cases, exacerbated by impaired lactate clearance (see above). The prognostic significance of adrenaline-induced lactic acidosis is unclear, but this phenomenon emphasizes the limitations of using blood lactate levels as a guide to tissue hypoxia in shock, especially in those receiving adrenaline. In an experimental septic shock model adrenaline administration was associated with dose-related reductions in cardiac index, ejection fraction and pH, as well as increases in systemic vascular resistance and creatinine. Adrenaline also adversely affected systemic perfusion, organ function and survival when compared to noradrenaline and vasopressin (Minneci et al., 2004b).

Despite these disadvantages, adrenaline can be a useful agent in patients with refractory hypotension. It is very potent and may prove successful when other agents have failed, particularly following cardiac surgery, perhaps because it stimulates myocardial α-receptors. Adrenaline is still pre-

### Table 5.8 Adrenergic agents

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Action</th>
<th>Dose dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline (epinephrine)</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Low-dose</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Moderate-dose</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>High-dose</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Noradrenaline (norepinephrine)</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Isoprenaline</td>
<td></td>
<td>+++</td>
</tr>
<tr>
<td>Dopamine</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Low-dose</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Moderate-dose</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>High-dose</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Dopexamine</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Dobutamine</td>
<td></td>
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</tr>
</tbody>
</table>

Adrenaline stimulates both α- and β-receptors but, at low doses, β effects seem to predominate. This produces a tachycardia with an increase in stroke volume and cardiac index; peripheral resistance may fall. As the dose is increased, α-mediated vasoconstriction develops. If this is associated with an increase in perfusion pressure, urine output may improve. Particularly at higher doses and in severe septic shock, however, adrenaline can cause excessive vasoconstriction, with potentially worrying reductions in splanchnic flow and associated falls in gastric mucosal pH, indicative of gut mucosal ischaemia (De Backer et al., 2003; Levy et al., 1997a; Meier-Hellmann et al., 1997). Renal blood flow may fall with adrenaline and prolonged high-dose administration can cause peripheral gangrene. Adrenaline may also precipitate tachyarrhythmias. Lactic acidosis is a common complication of adrenaline administration (Day et al., 1996) and is probably explained by β₂-mediated accelerated glycolysis, often combined with other causes of increased lactate production and, in many cases, exacerbated by impaired lactate clearance (see above). The prognostic significance of adrenaline-induced lactic acidosis is unclear, but this phenomenon emphasizes the limitations of using blood lactate levels as a guide to tissue hypoxia in shock, especially in those receiving adrenaline. In an experimental septic shock model adrenaline administration was associated with dose-related reductions in cardiac index, ejection fraction and pH, as well as increases in systemic vascular resistance and creatinine. Adrenaline also adversely affected systemic perfusion, organ function and survival when compared to noradrenaline and vasopressin (Minneci et al., 2004b).

Despite these disadvantages, adrenaline can be a useful agent in patients with refractory hypotension. It is very potent and may prove successful when other agents have failed, particularly following cardiac surgery, perhaps because it stimulates myocardial α-receptors. Adrenaline is still pre-
ferred by some as a cheap, effective means of reversing hypotension and increasing oxygen delivery in septic shock (Bollaert et al., 1990), especially when haemodynamic monitoring is not available or is considered unwarranted. In order to avoid adverse effects the minimum effective dose should be used, and its administration should be discontinued as soon as possible.

**NORADRENALINE (NOREPINEPHRINE)**

Noradrenaline has both \( \alpha \) - and \( \beta \)-adrenergic actions, but the \( \alpha \)-mediated vasoconstrictor effect predominates. Noradrenaline is particularly useful in those with unresponsive hypotension associated with a low systemic vascular resistance and an adequate cardiac output, for example in septic shock resistant to dopamine. It is also increasingly used to maintain blood pressure in vasodilated patients post cardiac surgery. Administration of noradrenaline to patients with vasodilatory shock is associated with an increase in systemic vascular resistance and MAP, while cardiac output usually falls in line with the increased afterload. In some cases, however, cardiac output is unchanged and in patients with dobutamine-resistant septic shock noradrenaline has been shown to improve cardiac output and left ventricular stroke work, as well as increasing systemic vascular resistance and MAP (Martin et al., 1999). These findings indicate that noradrenaline can sometimes exert a positive inotropic effect in septic shock, probably via stimulation of cardiac \( \alpha \) and \( \beta \) receptors or possibly as a consequence of improved coronary perfusion (Martin et al., 1999). Moreover, provided cardiac output does not fall, restoration of blood pressure with noradrenaline may be associated with maintained or improved splanchnic perfusion and oxygenation (Marik and Mohedin, 1994; Meier-Hellmann et al., 1996) and reductions in blood lactate levels, as well as increases in urine flow and creatinine clearance (Martin et al., 1990). PAOP and mean pulmonary artery pressure are usually either unchanged or slightly increased. In some cases, large doses may be required to overcome \( \alpha \)-receptor downregulation but there is a risk of producing excessive vasoconstriction and masking hypovolaemia, with impaired organ perfusion, peripheral ischaemia and increased afterload. Administration of high doses of noradrenaline has been implicated as a contributory factor in the development of symmetrical peripheral gangrene (Hayes et al., 1992). Noradrenaline administration must, therefore, be accompanied by close haemodynamic monitoring and, certainly when higher doses are used, determination of cardiac output.

**ISOPRENALINE**

This \( \beta \)-stimulant has both inotropic and chronotropic effects, and also reduces peripheral resistance by dilating skin and muscle blood vessels. This latter effect means that much of the increased flow is diverted away from vital organs such as the kidneys and may account for the oliguria that can be associated with its use. Most of the increase in cardiac output produced by isoprenaline is due to the tachycardia and this, together with the development of arrhythmias, seriously limits its value. There are now few indications for isoprenaline in the critically ill adult, except, perhaps, as a treatment for bradycardia after cardiac surgery.

**DOPAMINE**

Dopamine is a natural precursor of noradrenaline that acts on \( \beta_1 \) and, to a lesser extent, \( \beta_2 \) receptors, \( \alpha \) receptors (via noradrenaline release) and dopaminergic DA1 and DA2 receptors. When used in low doses (1–3 \( \mu \)g/kg per min) dopaminergic vasodilatory receptors in the cerebral, coronary and splanchnic circulations are activated (DA1 receptors are located on postsynaptic membranes and mediate vasodilatation, whereas DA2 receptors are presynaptic and potentiate these vasodilatory effects by preventing the release of noradrenaline). Peripheral resistance falls, renal and hepatic blood flow increase, and urine output, GFR, fractional excretion of sodium and creatinine clearance can be improved. The importance of the renal vasodilator effect of dopamine has, however, been questioned and it has been suggested that the increased urine output is largely attributable to a rise in cardiac output and blood pressure, combined with a decrease in aldosterone concentrations and inhibition of tubular sodium reabsorption mediated via DA1 stimulation. Despite the increase in urine output, low-dose dopamine has no effect on the need for renal replacement therapy or mortality in patients with, or at risk of, acute renal dysfunction (Friedrich et al., 2005) (see also Chapter 13).

As the dose of dopamine is increased (3–10 \( \mu \)g/kg per min), \( \beta_1 \)-adrenergic effects predominate, producing an increase in heart rate and cardiac contractility. Dopamine also increases noradrenaline release contributing to its cardiac effects, and at higher doses (> 10 \( \mu \)g/kg per min), vasoconstriction occurs, increasing blood pressure and afterload and raising ventricular filling pressures. This can be dangerous in patients with cardiac failure in whom filling pressures are already high. There is also some evidence to suggest that in septic shock the use of high-dose dopamine to achieve a target MAP > 75 mmHg may precipitate gut mucosal ischaemia, perhaps by redistributing flow, whereas noradrenaline can improve splanchnic oxygenation (Marik and Mohedin, 1994). In another study dopamine (5 \( \mu \)g/kg per min) was associated with a reduction in gastric mucosal blood flow and pH (Neviere et al., 1996). Dopamine consistently increases pulmonary shunt fraction and in some patients the dose of dopamine is limited by \( \beta \) effects such as tachycardia and arrhythmias. In septic shock dopamine restores MAP primarily by increasing stroke volume and cardiac index, with minimal effect on heart rate and systemic vascular resistance. Central venous, pulmonary artery and PAOPs are usually unchanged. At doses higher than 20 \( \mu \)g/kg per min, however, right heart pressures may increase and this dose should not normally be exceeded. The median dose of dopamine required to restore blood pressure in septic shock is 15 \( \mu \)g/kg per min (Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine, 1999).
Dopamine also suppresses the circulating concentrations of all the anterior pituitary-dependent hormones except cortisol (Van den Berghe and de Zegher, 1996). Although the clinical implications of this effect are unclear, such changes are unlikely to be beneficial and suggest that long-term administration of dopamine to critically ill patients should be avoided. Indeed an observational study has suggested that dopamine administration may be associated with increased mortality rates in shock (Sakr et al., 2006).

**DOPEXAMINE**

Dopexamine is an analogue of dopamine which activates β receptors as well as DA1 and DA2 receptors. It is more potent at DA1 than DA2 receptors, is a weak β agonist and inhibits neuronal reuptake of noradrenaline. Dopexamine is a very weak positive inotrope, but is a powerful splanchnic vasodilator, reducing afterload and improving cardiac output and blood flow to vital organs, including the kidneys. It is an effective natriuretic and diuretic agent. At higher doses a fall in diastolic pressure and MAP may reduce regional blood flow. In septic shock, dopexamine can increase cardiac index and heart rate, but causes further reductions in systemic vascular resistance (Colardyn et al., 1989) and the dose may be limited by tachycardia. Although some early studies suggested that dopexamine can improve gut mucosal perfusion, in a later study in patients with severe sepsis (who were already receiving dobutamine) dopexamine only increased splanchnic oxygen delivery in proportion to the increase in cardiac output and caused a dose-dependent reduction in intramucosal pH (Meier-Hellmann et al., 1999). Moreover, in patients with septic shock receiving noradrenaline, the addition of dopexamine failed to improve hepatosplanchnic haemodynamics, oxygen exchange and energy balance, despite increases in oxygen delivery (Kiefer et al., 2000). It has been suggested that dopexamine is likely to be most useful in the management of low-output left ventricular failure, but this agent is not generally recommended for the management of sepsis/septic shock.

**DOBUTAMINE**

Dobutamine is a racemic mixture of two isomers, a D-isomer with β- and β1-activity and a 1-isomer with β1- and α1-adrenergic actions. Dobutamine causes less tachycardia and arrhythmias than isoprenaline but when compared with dopamine the relative effects of the two agents on heart rate and rhythm are a matter of dispute. An advantage of dobutamine is its ability to reduce systemic resistance, as well as improve cardiac performance, thereby decreasing both afterload and ventricular filling pressures. Dobutamine is therefore useful in patients with cardiogenic shock and cardiac failure, although the associated vasodilatation may be complicated by hypotension. In septic shock dobutamine increases heart rate, stroke volume, ventricular stroke work, cardiac output, DO2 and VO2 while, in some cases, systemic vascular resistance falls (Vincent et al., 1990). Dobutamine may be particularly useful in septic patients with fluid overload or myocardial failure (Jardin et al., 1981). In adrenaline-treated patients with septic shock, the addition of dobutamine (5 μg/kg per min) selectively improved gastric mucosal perfusion without altering systemic haemodynamics (Levy et al., 1997b) and in another study the same dose of dobutamine improved gastric mucosal perfusion in septic patients, whereas dopamine was deleterious in this respect (Neviere et al., 1996). Dobutamine has no specific effect on the renal vasculature or dopamine receptors, although urine output and, in some cases, creatinine clearance often increase as cardiac output and blood pressure improve.

**PHOSPHODIESTERASE INHIBITORS (E.G. AMRINONE, MILRINONE, ENOXIMONE)**

These agents have both inotropic and vasodilator properties. They inhibit phosphodiesterase type III (PDE III), thereby increasing concentrations of cyclic adenosine monophosphate (AMP) and improving cardiac contractility, whilst inhibition of other PDE isoforms increases cGMP and produces vasodilatation. Cardiac index and stroke work indices usually increase, whilst systemic and pulmonary vascular resistances fall. Vasopressors such as noradrenaline may be required to counteract excessive vasodilatation. These agents have a relatively long half-life (e.g. 4–7 hours for enoximone) and are usually administered as a loading dose followed by a continuous infusion, although single doses may be sufficient for weaning from cardiopulmonary bypass. Because PDE III inhibitors bypass the β-adrenergic receptor they do not cause significant tachycardia, are considerably less arrhythmogenic than sympathomimetic agents and can potentiate the effects of β-agonists. PDE III inhibitors may be particularly useful in patients with adrenergic receptor downregulation, those receiving β-blockers, for weaning patients from cardiopulmonary bypass, and for patients with cardiac failure. In vasodilated septic patients, however, they may precipitate or worsen hypotension, an effect which can be prolonged. Although PDE III inhibitors are not generally recommended for patients with sepsis/septic shock, they can occasionally be useful in combination with adrenergic agents. Indeed, one study suggested that enoximone could improve hepatosplanchnic function in fluid-resuscitated septic shock patients in whom MAP was maintained with noradrenaline, perhaps in part by inhibiting the inflammatory response, as well as by improving regional perfusion (Kern et al., 2001).

**VASOPRESSIN**

Vasopressin is an ADH with thermoregulatory, haemostatic and gastrointestinal effects which also acts as a potent vaso-pressor via activation of V1 receptors on vascular smooth muscle. Its antidiuretic action is mediated via V2 receptor activation in the renal collecting duct system. In addition, vasopressin, at low concentrations, mediates vasodilatation in coronary, cerebral and pulmonary arterial circulations. Although circulating levels of vasopressin are usually increased in response to stress, inappropriately low levels have been described in patients with septic shock, possibly because of impaired secretion or depletion of vasopressin.
stores in the neurohypophysis (Landry et al., 1997; Sharshar et al., 2002). Moreover, in contrast to the blunted response to adrenergic agents, patients with vasodilatory shock appear to be hypersensitive to the pressor effects of exogenous vasopressin and administration of vasopressin to these patients potentiates the vasoconstrictor effects of noradrenaline. In a randomized double-blind study, a short-term vasopressin infusion reduced the requirement for conventional vasopressors and improved renal function (Patel et al., 2002). Cardiac index was maintained whilst ventricular filling pressures, pulmonary artery pressures, pulmonary vascular resistance and heart rate were unchanged, as was gastric mucosal perfusion. The increase in urine output and creatinine clearance following vasopressin administration may be a consequence of increased systemic blood pressure combined with preferential constriction of renal efferent arterioles leading to increased glomerular perfusion pressure. Also vasopressin may directly activate oxytocin receptors, causing natriuresis and diuresis, as well as releasing atrial natriuretic peptide. At high doses, however, there is a danger that vasopressin will precipitate excessive renal, coronary, mesenteric and systemic vasoconstriction, as well as causing a significant reduction in cardiac output. A recent randomised controlled trial, however, found that low dose vasopressin did not reduce mortality rates when compared to noradrenaline, although there was a suggestion of benefit in those with less severe septic shock (Russell et al., 2008).

Vasopressin is relatively contraindicated in hypovolaemia, heart failure and in those with a history of coronary artery disease, although there are studies showing utility in cardiogenic shock. An alternative is to use terlipressin, a cheaper, longer-acting, synthetic analogue of vasopressin. Small doses (0.25–0.5 mg), repeated at 20-minute intervals to a maximum of 2 mg, should be used with close observation for signs of peripheral ischaemia and with cardiac output monitoring. In sepsis patients a single dose is often sufficient to improve blood pressure, reduce vasopressor requirements and improve renal function (Leone et al., 2004).

Angiotensin has been used in resistant septic shock (Wray and Coakley, 1995) but there is a danger of excessive vasoconstriction with associated falls in cardiac output and tissue perfusion. This agent is no longer available in the UK.

**INHIBITION OF NITRIC OXIDE SYNTHESIS**

Experimental studies have demonstrated that the vascular hyperreactivity to adrenergic agonists and the peripheral vascular failure associated with endotoxaemia can be reversed by inhibiting NO synthesis with 1-arginine analogues, and prevented by inhibiting the induction of inducible NOS with dexamethasone. There is evidence that NO production is increased in human sepsis (Evans et al., 1993) and preliminary studies in patients with septic shock suggested that administration of the non-selective NOS inhibitor N-monomethyl-1-arginine hydrochloride (L-NMMA) was safe and could restore vasomotor tone and maintain blood pressure (Grover et al., 1999). At higher doses, however, cardiac output and oxygen delivery fell, although oxygen consumption was maintained by an increase in oxygen extraction. There were also concerns about the effects of inhibiting NO production on regional perfusion, the microcirculation, the pulmonary vasculature, coagulation, free radical injury and immune function. These concerns were highlighted when a phase III study of L-NMMA was terminated prematurely because of excess mortality in the treatment group, perhaps partly explained by the inclusion of patients with hypodynamic septic shock in this trial and the deleterious effect of higher doses of NOS inhibitor (Lopez et al., 2004).

**Methylene blue** inhibits guanylate cyclase and possibly also NOS. Administration of methylene blue to patients with septic shock can increase arterial blood pressure, although stroke volume, left ventricular stroke work and oxygen delivery are unchanged (Kirov et al., 2001). Further studies are required to determine whether this agent has a role in routine clinical practice.

**RECEPTOR DOWNREGULATION**

Many of the most seriously ill patients become increasingly resistant to the effects of pressor agents, an observation attributed to downregulation of adrenergic receptors. This may be due to a reduction in receptor numbers, a decreased affinity of the receptor for its ligand induced by overstimulation, or a direct effect of inflammatory mediators on signal transduction either at or distal to the receptor. This affects intracellular calcium levels and the resultant vascular hyperreactivity to both endogenous and exogenous catecholamines is a particular feature of septic shock.

**Guidelines for the use of inotropics and vasopressor agents** (Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine, 1999)

Many still consider dopamine in low to moderate doses to be the first-line agent for restoring blood pressure, although others favour dopexamine as a means of increasing cardiac output and organ blood flow. High-dose dopamine is usually best avoided. Dobutamine is particularly indicated in patients in whom the vasoconstriction caused by dopamine could be dangerous (i.e. patients with cardiac disease, those with a low cardiac output after fluid resuscitation and septic patients with fluid overload or myocardial failure). The combination of dobutamine and noradrenaline is currently popular for the management of patients who are hypotensive with a low
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