Hypertension

Hypertension (HTN) is a common disease with a worldwide incidence of 1 billion individuals. It is found in all societies except primitive, isolated countries; it accounts for about 6% of all deaths. The World Health Organization predicts that one-third of the world’s population will have HTN by the 2025.1

In the United States, there are approximately 72 million patients with HTN. The incidence increases with age: 30% of people older than 20 years and 60% to 70% of people older than 70 years. Patients who are normotensive by 55 years of age still have a 90% chance of developing HTN.2

Adult men have a higher incidence than women, but the reverse is seen in the senior population. The incidence in blacks is twice that of Caucasians, and their morbidity and mortality from coronary artery disease (CAD), stroke (cerebrovascular accidents [CVA]), left ventricular hypertrophy (LVH), myocardial infarction (MI), and renal failure is more pronounced.

HTN is a major risk factor for the development of cardiovascular, cerebrovascular, and renal diseases. Appropriate antihypertensive therapy reduces these risks, but only 29% of patients with HTN seek care; of those patients, only 49% have the appropriate therapy and control of the disease.

If patients are well controlled, stroke reduction is 35% to 40%, MIs are reduced by 20% to 25%, and heart failure (HF) reduction is greater than 50%.3

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) established categories for HTN and outlined the steps for management. The 3 categories are illustrated in Table 1.
A new category was created called prehypertension. Prehypertension is defined as a systolic blood pressure (SBP) of 130 to 139 mm Hg and a diastolic BP (DBP) of 80 to 90 mm Hg. Patients in this category are twice as likely to have HTN than patients with lower BPs.

Historically, antihypertensive therapy targeted DBP control, but current data show elevations in SBP as a greater risk for cardiovascular disease (CVD), especially in patients older than 50 years. For patients between the ages of 40 and 70 years, each incremental increase of 20 mm Hg in SBP and/or 10 mm Hg increase in DBP, doubles their risk for CVD. This effect occurs over a pressure range of 115/75 to 185/115 mm Hg.

The management of HTN requires a multimodal approach. Medications are almost always the primary step, but other treatments are initiated simultaneously with these drugs. Lifestyle changes are indicated. Diets are necessary to induce weight loss in overweight and obese patients; this includes a low-fat, sodium-restricted diet for chronic BP control. Patients also need to increase their aerobic physical activity and reduce their alcohol intake to a daily maximum of 3 oz of 80-proof spirits, 24 oz of beer, or 10 oz of wine.

BP can be controlled by antihypertensive medications, but most patients will require 2 or more agents. Typically, the thiazide diuretics are the first-line agents used in HTN, and they are augmented as needed by beta-blockers (BB), calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEI), and angiotensin receptor blockers (ARB). Some practitioners will skip the diuretic and immediately go to the other agents. The metabolic syndrome is an example whereby many patients are not on diuretics, and the first-line drug used is an ACEI agent. The goal is to reduce BP to less than 140/90 in most patients, but an additional reduction to less than 130/80 is the goal for patients with diabetes or renal disease. In most patients, once the SBP goal is achieved, the DBP will be controlled (Fig. 1).

In special circumstances, as illustrated later, certain agents are more effective than others in controlling HTN. Existing comorbidities make one drug better than another (Table 2).

### TYPES OF HTN

Essential HTN (also known as primary or idiopathic HTN) is of an unknown cause, but there is a familial incidence. It accounts for 80% to 90% of all HTN. Patients typically have an increased sympathetic discharge with an increased beta-receptor activity. The incidence increases with age; it frequently has associated comorbidities, like diabetes, obesity, and obstructive sleep apnea.

Secondary HTN accounts for the remaining 5% to 20% of cases, with renal disease being the primary cause. The causes of secondary HTN are listed in Box 1.

### PATHOLOGIC EFFECTS OF HTN

HTN is a major risk factor for developing CVD, which is the leading cause of death in patients with HTN. In trying to pump blood against elevated pressures, the heart eventually fails, leading to a variety of complications. The following table summarizes the key effects of HTN.

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Systolic Blood Pressure (mm Hg)</th>
<th>Diastolic Blood Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>80–89</td>
</tr>
<tr>
<td>Stage I HTN</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage II HTN</td>
<td>≥160</td>
<td>≥100</td>
</tr>
</tbody>
</table>


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BPs (afterload), structural and functional defects develop in the heart. LVH, a thickening of the heart wall muscle mass, develops resulting in a less compliant heart that is unable to effectively withstand the increases in left ventricular end diastolic pressures and volumes (LVEDP and LVEDV). The end result is myocardial ischemia, injury, infarction, dysrhythmias, and HF.

Cardiovascular effects from HTN are far more common than the cerebrovascular effects, but the central nervous system (CNS) complications from hypertension can be just as significant. HTN increases a patients’ risk for cerebral ischemic infarcts and hemorrhagic stroke. This risk is amplified in patients older than 65 years. These patients are also at an increased risk for cognitive dysfunction and dementia.

In severe HTN, the autoregulation of cerebral blood flow fails and ischemia, edema, or encephalopathy can develop. In normotensive patients, blood flow is maintained over a mean arterial pressure (MAP) of 50 to 150 mm Hg; but in severe HTN, there is vasodilation and hyperperfusion of cerebral tissues that can cause death within hours if not managed properly.

Renal disease is the most common cause of secondary HTN. Patients with chronic renal failure have an 80% incidence of HTN.

**METABOLIC SYNDROME**

The metabolic syndrome is a combination of HTN, insulin resistance, and dyslipidemia. In the United States, 44% of the population who are older than 50 years have metabolic syndrome. The incidence increases with age, resulting in rates of 34% in men and 35% in women. These patients are at increased risk for CAD, stroke, and diabetes.

The primary approach to treatment is weight loss. A low-carbohydrate diet will lead to rapid weight loss, but a diet of fruits, vegetables, whole grains, lean poultry, and fish is the preferred long-term diet. Diet control needs to be followed by an increase in physical activity and reduced alcohol intake just like in any patient with HTN. BP control is usually accomplished by the use of angiotensin agents, either ACEI or ARB, which have been found to not only decrease BP but to also decrease the onset of type 2 diabetes.

**PHYSIOLOGIC EFFECTS OF HTN**

With new-onset HTN, there is an increased sympathetic activity that results in changes in cardiac output (CO), heart rate, systemic vascular resistance (SVR), and circulating blood flow.

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**Table 2**

<table>
<thead>
<tr>
<th>Medication</th>
<th>HF</th>
<th>Post MI</th>
<th>Diabetes</th>
<th>Chronic Kidney Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretic</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>BB</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>ACEI</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>ARB</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CCB</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>


**Box 1**

Causes of secondary HTN

- Renal disease
- Pheochromocytoma
- Oral contraceptives
- Obesity and obstructive sleep apnea
- Primary aldosteronism
- Hyperthyroid
- Hypothyroid
- Cushing syndrome
- Postoperative hypertension
- Drugs of abuse
  - Cocaine, amphetamines, and alcohol
- Hyperparathyroid

**Table 3**

<table>
<thead>
<tr>
<th>Risk factors for metabolic syndrome</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>≥130/85</td>
<td>≥130/85</td>
</tr>
<tr>
<td>Abdominal waist size</td>
<td>&gt;102 cm</td>
<td>&gt;88 cm</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>&gt;100 mg/dL</td>
<td>&gt;100 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&gt;150 mg/dL</td>
<td>&gt;150 mg/dL</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>&lt;40 mg/dL</td>
<td>&lt;50 mg/dL</td>
</tr>
</tbody>
</table>

Abbreviation: HDL, high-density lipoprotein.

Vasoconstriction of the arterial vessels causes an increase in SVR, so there is an increase in the afterload that the heart pumps against. The vasoconstriction also reduces the pooling of blood in the venous vessels, so there is an increase in blood return to the heart and, therefore, an increased preload; this results in an increase in the heart rate and the CO.

The resultant increase in BP (HTN) and heart rate (tachycardia) is not without adverse side effects. There are imbalances between oxygen supply and demand. The increased myocardial oxygen consumption can lead to ischemia, injury, and infarction. Tachycardia and HTN are the two most important determinants of imbalances in oxygen supply and demand. These effects are tolerated in young adults, but they are significant in the middle-aged and senior populations.

Coronary blood flow is dependent on diastolic filling time and pressure. If there is a decrease in filling time caused by tachycardia or an increase in LVEDP and LVEDV caused by HTN, coronary blood flow and volume will be decreased and ischemia will result. The resultant ischemia causes a decrease in CO over time, and this ultimately leads to signs of congestion and HF (Table 4).6

ANESTHESIA AND HTN

Patients with HTN can develop exaggerated hypotension and HTN perioperatively. With chronic HTN, there is a relative decrease in intravascular volume; if the anesthetic agents cause vasodilation, the decreased intravascular volume cannot fill those dilated vessels. The result is a decrease in venous return to the heart, a decrease in CO, and an exaggerated hypotensive event.

Chronic HTN also causes vascular smooth muscle hypertrophy. Surgical stimulation can activate the sympathetic nervous system; this results in vasoconstriction of the hypertrophic muscle in those vessels, and you see an exaggerated hypertensive event. This reaction is not uncommon during intubation or the maintenance phase of anesthesia if patients are not in a deep enough stage of anesthesia.6

<table>
<thead>
<tr>
<th>Table 4 Heart rate and cycle time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate (beats per min)</td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>90</td>
</tr>
<tr>
<td>120</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

PERIOPERATIVE HTN

Perioperative HTN does increase the risk of ischemia, infarction, HF, CVA, and renal disease. The incidence of complications is 30% in patients with untreated HTN, 36% in poorly controlled patients, and 16% in well-controlled patients. The overall incidence of perioperative HTN is 25%.9

Patients with pre-HTN or stage 1 HTN (SBP 120–159 mm Hg or DBP 80–99 mm Hg) do not have an increased risk for cardiovascular complications. The parenteral use of antihypertensive agents is unnecessary preoperatively, and there is no apparent benefit in delaying the surgery. During surgery, if an acute exacerbation occurs, medications are indicated to control BP, and patients' antihypertensive medications should be maintained during the perioperative period.

Patients with a DBP less than 110 mm Hg behave very similar to normotensive patients. BPs that are less than 180/110 without evidence of target organ disease are not independent risks for perioperative cardiovascular complications. Therefore, it is unnecessary to reduce these pressures to normal before surgery. In fact, aggressive lowering of BP (too fast, too low) may increase the risk of ischemic injury to the heart, brain, and kidneys.

Surgery must be deferred regardless of BP in the presence of ischemia, HF, renal failure, or CNS dysfunction. Patients at high risk (previous stroke or active CAD) should have surgery postponed when the SBP is more than 180 mm Hg or the DBP is more than 110 mm Hg. These patients need optimization of BP before surgery to reduce risks.

Surgery in patients with poorly controlled HTN has increased complications. The decision to proceed with surgery is based on the surgical risk (low vs high), comorbidities, and patients’ presentation. Patients with no evidence of target organ disease despite BPs of 180/110 or more may still be candidates for elective surgery. There is no data to support delaying surgery solely based on the BP reading. If you decide to proceed, those patients will need parenteral perioperative antihypertensive medications. BB like metoprolol or labetalol are typical agents that are used along with a benzodiazepine to reduce anxiety. The target BP decrease should be no greater than 20% of the baseline. These cases are not office-based cases. They should be done in a hospital-based ambulatory center or an in-patient facility.

Pulse pressure (PP) is the difference between the SBP and the DBP. Patients with PPs greater than 80 mm Hg have a greater risk for perioperative stroke, death, and renal dysfunction. Increased PPs in ambulatory patients is a better
indicator of cardiovascular and cerebrovascular risk than SBP or DBP readings.

Studies have shown that death rates in the middle-aged and senior populations are highest in patients with HTN with an SBP more than 160 and a DBP less than 70, which result in PPs more than 90 mm Hg. The morbidity and mortality rates increase as PPs increase more so than in SBP at fixed PPs. This increase is caused by decreased coronary perfusion and increased myocardial oxygen consumption in pumping blood against the increased afterload.10

OFFICE SURGERY AND HTN

Patients with an SBP of 180 mm Hg or more and/or a DBP of 110 mm Hg or more may be at low risk in the absence of target organ damage, but they still have risks. It would be wise to defer elective office surgery and anesthesia until the BP can be optimized. Anecdotally, surgeons try test doses of sedation to see if the BPs can be lowered; if so, they assume that patients have white coat syndrome, and this is why the pressure is elevated. Anxiety may be a contributing factor, but these patients can still develop HTN/hypotension episodes under anesthesia. A more conservative approach would be to discuss these patients with the physician to see if additional antihypertensive agents are indicated and then proceed with surgery.

The JNC-7 report classifies a SBP of more than 180 mm Hg and a DBP of more than 110 mm Hg as a hypertensive crisis. This crisis can be further classified as an emergency or an urgency, and the treatments differ for both. Hypertensive emergencies result in target organ damage. It was first described in 1914 as severe HTN with signs of vascular injury to the heart, brain, kidney, and eyes. In 1939, the term malignant hypertension was used to describe the event. Before the use of antihypertensive agents, 7% of patients with HTN suffered an emergency, and there was a 79% 1-year mortality rate.

In the United States, men have twice the incidence as women. The elderly and black populations have a higher incidence than middle-aged white men. Sympathetic stimulation with the release of vasoconstrictors increases the SVR and subsequently damage the endothelial lining of vessels. Ischemia develops over time, and the renin angiotensin system is activated to cause additional vascular constriction. The overall result is end organ hypoperfusion, ischemia, and dysfunction.11

The most common clinical signs are dyspnea, chest pain, headache, altered mental status, and focal neurologic deficits. Patients who present with severe HTN should be examined to rule out target organ injury.8

BRAIN

As BP increases, intracranial pressure and cerebral blood flow increase. This increase disrupts the blood-brain barrier and causes fluid leakage and cerebral edema. As this process progresses, hypertensive encephalopathy develops; although it is uncommon, it is a true emergency. Clinical signs include severe, generalized headache; confusion; somnolence; projectile vomiting; visual disturbances (blurred vision to blindness); and transient focal neurologic deficits.12

Retinal examination shows arteriolar spasm, exudates, hemorrhage, cotton wool spots, and papilledema. This progressive deterioration may take 12 to 24 hours before all the signs are evident. Treatment is to reduce the MAP 10% to 15%, with a maximum reduction of 20% in the first hour. Further reduction in pressure to 160/100 is done over the next 2 to 6 hours. If the reduction is too rapid, cerebral perfusion decreases and cerebral ischemia and infarcts can develop (Table 5).13

Hypertensive urgencies are elevations in BP of more than 180/120, but there is no target organ disease. These patients are usually given oral antihypertensive agents to reduce BP over several hours or days. In the perioperative setting, this is usually not possible because the patients are under anesthesia. The potential problem with not treating these patients is that the urgency may be a transitioning period, which can lead to a true emergency. In this setting, parenteral agents are used, but aggressive therapy is to be avoided. Avoid lowering too fast and too low to prevent hypoperfusion and prolonged postoperative hypotension.14

HTN during elective office anesthesia is usually a hypertensive urgency, not an emergency. There is no target organ failure. Patients who present to the office with well-controlled HTN have less than a

<table>
<thead>
<tr>
<th>Table 5</th>
<th>Target organ disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral Infarction</td>
<td>Brain</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>Hypertensive encephalopathy</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>Ischemia, injury, infarction</td>
</tr>
<tr>
<td>Dysrhythmias</td>
<td>Pulmonary edema</td>
</tr>
<tr>
<td>HF</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>Renal ischemic injury</td>
</tr>
<tr>
<td>Renal failure</td>
<td></td>
</tr>
</tbody>
</table>
10% risk of developing SBP of more than 160 mm Hg intraoperatively. Data support low complication rates perioperatively as long as the preoperative BP is less than 180/110.

**Intraoperative HTN**

Fluctuations in BP are very common during anesthesia induction and intubation. These fluctuations happen with both normotensive patients and patients with HTN. Patients with HTN will exhibit the most dramatic changes in pressure.

In normotensive patients, general anesthesia induction can increase BP by 20 to 30 mm Hg and elevate the heart rate by 15 to 20 beats per minute. In patients with HTN, there can be increases in BP up to 90 mm Hg and increases in heart rate up to 40 beats per minute.

Intraoperatively, the BP usually decreases from direct vasodilation of vessels by the anesthetic agents and inhibition of the sympathetic nervous system. In normotensive patients, BP will decrease up to 30 mm Hg; in the patients with HTN, this decrease can exceed 60 mm Hg. This hypotension can result in hypoperfusion with ischemia, dysrhythmias, HF, and renal failure. Goldman found that intraoperative hypotension (BP <50% of baseline or a 33% decrease for 10 or more minutes) will increase these risks. Beyer and colleagues found that HTN will increase the risk of intraoperative dysrhythmias and hemodynamic changes by 40%. During surgery, fluctuations in MAP more than 20% will increase postoperative cardiovascular complications.

The management of intraoperative HTN is complicated by patients’ comorbidities, volume status, anesthetic depth, and choice of anesthetic agents (Box 2).

**ACUTE POSTOPERATIVE HTN**

It is not uncommon to see postoperative HTN. There is no universally accepted definition for acute postoperative HTN (APH). Some practitioners define APH as an SBP of more than 20% of the baseline preoperative pressure or an increase in DBP of more than 110 mm Hg. Others use an SBP of more than 160 mm Hg, a DBP of more than 90 mm Hg, or an MAP that exceeds 110 mm Hg. Regardless of the definition, APH can increase the risk of cardiovascular and cerebrovascular complications (Box 3).

The onset is usually within 10 to 15 minutes after surgery, but it can take up to 2 hours to develop. The duration is less than 6 hours, and the incidence is 4% to 35%. The major component of APH is activation of the sympathetic nervous system as demonstrated by the increased plasma concentration of circulating catecholamines. The renin angiotensin system is a minor component in APH (Box 4).

One specific cause of APH is the clonidine withdrawal syndrome. Although rare, it can happen because patients are NPO for anesthesia and they do not take the oral clonidine, and there is no parenteral substitute in the United States. The reaction develops 18 to 24 hours after the drug is stopped. Patients have increased sympathetic stimulation with rebound HTN.

If oral clonidine is stopped for surgery, a transdermal clonidine patch is available for use until patients can take oral medications. Patients who also use nonselective BB are at an increased risk because the beta-2 sites (vasodilation) are blocked, and the alpha vasoconstrictor sites are now unopposed, which leads to significant HTN. Dexmedetomidine may have some use in these cases because of its alpha-2 agonist activity (vasodilation).

**MEDICATIONS FOR PERIOPERATIVE HTN**

Perioperative HTN management should include the use of sedation, either moderate or deep, to reduce the anxiety component of HTN. Pain management using profound local anesthesia and perioperative opioids is appropriate as is optimal oxygenation.

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**Box 2**

**Causes of intraoperative HTN**

- Intubation and airway manipulation
- Light anesthesia and pain
- Exogenous epinephrine
- Hypoxia and hypercarbia
- Hypovolemia
- Hypothermia
- Volume overload and/or bladder distention
- Holding perioperative antihypertensive medications

**Box 3**

**Acute postoperative HTN complications**

- Myocardial ischemia and infarction
- Cerebral ischemia and infarction
- Dysrhythmias
- Congestive HF
- Pulmonary edema
- Intracranial bleeding
- Incisional bleeding
and ventilation. Antihypertensive medications are usually maintained perioperatively, but patients may still require intraoperative medications to control the BP.

The ideal antihypertensive agent should have a rapid onset and short duration of action to avoid prolonged recovery times. Bolus agents are preferable to infusion agents in the office because they can be given fast and they do not require additional equipment to administer the drug. These agents should also have minimal side effects that will not disrupt cardiac conduction or reduce myocardial contractility. Agents that vasodilate the arteriolar resistance vessels are good because they decrease afterload and myocardial oxygen consumption, and any agent that has limited reflex tachycardia is good because it too will limit oxygen consumption.19

**BB**

BB have a long history in the management of HTN. They have been found to decrease post-MI mortality. Perioperatively, they reduce ischemia and attenuate fluctuations in intraoperative BP. Patients at risk for cardiovascular complications have less perioperative events while maintaining the beta agent. There are fewer episodes of ischemia, infarction, dysrhythmias, HF, or death. However, these agents are not without risk. Deveraux20 found that although the risk of perioperative MI is reduced, the risk for stroke actually increased.

**Should BB Be Maintained Perioperatively?**

Major cardiovascular complications, such as infarctions or unstable angina, only occur in 1% of elective inpatient surgery; but that risk can increase to 5% in patients who have underlying CVD.21

In high-risk patients undergoing high-risk surgery, there is a benefit to perioperative BB therapy. Withdrawal of the BB is associated with an increased mortality at 30 days and 1 year.22

For office and ambulatory surgery, if patients are not taking a BB and there is no indication for long-term beta blockade, there is no indication to support the initiation of BB therapy.23

BB reduce BP by decreasing the heart rate and myocardial contractility. The result is a decrease in CO and BP. Most patients using BB are on selective BB to limit side effects. However, at high doses, even the selective beta-1 agents lose selectivity and have crossover effects that inhibit beta-2 vasodilation. BB are not used in acute HF because they reduce heart rate and contractility in a failing heart. These agents are also restricted in patients with atrioventricular (AV) heart block.

**SHOULD BB BE USED IN PATIENTS WITH OBSTRUCTIVE AIRWAY DISEASE?**

There are 3 types of beta-receptors. Beta-1 receptors are typically found in the heart and when activated cause an increase in heart rate and force of myocardial contraction. These receptors also compose up to 30% of the beta-receptors in the alveolar walls of the lung. Beta-2 receptors cause bronchial and vascular smooth muscle to dilate. These receptors are also found in the heart and account for about 20% to 25% of those beta-receptors. The role of beta-3 receptors is still to be determined.

Nonselective BB like propranolol act on beta-1 and beta-2 receptors. Patients with asthma or chronic obstructive pulmonary disease (COPD) that are exposed to these drugs orally can see a 66-fold increase in airway hyperresponsiveness and a 6-fold increase to intravenous (IV) drug exposure as compared with the response in nonasthmatic patients. Therefore, nonselective BB should not be used in these patients because of a potentially life-threatening bronchospastic response.24

Studies have shown that cardioselective BB do not cause significant changes in patients’ forced expiratory volume in 1 second or affect the response of rescue beta-2 agents. Patients with COPD typically have more significant airway disease than most patients with asthma, and they are also more prone to have a coexisting CVD. If these patients require antihypertensive therapy and would benefit from the use of a cardioselective BB, they should not be withheld.

Because of its short duration and demonstrated lack of airway dysfunction in patients with asthma, IV esmolol may be useful in perioperative HTN. Labetalol may also have a role because of its alpha-1 blockade. Alpha-1 antagonists are weak bronchodilators, and they also have antihistamine and anti-serotonin activity.

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**Box 4**

**Causes of APH**

- Pain and anxiety
- Hypoxia and hypercarbia
- Hypothermia
- Volume overload and/or bladder distention
- Emergence delirium
- Endotracheal tube irritation
- Rebound HTN from withholding antihypertensives
However, some investigators caution against using these agents in patients with airway hyperresponsiveness. Certainly, they would be contraindicated in patients with acute bronchospasm, but elective anesthesia would also be contraindicated in these patients. It remains up to the practitioner to assess risk versus benefit in this group of patients with perioperative HTN.25,26

ESMOLOL

Esmolol is an ultrashort-acting beta-1 selective blocker. The elimination half-life is about 8 minutes because of hydrolysis of its ester linkage by red blood cell esterases. This metabolism is independent of renal or liver function. The onset of action is 60 seconds after the IV bolus dose, and the duration is about 10 to 20 minutes after the infusion is stopped.18

Esmolol competitively blocks the beta-1 receptor; but at high doses, there is also beta-2 blocking. This crossover can precipitate bronchospasm in patients with reactive airway disease, asthma, or COPD. There is less risk of bronchospasm with esmolol versus labetalol because of esmolol’s short duration of action. Esmolol has no direct vasodilatation effects. The reduction in BP is by decreasing heart rate and myocardial contractility. Clinical effects are a reduction in heart rate, CO, SBP, and DBP.10

Esmolol is an excellent agent for perioperative HTN, especially when tachycardia is present. This BB reduces BP, but it reduces heart rate to a greater degree than BP. It should not be used in patients who present with bradycardia, acute HF, or AV heart block (second or third degree).27

In most cases, an IV bolus is given over 30 seconds to 1 minute, and this is followed by an infusion because of the short duration of the agent. An alternative approach presented in an American Dental Society Anesthesiology (ADSA) general anesthesia review program is to give an IV bolus of 5 to 10 mg (0.5 mg/kg). As with other techniques, this dose would be given over 30 seconds, and you will see a decrease in heart rate of 1 beat per minute for every 1 mg of drug given. The maximum dose of esmolol by any schedule is 300 mcg/kg/min (Tables 6 and 7).

LABETALOL

Labetalol is a nonselective BB and a selective alpha-1 blocker. Beta blockade is 5 to 10 times greater than the alpha blockade, but the beta-1 and beta-2 sites are blocked to the same degree. The ratio of alpha to beta blockade is 1:7. Unlike other BB, labetalol maintains CO, and the heart rate is either maintained or slightly reduced. SVR is decreased, but cerebral, coronary, and renal blood flow is maintained.18

The onset of action is 2 to 5 minutes, with a peak effect within 5 to 15 minutes. The duration of action is 2 to 4 hours. Metabolism occurs in the liver. Labetalol, like esmolol, is an effective medication for perioperative HTN with tachycardia. It should not be used in bradycardia, HF, or AV heart block. Its use in airway disease is controversial. Certainly it would not be used in acute bronchospasm.

As stated previously, with most of these antihypertensive agents, it is better to go low, go slow in an office setting because we can precipitate other complications that can be worse. Although the initial bolus dose of labetalol is 20 mg IV, a conservative approach would be to give 5 to 10 mg IV with incremental dosing in 5 to 10 minutes at 20 mg or more. The use of 1 to 2 mg/kg as an initial dose should be avoided because significant hypotension can occur. The maximum daily dose of labetalol is 300 mg in 24 hours (Table 8).10,28

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Esmolol dosing schedules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus Dose Schedule</td>
<td>Infusion Dosage Schedule</td>
</tr>
<tr>
<td>80 mg over 30 s</td>
<td>150 mics/kg/min</td>
</tr>
<tr>
<td>500 mics/kg over 1 min</td>
<td>25–200 mics/kg/min</td>
</tr>
<tr>
<td>500 mics/kg over 1 min</td>
<td>25–50 mics/kg/min then increase the dosage by 25 mics/kg/min q 10–15 min</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 7</th>
<th>AAOMS office anesthesia manual for esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus Dose</td>
<td>Infusion Dose</td>
</tr>
<tr>
<td>80 mg (1 mg/kg) over 30 s</td>
<td>150 mics/kg/min to a maximum of 300/mics/kg/min</td>
</tr>
<tr>
<td>500 mics/kg over 1 min</td>
<td>50 mics/kg/min for 4 min, reevaluate, and if needed, try the bottom dose schedule</td>
</tr>
<tr>
<td>500 mics/kg over 1 min</td>
<td>100 mics/kg/min up to maximum of 300 mics/kg/min</td>
</tr>
</tbody>
</table>

Abbreviation: AAOMS, American Association of Oral and Maxillofacial Surgeons.

Metoprolol is a beta-1 selective blocker. Like the other BB, it reduces BP and CO by decreasing the heart rate and myocardial contractility. A secondary effect on BP is its suppression of the sympathetic nervous system to pain and anxiety. Patients who use metoprolol for maintenance therapy for HTN have decreased renin release and decreased levels of angiotensin II.

IV metoprolol is used to control the ventricular response in atrial fibrillation and paroxysmal supraventricular tachycardia (PSVT). It is not a first-line drug for perioperative HTN; as a solo agent, it is not always effective. If a vasodilating antihypertensive agent is used to reduce BP, a reflex tachycardia will occur. If metoprolol is added to the treatment, it will prevent the reflex tachycardia. The initial dose is 1 to 2 mg IV. The onset of action is 2 to 3 minutes, with a peak effect within 20 minutes. The duration of action is 4 hours. Additional doses of metoprolol of 1.25 to 5.0 mg can be given every 6 hours.15

Other BB that can be used for perioperative HTN include the following: Propranolol is a nonselective BB that is rarely used for perioperative HTN because there are better cardioselective BB. Atenolol, a cardioselective BB, has a slow onset, so it is not a first-line agent. Nebivolol is a third-generation BB that also has vasodilating properties. Both arteries and veins are dilated through the L-arginine-nitric acid pathway. It is a BB plus a vasodilator, which makes it a promising agent for the future.

### CCB

There are 6 types of CCB. The L-type agents act on vascular and myocardial functions. This drug class inhibits the influx of extracellular calcium (Ca) ions through the Ca channels. This inhibition causes vascular smooth muscle to vasodilate, and it inhibits myocardial contractions and cardiac conduction pathway transmissions.

There are 3 classes of L-type CCB

- Phenylalkylamines: verapamil
- Dihydropyridines: nifedipine, amlodipine, nicardipine (Cardene), and clevidipine (Cleviprex)
- Benzothiapines: diltiazem

The dihydropyridines are used as vasodilators, whereas the phenylalkylamines and the benzothiapines are antidyssrhythmics.

### DIHYDROPYRIDINES

These drugs include nifedipine, nicardipine, and clevidipine. They are selective for vascular smooth muscle with cerebral vessels having the highest affinity followed in descending order by coronary, muscle, and renal vessels. There is little to no activity on cardiac muscle contractility or sinoatrial node transmission. The net effect of these agents is vasodilation, which acts to reduce BP.

**Nicardipine is a second-generation dihydropyidine.** In cerebral vessels, it dilates small resistance arterioles to relieve cerebral ischemia without changing intracranial pressure or intracranial volume. Nicardipine reduces SVR by vasodilation and reduces coronary ischemia by increasing coronary blood flow. There will be an increase in the heart rate and CO, whereas the afterload is decreased. Side effects are headache, hypotension, and nausea and vomiting.11

Nicardipine is usually given as an infusion, and the dose is independent of weight. Nicardipine comes in premixed bags for IV infusion use.

Nicardipine: Use 20 mg in 200 mL fluid, 40 mg in 200 mL fluid, or 2.5 mg/mL in a 10-mL vial.

**Dosing instructions**

The initial dosage is 5 mg/h as an IV infusion. This dosage is increased by 2.5 mg/h every 5 minutes for a rapid reduction of BP. For a gradual reduction of BP, the dosage can be increased by 2.5 mg/h every 15 minutes. This dosing is done until the BP is controlled or a maximum dosage of 30 mg/h.

When the target pressure is achieved, the dosage is reduced by 3 mg/h. This dosage is single use only; discard any unused portion. Do not mix or run the drug in the same line as other medications.

Nicardipine is an excellent drug for perioperative HTN. The onset of action is 5 to 15 minutes, with a

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**Table 8**

<table>
<thead>
<tr>
<th>Initial Bolus</th>
<th>Repeat Bolus in 10 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>5–10 mg IV</td>
<td>20 mg IV</td>
</tr>
<tr>
<td>20 mg IV</td>
<td>20–80 mg IV</td>
</tr>
<tr>
<td>5–20 mg IV over 2 min</td>
<td>2 mg/min up to 300 mg maximum dose</td>
</tr>
<tr>
<td>Infusion of 0.5–2.0 mg/min</td>
<td>Increase by 0.5 mg/min q of 6 mg/min</td>
</tr>
</tbody>
</table>

duration of 4 to 6 hours. At present because of its cost and the need for infusion administration, this agent has limited usefulness in the office. However, bolus nicardipine has been used to control BP during cardiac surgery and to limit the cardiovascular response in rapid sequence intubations. An IV bolus of 0.5 to 1.0 mg decreased the SBP by 32 to 36 mm Hg. It also decreased the MAP by 21 to 24 mm Hg, with a maximum response in about 60 seconds in both instances. IV doses of 20 mics/kg have been used for intubations with an onset of action in 2.5 ± 0.6 minutes and a duration of 24 ± 5 minutes.\textsuperscript{29,30}

**Clevidipine**

Clevidipine is an ultrashort-acting third-generation dihydropyridine CCB. The onset of action is within 2 to 4 minutes from the start of the infusion, and there is a return to baseline pressures within 10 to 15 minutes after stopping the infusion. The short duration is caused by redistribution effects similar to what is seen with propofol. The rapid metabolism is from tissue and red blood cell esterase hydrolysis.

This agent reduces SVR by arterial smooth muscle vasodilation, so there is a decrease in the afterload. There is no effect on venous capacitance vessels, so the preload of the heart is maintained. CO increases, as does coronary blood flow; but unlike other vasodilators, there is no reflex tachycardia seen with clevidipine. Clinically, there is a reduction in SBP, DBP, and MAP.\textsuperscript{33}

**Dosing schedule for clevidipine**

The initial dosage is 1 to 2 mg/h. This dosage may be doubled at 90-second intervals until you approach the target BP reduction. As the pressure approaches the target pressure, the dosage is increased by less than double at an interval of every 5 to 10 minutes. Most patients reach the target reduction at rates of 4 to 6 mg/h in less than 30 minutes. The maximum dosage is 32 mg/h.

Use clevidipine 0.5 mg/mL in 50-mL or 100-mL vials. Clevidipine is a lipid emulsion, so as with propofol, there is a concern in patients with soy and egg allergy. The unused portion of the drug must be discarded after 4 hours to avoid contamination. Side effects include onset of atrial fibrillation, headache, flushing, fever, and nausea and vomiting. The advantages of clevidipine are its ultrashort half-life, along with ease of titration, predictable response, and lack of toxicity and drug interactions.\textsuperscript{34}

**HYDRAZINE**

Hydralazine is a direct arteriolar vasodilator with little to no effect on venous capacitance vessels. The drug causes reflex sympathetic activity with an increase in circulating catecholamines. This vasodilation and sympathetic discharge causes an increase in CO, myocardial contractility, and reflex tachycardia.

The tachycardia will increase the myocardial oxygen demand and myocardial oxygen consumption, so hydralazine should be avoided in patients at risk for myocardia ischemia. Cerebral vessels also vasodilate and that will allow an increase in intracranial pressure. The clinical relevance of this effect is debatable; but to be safe, hydralazine is contraindicated in closed head injury.

The onset of activity is 5 to 15 minutes, but the onset may be followed by an unpredictable and severe decrease in BP that can last for up to 12 hours. The circulating blood half-life is 3 hours, but the drug’s clinical half-life is up to 10 hours. The duration of action is between 2 to 10 hours, depending on the ability of the liver to metabolize the drug. The maximum decrease in BP in most cases is 10 to 80 minutes after bolus injection. Clinically, there is a decrease in SBP, DBP, and MAP.\textsuperscript{11,35}

There are multiple dosing guidelines found in the literature. The reason is that the response is unpredictable and the risk of prolonged hypotension is real. In using this drug, a conservative approach is necessary; and we need to remember that although the perioperative BP readings may be high (SBP $\geq$180 mm Hg), most of these cases, at least initially, are urgencies and not emergencies. We have the time to slowly decrease the BP.

**One approach to consider**

The initial dose of hydralazine is 2.5 to 5.0 mg IV over 2 minutes. Wait for 10 to 15 minutes, then give a repeat of the initial dose or increase that dose. The maximum dose in the office should be 20 to 25 mg (Table 9).\textsuperscript{36}

Hydralazine has been used as an office treatment of perioperative HTN for many years. It is
no longer a first-line agent because there are other options with less risk of hypotension and tachycardia-induced ischemia. This availability of other options is certainly true in a hospital setting. But in the office, these newer agents are not readily available; they are expensive, and they require infusion technology. When left with hydralazine as a treatment option, we need to assess the risk of such treatment in our consultation visit. In doing so, the potential harm to patients may lead us to doing this case in a facility that has more medication options. It is up to each practitioner to make that judgment.

NITROGLYCERIN

Nitroglycerin (NTG) is primarily an antianginal agent because it dilates coronary arteries, relieves coronary vessel spasms, and increases blood flow to ischemic myocardial tissues. At low doses, it is a potent venodilator decreasing the preload and the LVEDP and LVEDV. The result is a decrease in myocardial oxygen demand and a relief of ischemia and pain. The decrease in BP is secondary to reductions in the preload and CO. These effects are seen regardless of the route of administration (sublingual, patch, or IV).

At higher doses of NTG, arterial vessels dilate, which then decreases the afterload of the heart. This decrease makes it easier to pump blood to the aorta with less myocardial oxygen consumption. The IV dosage of NTG is 5 to 10 mics/min or 0.075 to 0.15 mics/kg/min. This dosage can be increased by 5 to 10 mcg/min every 3 to 5 minutes.

The onset of action is within 2 to 5 minutes, with a duration of 10 to 20 minutes after the infusion is stopped. Side effects are headache, reflex tachycardia, and, on rare occasions, methemoglobinemia.\(^\text{18}\)

APH can lead to hypovolemia. If NTG is administered in the presence of hypovolemia, an exaggerated hypotensive episode will follow. NTG is not a first-line agent for APH because of this possibility along with the reflex tachycardia that most always occurs at doses of NTG that can decrease BP. NTG is an adjunct therapy to other antihypertensive medications in patients that present with acute ischemia, infarction, or pulmonary edema, which are situations when you need a decrease in preload, afterload, and myocardial oxygen consumption.\(^\text{1}\)

Before NTG is used, patients should be asked about erectile dysfunction medications, the phosphodiesterase-5-inhibitors. Patients need a 48-hour washout period for these agents, otherwise NTG can cause severe hypotension that may be unresponsive to most vasopressors.

<table>
<thead>
<tr>
<th>Table 9</th>
<th>Hydralazine dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Dose Bolus</strong></td>
<td><strong>Repeat Dose Bolus</strong></td>
</tr>
<tr>
<td>10–20 mg IV</td>
<td>None given</td>
</tr>
<tr>
<td>10–50 mg IM dose not IV</td>
<td>None given</td>
</tr>
<tr>
<td>5–10 mg IV over 2 min</td>
<td>5–20 mg IV q 6 h</td>
</tr>
<tr>
<td>10–20 mg IV</td>
<td>Repeat q 4–6 h</td>
</tr>
<tr>
<td>2.5–5.0 mg IV</td>
<td>None given</td>
</tr>
<tr>
<td>3–20 mg IV</td>
<td>Repeat q 20–60 min</td>
</tr>
<tr>
<td>AAOMS manual, eighth edition</td>
<td>Titrate up to 25 mg</td>
</tr>
<tr>
<td>5 mg IV</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AAOMS, American Association of Oral and Maxillofacial Surgeons; IM, intramuscularly.

Is There a Role for Sublingual NTG in Office Perioperative HTN?

Most practitioners have limited choices for managing HTN in the office. Typical IV agents are labetalol, esmolol, and possibly hydralazine. A beta agent is not a good choice for a hypertensive event in patients with acute, severe bronchoconstriction. Patients with acute angina who are hypertensive do not need an agent like hydralazine whereby the tachycardia will make the ischemia worse, so what is left?

In this circumstance, the use of low-dose sublingual NTG can help. It certainly is indicated in patients who are anginal; in patients with asthma, if you do not have hydralazine, the NTG can be helpful. Where is the peer-reviewed literature to back this up? At present, it is lacking, but there are practitioners who use it.

A recommendation found in a 2005 ADSA General Anesthesia Review course outlines the use of sublingual NTG for HTN. Using 0.4-mg sublingual tablets, 1 to 2 tablets are placed under the tongue. The onset of action is within 15 to 20 minutes, with a duration of 5 to 7 minutes, and the onset may be faster. It may be more useful to use ACLS dosing guidelines of every 5 minutes. Anecdotally, emergency medical services (EMS) providers that treat far more cardiac complications than OMFS, use sublingual NTG for HTN on route to the hospital. Anesthesiologists have used NTG spray for short-term hypertensive reactions from exogenous epinephrine; in the cardiac catheterization laboratory, cardiologists have used the spray during their procedures. Because of a lack of published data, a recommendation cannot be made; but practitioners do use off-label treatments. It is up to the surgeon to make that call.
CLONIDINE

Clonidine is a centrally acting alpha-2 adrenergic receptor agonist that prevents the release of norepinephrine from the sympathetic nervous system and acts on CNS I-1 receptors to cause centrally mediated vasodilation and hypotension. Clinically, there is a reduction in peripheral vascular resistance, heart rate, and BP.18

As an anesthetic agent, it reduces the MAC (minimum alveolar concentration) of volatile gases and opioid requirements for pain. It also reduces the sympathetic response to intubation. In the United States, it is only available in oral and transdermal patches, but other countries have an IV formulation.15

There is a lack of published data to support the routine use of clonidine for acute postoperative HTN, most likely because of the lack of an IV route of administration. However, there are data for the perioperative effects of clonidine. Oral or transdermal clonidine the night before surgery decreases the MAP for up to 24 to 48 hours and reduces the levels of circulating catecholamines.37

Wallace38 studied preoperative clonidine in patients at risk for CAD who required noncardiac surgery. They used a 0.2-mg oral dose plus an applied transdermal patch the night before surgery; they also gave patients a 0.2-mg oral dose 1 hour before surgery. Patients continued to receive 0.2 mg oral clonidine postoperatively for 4 days, and the patch was removed at that time. The results showed less episodes of perioperative HTN and ischemia. The patients did have more episodes of tachycardia than patients on BB, but the ischemia improvement was similar to the BB.

Side effects are headache, nausea and vomiting, and hypotension that responds to IV fluids. These reactions occur within 30 minutes to 1 hour after taking the drug, but they can last up to 10 hours.3

There is a role for clonidine in office anesthesia. Friedberg uses an office plastic surgery technique where clonidine is given preoperatively taking the place of midazolam, and this is followed by an intravenous anesthetic consisting of ketamine and propofol.

Another indication for clonidine would be patients with HTN who present in the office for a minor oral surgical procedure under local anesthesia but have a BP more than 180/100. When you ask patients about antihypertensive medication compliance, they tell you, “I take my meds daily, my BP is high just because I am here.” The primary care physician (PCP) tells you, “The BP is controlled and this is just white coat syndrome, so just take out the teeth.”

Clonidine is useful here. It can be given 0.1 to 0.2 mg orally as a solo agent or it can be combined with an anxiolytic. Clonidine will decrease BP, and it also has a sedative effect. The patch is not useful because it takes too long for an effect.

PHENTOLAMINE

Phentolamine is a pure alpha-adrenergic antagonist. The primary indication for this agent is a catecholamine-induced hypertensive emergency like a pheochromocytoma or a monoamine oxidase inhibitor hypertensive crisis. It is not a first-line drug for perioperative HTN.

The dosage in perioperative HTN is 1 mg every 5 to 10 minutes, with a range of 1 to 5 mg. The onset of action is within 1 to 2 minutes, with a duration of 3 to 15 minutes. Side effects include flushing and headache. This agent is often difficult to obtain because it is rarely indicated, so its usefulness as compared with other agents is minimal.19,39

NITROPRUSSIDE

No discussion of the management of acute HTN is complete without nitroprusside. It was the gold standard of care for hypertensive emergencies. The drug is both a venous and arterial vasodilator that reduces preload, afterload, and peripheral venous resistance. IV infusion has a near-immediate response, with a range of 1 to 2 minutes; once the infusion is stopped, the duration of action is about 2 minutes.

The side effects are problematic. Cerebral blood flow is diminished, whereas the intracranial pressure is increased. In the heart, coronary steal (a process whereby blood flow is diverted away from ischemic areas) happens frequently. Renal function and blood flow are also decreased.39 Cyanide and thiocyanate toxicity are side effects from prolonged infusions of nitroprusside. Nitroprusside metabolism releases cyanide, which is then detoxified by circulating thiosulfate molecules. The amount of cyanide depends on the amount of available thiosulfate in the circulation.

Infusions of nitroprusside exceeding 4 to 5 mics/kg/min for as little as 2 to 3 hours cause cyanide toxicity. Signs include headache, anxiety, confusion, lethargy, and coma. Cardiovascular signs are ischemia, dysrhythmias, AV heart block, and cardiovascular collapse. Patients may also report nausea and vomiting, abdominal pain, and increased salivary flow.1

To prevent cyanide toxicity, thiosulfate is added to the infusion at a ratio of 10:1. It will not decrease the antihypertensive effect of nitroprusside. The
byproduct of cyanide metabolism by thiosulfate is thiocyanate, which is 100 times less toxic than cyanide.\textsuperscript{2}

The dosage for nitroprusside is 0.25 to 0.5 mics/kg/min increased by 0.5 mics/kg/min every 5 to 10 minutes. Do not exceed a total dosage of 5 mics/kg/min.

Nitroprusside is no longer a first-line agent for hypertensive urgencies and emergencies. Its renal, cerebral, and cardiac side effects are significant. In addition, it is mandatory to use arterial line catheters to monitor BPs with this agent. There is no reason to consider the use of this drug in an office.\textsuperscript{11}

RENIN ANGIOTENSIN SYSTEM

This system regulates BP and intravascular volume. Antihypertensive drugs in the category are ACEI and ARB. ACEI block the conversion of angiotensin I to angiotensin II, a vasoconstrictor. ARB block the effect of circulating angiotensin II.

Intraoperative HTN can be treated with enalaprilat, an ACEI. It will reduce MAP, SBP, DBP, and the preload. The vasodilation decreases the afterload, but there is no reflex tachycardia. Enalaprilat maintains cerebral blood flow with no change in intracranial pressure.

The dose is 0.015 mg/kg or 0.625 to 1.25 mg IV over 5 minutes, and it can be repeated in 20 to 30 minutes if the first dose was ineffective. Additional doses can be given every 6 hours. The onset of action is within 15 minutes; it peaks in 1 hour, and the duration of action is more than 4 hours. This drug would not be a first-line agent for perioperative HTN.\textsuperscript{10,18}

OFFICE AND AMBULATORY ANESTHESIA AND ANTIHYPERTENSIVE AGENTS

Do We Hold These Agents or Maintain Them During Surgery?

BB should be maintained perioperatively, and this was discussed earlier in the article.

CCB may not be cardioprotective during surgery, but there is no evidence to suggest any detrimental effects, so they too are maintained perioperatively.

ACEI and ARB

These drugs are frequently used to manage HTN, HF, and chronic renal failure. Pharmacologically they should be cardioprotective during surgery, but they are the most likely antihypertensive agents to cause significant intraoperative hypotension. This hypotension is less responsive to IV fluid challenges and vasopressors like ephedrine, phenylephrine, and epinephrine. At present, there is controversy as to holding these drugs preoperatively or maintaining them perioperatively.\textsuperscript{23}

During the first 30 minutes of anesthesia, there is greater volatility in BP. This volatility is related to possible decreased intravascular volume from being NPO or chronic HTN. Anxiety also has a role, and the pharmacology of the anesthetic induction drugs has a major role. After the first 30 minutes, BP changes tend to be less volatile and more stable.

ACEI and ARB have a typical half-life of about 10 hours. Comfere and colleagues\textsuperscript{40} examined the incidence of hypotension during the first 30 minutes of anesthesia in patients who stopped their medications in less than 10 hours and 10 hours or more preoperatively. The incidence of moderate hypotension (SBP ≤ 85 mm Hg) was 60.4% in the less-than-10-hour group and 46.3% in the 10-hour-or-more group. There was no difference between groups in the incidence of severe hypotension (SBP ≤ 65 mm Hg), and there was no difference in the response to vasopressor treatment.

The presence of other antihypertensive drugs did not affect the incidence of hypotension. They concluded that ACEI and ARB drugs are significant risk factors for moderate hypotension during the first 30 minutes of general anesthesia. Because this hypotension did not result in significant adverse effects, there is no support for stopping these drugs preoperatively in all patients. However, a practitioner should consider holding these drugs for patients that cannot tolerate acute hypotensive episodes.\textsuperscript{40}

ARB induce more profound and more frequent episodes of intraoperative hypotension than do ACEI. When diuretics are combined with ARB drugs, the hypotension is more exaggerated. Brabant\textsuperscript{41} reported that perioperative hypotension occurred in 100% of patients who maintained their ARB the morning of surgery. Bertrand and colleagues\textsuperscript{42} found that intraoperative hypotension was greater and required more vasopressor treatment when the ARB was taken the morning of surgery.

WHAT SHOULD WE DO?

If ACEI and ARB drugs are not stopped, the risk of hypotension is significant; but it still can occur if the drugs are stopped 24 hours before surgery. Although omitting 1 dose does not seem to cause adverse effects, most of the hypotensive episodes will respond to IV fluids and the usual vasopressors found in the office. For office anesthesia, the risk is minimal if ACEI and ARB drugs are maintained. However, consideration should be given to holding the morning dose of the diuretic.
because it exacerbates the level of hypotension with ACEI and ARB. We can further decrease the risk of hypotension by infusing at least 500 ml of lactated ringers (LR) or normal saline (NSS) for our office anesthetics. The first treatment of hypotension is a fluid challenge, so butterfly IV anesthesia without IV fluids needs to be abandoned.  

**GENERAL MANAGEMENT OF PERIOPERATIVE HTN**

**HTN with Bradycardia**

Where do we start the treatment, the bradycardia or the HTN? If you initiate treatment aimed at the bradycardia, you can make the situation worse. There is already an increased afterload consuming myocardial oxygen, so if you speed up the rate, you increase myocardial oxygen demands and decrease coronary oxygen supply. In this case, the use of the anticholinergic drug atropine should be avoided.

How do we treat the HTN? BB are not a good choice because they work by decreasing the heart rate, and patients are already bradycardic. There are many other drugs that can be used, but the question is what do we have in the office? The most likely agents would be hydralazine or NTG tablets.

**HTN with Tachycardia**

Patients who have CVD do not tolerate prolonged tachycardia or HTN. These two factors significantly increase the heart’s need for coronary blood flow to prevent ischemia. In this case, you need to assess the level of anesthesia. Are patients too light? Do patients need an increase dose of opioids for pain, or do they need additional local anesthesia?

The antihypertensive management in this case would be a BB. The BB will decrease the heart rate and lower the BP. Esmolol or labetalol would be excellent agents to use in this case.

**PCP AND EMERGENCY DEPARTMENT REFERRALS**

In the office, patients with stage 1 HTN (SBP 140–159 mm Hg, DBP 90–99 mm Hg) with no symptoms pose little risk for treatment in the office. They need to be referred to their PCP for a nonurgent appointment. What is your protocol for patients with HTN who arrive in the office for treatment but their BP is more than 180/120? By JNC guidelines, this is a hypertensive crisis, and treatment depends on differentiating an emergency versus an urgency. Our primary obligation to these patients is to inform them of the pressure reading and explain why this should not be ignored. A referral is made that day to their PCP or to the emergency department. They will make the diagnosis of emergency or urgency and proceed from there.

A brief history and physical examination is necessary in these cases. Are antihypertensive medications being prescribed for patients and, in fact, are they taking them as directed? Do they have a past history of MI, HF, stroke? Do they use any recreational drugs?

At present are they experiencing chest pain, dyspnea, severe headache, confusion, visual disturbances, or nausea and vomiting. Call the PCP with the findings; if they are unavailable, tell patients you think it is in their best interest to go to the emergency department. Expect patients to be resistant, but tell them there is a possibility of complications, including heart attack if this is not addressed. It is up to patients to take responsibility, but no oral surgery care will be done until this is addressed.

The emergency department or the PCP is necessary to rule out target organ disease. Fundoscopic examination will rule out hemorrhage, exudates, and papilledema. A 12-lead ECG and troponin levels are indicated for cardiac at-risk patients, and a neurologic evaluation should also be done.

If there is no evidence of end organ damage, this is a hypertensive urgency. In newly diagnosed patients, the emergency department may refer to the PCP for an urgent (1–5 days) follow-up. Some patients may be given an antihypertensive medication in the emergency department and kept for a few hours for observation.

In rare cases, patients may be admitted, especially if they have no PCP of record and will not be able to find a physician in the next few days. BP therapy is started; patients are admitted; social work arranges for follow-up.

In cases of a hypertensive emergency, patients are admitted for antihypertensive therapy. The MAP will be reduced 20% to 25% over the first hour, and then target BP is achieved over the next 6 hours.

Anecdotally, some of us have had the experience of sending a patient to the emergency department for severe BP and received a call questioning our reasoning for this nonurgent referral. It is not our responsibility to make the diagnosis of a hypertensive urgency versus and emergency; we need a **physician to rule out the possibility of a hypertensive emergency.**

**COSTS OF ANTIHYPERTENSIVE AGENTS**

The past few years have seen critical shortages of medications along with costs that have increased...
dramatically. Availability of drugs used on a daily basis is unpredictable and frustrating. The following chart lists agents discussed in this article along with estimated pricing, which varies frequently (Table 10). Also, tables of stage I and II hypertension drug therapy are presented (Tables 11 and 12).

PERIOPERATIVE HYPOTENSION

Syncope is the most common medical emergency in the dental office. Hypotension develops as a result of peripheral venous pooling of blood. This condition causes a decrease in the preload, so BP decreases and cerebral blood flow is decreased to the point of a loss of consciousness. During the third trimester of pregnancy, patients in the supine position will experience the supine hypotensive syndrome from compression of the inferior vena cava. The treatment is to turn patients onto their left side to reestablish vena cava blood flow. Patients can also experience hypotensive episodes if they stand up too quickly from the dental chair. This postural hypotension frequently occurs in the senior population, but medications with this side effect can make patients in any age group more susceptible.

Patients are NPO before anesthesia, so they do have an intravascular volume deficit; but this minor decrease in volume by itself is unlikely to cause hypotension. Patients arriving in the office for anesthesia usually do not have preoperative hypotension and tachycardia. Their anxiety is more likely to present as minor elevations in BP as compared with their consultation BP along with tachycardia. However, the combination of volume status from being NPO and anesthetic induction medications can cause a hypotensive episode. Propofol and/or volatile anesthetic gases are known to decrease BP.

During the maintenance phase of anesthesia, medications can continue to affect BP. Propofol, when used as a solo general anesthetic agent, will decrease BP. The amounts of propofol needed to maintain that general anesthetic state can decrease MAP to a point of hypoperfusion that will require small doses of vasopressors.

Allergic reactions during anesthesia are another source of hypotension, so the anesthesia team needs to monitor patients for signs of rash, hives, or angioedema during the case. Other causes of hypotension include hypoxia and hypercarbia; but with the use of the precordial stethoscope, pulse oximetry, and capnography, early detection and intervention can eliminate these as causes of hypotension.

Rare but possible causes of hypotension are pneumothorax and pulmonary embolism. Medication errors are another possibility.

Initial Management of Hypotension

The first step would be to place patients in a supine position and possibly elevate the legs. The next step is to evaluate patients for the cause of the event.

Oxygenation and ventilation need to be assessed. Surgeons will need to auscultate all of the lung fields and then check the equipment. Is the oxygen delivery system working and is it connected to the patients? Are the monitor alarms disabled? Is the pulse oximeter probe connected? Is the capnograph connected?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Size</th>
<th>Average Cost ($)</th>
<th>Availability</th>
<th>Usual Supply Houses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>5 mg/mL 20 mL</td>
<td>5.00–6.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Esmolol</td>
<td>10 mg/mL 10 mL</td>
<td>22.00–26.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>5 mg/5 mL</td>
<td>7.00–20.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Hydralazine</td>
<td>20 mg/mL</td>
<td>18.00–20.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>NTG</td>
<td>5 mg/mL 10 mL</td>
<td>8.00–9.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Diltiazem</td>
<td>5 mg/mL 5 mL</td>
<td>3.50–4.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Verapamil</td>
<td>2.5 mg/mL 2 mL</td>
<td>5.00–10.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>1.25 mg/mL 2 mL</td>
<td>9.00–10.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Phentolamine</td>
<td>5 mg/2 mL</td>
<td>95.00–112.00</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Clevidipine</td>
<td>0.5 mg/mL</td>
<td>&gt;&gt;100.00</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td>25 mg/mL</td>
<td>&gt;&gt;100.00</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

Costs accessed on the Internet on 11/29/2012 from multiple sites and then averaged. Prices and availability vary weekly.
**TREATMENT OF PERIOPERATIVE HYPOTENSION**

Before vasopressors are given, the depth of anesthesia should be reduced and a bolus of IV fluid should be tried. The dose can be up to 10 mL/kg, and a typical starting dose in adults is 250 mL of LR or NSS. These doses can be repeated as needed.

If an allergic reaction is suspected, then epi-
nephrine should be the agent of choice. An intra-
muscular adult dose is 0.3 mg of 1:1000. In the event of a severe reaction, an IV dose of 10 to 20 μg of 1:10 000 can be used but expect to see cardiac side effects. If this is the start of an anaphy-
lactic reaction, the side effects from the IV epi-
nephrine are far less a problem than the cardiac arrest that will follow if we do not use the epinephrine. If an allergic reaction is not suspected, epinephrine will not be the drug of choice for the perioperative hypotension.

Patients that present with hypotension and brady
cardia (heart rate <60 beats per minute) are sometimes treated with an anticholinergic agent like atropine. The dosage is 0.5 mg IV every 3 to 5 minutes up to a maximum dose of 3.0 mg. It may be difficult to get vials of 0.5 mg or 1.0 mg unless you order a prefilled syringe. Most of the time, atropine comes in 0.4 mg/mL, so this dose can be used. The reasoning behind this technique is that if you increase the heart rate, cardiac out-
put will increase and BP increases will follow. A better alternative would be to use ephedrine or phenylephrine.

Ephedrine is an alpha and beta agonist that increases heart rate, SBP, and DBP. It affects venous constriction more than arterial constriction, and this results in an increase in preload and CO to increase BP. There is a minor increase in afterload but far less than the preload, so it is easier for the heart to eject blood; so there is less myocardial ox-
ygen consumption than with epinephrine. Side ef-
tects that may be beneficial are bronchodilation and a minor antiemetic effect.

The dosage in adults is 5 mg IV bolus every 5 to 10 minutes as needed. The onset of action is within 10 minutes, with a peak effect in 20 minutes. The duration of action is 4 hours. The drug comes in a 50-mg/1 mL vial, so it is diluted in 9 mL of fluid making the dose 5 mg/mL. In patients with CVD, ephedrine should be limited to cases of hypotension without tachycardia.

Phenylephrine is an alpha agonist that causes vasoconstriction. It too has more of an effect on venous vessels than arterial, so the preload is increased, which increases CO and BP. This drug causes a reflex bradycardia, so it is an excel-
lent choice in patients with hypotension plus tachycardia.

Phenylephrine 1% usually comes in a 10-mg/1 mL vial. This drug requires a double dilution technique to get to the 100-μg/mL dose. The phenylephrine is diluted into 9 mL of fluid, and then 1 mL from that syringe is diluted into another 9 mL of fluid. This now gives you a concentration of 100 μg/mL. The dose is 100 μg in adults. The onset of action is within 2 to 3 minutes, with a duration of 15 minutes. Repeat dosing in every 5-minute intervals.

**How Do You Manage a Case of Refractory Perioperative Hypotension?**

Most patients respond to vasopressors like ephed-
rine or phenylephrine along with IV fluids. If that is ineffective, epinephrine mini-boluses of 10 μg IV
can be started, and the dose can be increased up to 20 mics as needed. An infusion of 2 to 10 mics/min can be titrated to an effect. Diluting 1 mg of epinephrine in 500 mL of D5 W yields a 2 μg/mL concentration. The use of epinephrine for hypotension is a treatment of last resort because of potential side effects. If patients require this type of support, EMS should be called for immediate transfer to a hospital.

Patients taking ACEIs or ARBs are well known to have more episodes of perioperative hypotension, and they are also less likely to respond to the vasopressors discussed earlier, including epinephrine. Vasopressin, a peptide hormone secreted by the hypothalamus, can stimulate V1 receptors found in vascular smooth muscle; this results in vasoconstriction.

Vasopressin can be given as an IV bolus starting at 0.4 U every 10 minutes; if that is ineffective, it can be increased to 2 U every 10 minutes, or an infusion of 0.04 U can be started and increased as needed. Vasopressin has a half-life of only 6 minutes and has a side effect of decreasing renal perfusion, so urine output must be monitored. The cost of vasopressin is approximately $5.00 for a dose of 20 U/1 mL.

**CONTROLLED HYPOTENSIVE ANESTHESIA**

Controlled hypotensive anesthesia has been used for more than 50 years. The benefits are a reduction in blood loss with less need for blood transfusions, a clear view of the operating field, and a reduction in surgical time. Multiple agents have been used in this technique: volatile anesthetics, sodium nitroprusside, IV NTG, and nicardipine.

It is defined as a reduction in SBP to 80 to 90 mm Hg or a reduction in MAP to 50 to 65 mm Hg. In normotensive healthy patients, reductions in MAP to 55 to 65 mm Hg did not result in target organ damage from hypoperfusion. A growing concern in all of anesthesia is postoperative cognitive dysfunction. Choi and colleagues studied the effects of NTG and nicardipine hypotensive anesthesia on cerebral oxygen saturation, and they found that at MAP of 60 to 65 mm Hg, the saturation was unaffected and cerebral cognitive function was not impaired.

The vasodilating agents used in these techniques can cause a reflex tachycardia. It will not occur in all cases, but the incidence has been reported to be about 70%. The concern is the increased myocardial oxygen consumption from the tachycardia. BB have been used both preoperatively and intraoperatively to reduce tachycardia. Preoperative propranolol, 10 mg orally, and esmolol 0.5 mg/kg IV for intraoperative heart rates of more than 95 beats per minute have been found to be safe and effective.

Controlled hypotension requires indwelling arterial line catheters to monitor BP along with urine output measurements to decrease the risk of hypoperfusion. In the future, the use of cerebral oximetry may become a standard of care to decrease the risk of postoperative cognitive dysfunction.

**CONTROVERSIES IN PERIOPERATIVE HTN AND HYPOTENSION**

In an operating room, most of our surgery is done in the supine position on an operating room table. However, in the office, our patients are in a dental chair and the surgeon is usually standing. This means that patients are in a head-up position of 30° or more. Does this place patients at an increased risk of cerebral hypoperfusion?

Cerebral autoregulation is the body’s ability to maintain cerebral blood flow over a range of BP. For normotensive patients, this range is reported to be a MAP of 50 to 150 mm Hg. With chronic HTN, there is a shift to the right, so an MAP of 50 mm Hg will now result in hypoperfusion of the brain, placing patients at risk for injury, ischemic infarcts, or postoperative cognitive dysfunction. Immink and colleagues reported the range of cerebral autoregulation to be 60 to 150 mm Hg, and a range of 115 to 170 mm Hg in patients with HTN. The upper limits cannot be tested in humans, so these values come from studies in baboons.

In normotensive patients despite cerebral autoregulation, the baseline cerebral blood flow in the supine position can decrease by 14% to 21% when patients stand up. Any elevations in head position more than 20° from the horizontal position will cause a decrease in cerebral blood flow. In awake patients, these effects are compensated by increases in the SVR to maintain flow; but during anesthesia, the vasodilating anesthetic agents block this sympathetic response.

Cerebral perfusion pressures even in awake patients will decrease by 15% when they sit down, so it is safe to assume that during anesthesia, those pressures will decrease to a greater degree from the anesthetic agents.

Since 2007, the Anesthesia Patient Safety Foundation has been investigating the effects of patient positioning and controlled hypotensive anesthesia on cerebral blood flow. Some of their preliminary findings are quite revealing.

During surgery in a supine position, the BP measured at the arm is equal to the BP in the brain. However, in a head-up position, the cerebral BP is less than the arm reading. This difference is 1 mm
Hg for each vertical measurement of 1.25 cm as measured from the arm to the external auditory meatus of the ear (level of the base of the brain). F52

Drummond, F53 in a review of the literature, now recommends a lower limit of 70 mm Hg for autoregulation in the supine position for normotensive patients. One of his reasons is that 45% of patients have an incomplete Circle of Willis, which decreases autoregulation function. The workshop findings also recommended that surgery done in a beach chair position (head elevated 30°–90° from horizontal) should have BP adjusted for hydrostatic gradients from the arm to the ear and that controlled hypotensive anesthesia should be avoided in this position. Reductions in baseline pressures should not exceed 30% in the sitting position. F53

Sanders and colleagues, F54 in an editorial, recommended that in patients with HTN and those with vascular disease hypoperfusion and hypoperfusion must be avoided. Their goal is to avoid HTN (SBP >160 mm Hg) and to keep hypotension to no greater than a 20% decrease in baseline pressure.

To no one’s surprise, there are also studies that say this risk of stroke and cognitive dysfunction is being overstated because the incidence of perioperative stroke in noncardiac and non-neurosurgery is low (0.1%), and most of the reported strokes are thromboembolic in nature. Data also show that during sleep, BP decreases about 30% from baseline, so intraoperative pressure decreases of 30% are acceptable, but you must keep in mind that this is in the supine position. The American College of Surgeons National Surgical Quality Improvement Program’s report in 2011 failed to establish perioperative hypotension as a risk factor for stroke in noncardiac and non-neurologic surgery. F55, F56 The debate will continue, and we need to remain in the loop for further information.

SUMMARY

Perioperative HTN does increase the risk of ischemia, infarction, HF, and stroke. For office-based anesthesia/surgery, it would be best to defer patients with an SBP of 180 mm Hg or more and a DBP of 110 mm Hg or more until their BP can be optimized. The antihypertensive agents that are typically found in offices will allow us to treat most of the hypertensive episodes that we will encounter, but we also have to realize that there are other agents that may be better in some instances but are, as yet, impractical for office use. The agents that we should consider stocking are esmolol, labetalol, NTG (spray or tablets), and maybe hydralazine.

Patients on maintenance antihypertensive agents should have those agents maintained during surgery, and this includes BB, CBC, and, in most cases, the angiotensin blockers ACEI and ARB. However, if patients are on a diuretic in addition to the angiotensin agents, that diuretic may be held preoperatively to reduce the incidence of hypotension.

Hypotension is usually managed by decreasing the depth of anesthesia, administering IV LR or NSS, and then adding vasopressors. Most offices have phenylephrine and ephedrine for these episodes, along with the ability to administer mini-bolus epinephrine. There may be an indication for vasopressin, and that decision should be up to the individual practitioner.

A conservative approach for perioperative hypotension prevention and management would be to replace NPO fluid deficits with IV fluids preoperatively and intraoperatively. Vasopressors should be used when MAP decreases to less than 60 mm Hg in normotensive, healthy adolescents or adults. Most patients will tolerate baseline BP decreases of 30% without the risk of target organ damage, especially cerebral ischemia or postoperative cognitive deficits. However, there is an increasing concern, especially in the elderly, about postoperative cognitive deficits from the agents that are being used and the level of hypotension intraoperatively. We need to keep abreast of current literature regarding these issues.

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