Hypertension (HT) in children, although less common than its adult counterpart poses a far more serious risk with increased morbidity and mortality than adult HT. Pediatric HT is defined as the systolic or diastolic blood pressure (BP) above the 95th percentile for gender, age, and height [1-3]. Hypertensive crisis however, has a totally different definition and level of urgency and it is commonly divided into hypertensive emergencies and hypertensive urgencies.

A hypertensive emergency occurs when BP is severely elevated and signs and symptoms of end-organ involvement are present. Hypertensive urgency occurs, when despite a highly elevated BP there are no signs of end-organ damage. The management protocols for each of these two entities differ according to the underlying etiology and risk of further damage based on the therapeutic agent of choice. Etiology of HT as well as related end-organ damage must be considered in the work up and management of these two hypertensive crises [4-5].

The clinical presentation may vary among individuals; the symptomatic hypertensive child may have signs of hypertensive encephalopathy that include headache, seizures, vomiting, altered level of consciousness and papilledema [6].

MANAGEMENT

The management of hypertensive emergency should focus on lowering the BP in a safe and timely manner and treating any secondary complications that the HT may have caused. The goal of therapy should be a reduction in BP, but by no more than 25% of targeted reduction within the first 2 hours, then reduced gradually to normal over the next 3-4 days. This is because in long-standing HT cerebral vascular auto regulatory mechanisms are frequently overwhelmed and can no longer compensate for rapid changes in pressure. Rapid lowering of BP in such cases can result in serious neurological sequelae [7].

An asymptomatic child diagnosed as having a hypertensive urgency may have his or her BP reduced with the use of an oral antihypertensive medication administered over a period of 24 to 48 hours. It is recommended that one third of the total planned BP reduction be done during the first 6 hours, another third during the next 24 to 36 hours and the final third during the next 24 to 96 hours or even longer [8-9].

In children with hypertensive emergencies, vascular access should be established immediately and the patients should be place on cardiac and continuous BP monitoring (preferably by an intra-arterial catheter). Urine output should be monitored from the outset [10]. The child’s neurologic status should be observed closely for signs of cerebral hypoperfusion that include headaches, emesis, and confusion. If hypotension occurs or neurological signs are present during therapy, doses of antihypertensive medica-
tions should be adjusted and a fluid bolus administered [11]. Medications used to treat HT should be chosen according to availability, their side-effect profile, and physician familiarity with the drug. The intravenous route for medication administration is preferred because it allows for easier titration and more predictable absorption [12]. Commonly used drugs for the treatment of hypertensive emergencies in children are presented in Table I.

**Sodium Nitroprusside**
Sodium nitroprusside is the most commonly used pharmacologic agent for hypertensive emergencies. It is an arterial and venous vasodilator with minimal effects on the cardiac output [13]. It has an extremely short half-life and requires administration by continuous infusion. Once the infusion is discontinued, BP returns to previous levels as early as 30 to 60 seconds. The recommended starting dose is 0.3-0.5 µg/kg/min to a maximum of 8-10 µg/kg/min. Most patients respond to rates of 3 µg/kg/min [14].

Nitroprusside is metabolized by erythrocytes to cyanide, which is subsequently converted to thiocyanate in the liver and excreted by the kidneys. As a result, extreme caution should be exercised when using this drug in patients with impaired hepatic or renal function. Moreover, use of the drug for longer than 24 to 48 hours can lead to an accumulation of cyanide and thiocyanate in the blood, causing signs and symptoms of toxicity including metabolic acidosis, tachycardia, altered level of consciousness, decreased reflexes, and methemoglobinemia. Thiocyanate toxicity may also cause an alteration in mental status, as well as nausea, seizures, anorexia, and coma.

Because of this potential toxicity, cyanide and thiocyanate levels should be obtained when the medication is used in patients with hepatic or renal impairments, when infusions last more than 24 hours, or when used in doses higher than 3 µg/kg/min. Cyanide toxicity may be treated with amyl nitrite, sodium nitrate, and sodium thiosulfate. Sodium thiosulfate may also be used to prevent thiocyanate toxicity [15-16].

Sodium nitroprusside has been shown in adults to cause an increase in intracranial pressure, although it is believed that the accompanying drop in BP blocks the rise in cerebral blood flow. Consequently, nitroprusside is still recommended, in the adult literature, for use in patients with cerebrovascular accidents and hypertensive encephalopathy [17]. Nitroprusside for intravenous infusion should be admixed in 5% dextrose in water and should be protected from light to prevent its degradation. It should be avoided in pregnant adolescent patients [13].

**Labetalol**
Labetalol competitively blocks α and β receptors. It reduces BP by decreasing peripheral vascular resistance, with a minimal effect on heart rate and cardiac output. Its plasma half-life is 3 to 5 hours making it more difficult to titrate than sodium nitroprusside [1].

Labetalol may be administered by continuous infusion or bolus dosing. For continuous infusions, recommendations range from 0.2 to 3 mg/kg/hr. Labetalol may also be administered by intermittent boluses of 0.2 to 1 mg/kg, or by an initial bolus of 0.2 to 1 mg/kg followed by a continuous infusion of 0.25 to 1.5 mg/kg/hr [1].

As with many β-blockers, labetalol is contraindicated in patients with asthma and chronic lung disease as it may precipitate bronchospasm. It is also contraindicated in patients with congestive heart failure due to its negative inotropic and dromotropic effects. Labetalol may also mask signs and symptoms of hypoglycemia, and should be used with caution in children with diabetes mellitus [13].

**Nicardipine**
Nicardipine is a dihydropyridine calcium channel blocker, the first of its class approved for intravenous administration. It works by blocking the movement of calcium across vascular smooth muscle cells, thereby preventing contraction and decreasing total vascular resistance. Unlike other calcium channel blockers, nicardipine has limited effects on the function of the heart. Although nicardipine has been extensively studied in adults, experience in children is mostly limited to case reports. Most reports highlight use of the drug in cases where sodium nitroprusside or intravenous labetalol may be contraindicated, such as hepatic or renal failure, and in patients with asthma or lung disease [18-19].

The recommended starting dose of nicardipine is 0.5 to 1 µg/kg/min, to a maximum of 3 µg/kg/min. The rate of infusion should be increased every 15 to 30 minutes until the desired effect is achieved. Some authors recommend a starting dose of 5 µg/kg/min followed by 1 to 3 µg/kg/min once the desired mean arterial pressure is achieved. Nicardipine is metabolized in the liver. It begins to work within 1 to 2 minutes and has a duration of action of approximately 40 minutes [20].

Adverse effects of nicardipine include increased intracranial pressure. As a result, caution should be exercised in children with space-occupying lesions. Other side effects include headache, nausea, and hypotension [19].

**Esmolol**
Esmolol is a cardio selective β-adrenergic blocking agent with a very short half-life of 2 to 4 minutes. It has been used on a limited basis in children for the management of hypertensive crises associated with the repair of congenital heart disease [1].

When given by intravenous infusion, a loading dose of 100 to 500 µg/kg followed by a continuous infusion of 50 to 300 µg/kg/min should be administered. Side effects are similar to those of any other β-blocking agents; these may include bronchospasm, bradycardia, and congestive heart failure [8].

**Hydralazine**
Hydralazine is a potent arterial vasodilator that is used to reduce BP. Its onset of action is 5 to 30 minutes with a
Although it remains one of the oldest antihypertensive agents available, it has largely been replaced by faster acting, more effective drugs [1]. The drug is administered by the intravenous route, usually every 4 to 6 hours. The recommended dose of hydralazine is 0.1 to 0.5 mg/kg/dose to a maximum dose of 20 mg. Adverse effects include flushing, tachycardia, hypotension, and lupus-like syndrome [8, 15].

Fenoldopam
Fenoldopam is a selective dopamine agonist causing vasodilation of the renal, coronary, cerebral, and splanchnic vasculature, resulting in decrease in mean arterial pressure. The use of fenoldopam in pediatrics has increased in recent years. Case reports have demonstrated success with its use for controlled hypotension during spinal instrumentation, and in the intensive care setting when conventional therapy was unsuccessful [21-22].

In adults, peak effects of fenoldopam have been observed in 5 to 15 minutes, with steady-state serum levels achieved in 30 to 60 minutes. Infusion rates of 0.1 to 2 mg/kg/min have been reported for use in children. Side effects include reflex tachycardia, increased intracranial pressure, and increased intraocular pressure. Although pediatric experience with fenoldopam is limited, it appears to be a reasonable alternative to other more conventional therapies.

Diazoxide
Diazoxide is a potent vasodilator extensively used in children for hypertensive emergencies. It produces direct dilation of arterioles, resulting in a decrease in systemic BP, reflex tachycardia, and increased cardiac output. It has a rapid onset of action (1 to 5 minutes) and a long duration of action (3 to 12 hours). Recommended intravenous doses of diazoxide for children range from 1 to 3 mg/kg up to a maximum of 150 mg per dose when administered by rapid injection over a period of 30 seconds or less. It must be administered over 10 to 30 seconds because it is highly bound to albumin and its effects are dependent on the free drug reaching smooth muscle receptors. Doses can be repeated every 5 to 15 minutes until the BP is lowered to desired levels [13-14]. Although diazoxide is very effective, its use is limited by an unpredictable effect on BP and the propensity to cause hypotension, difficulty of dose titration, and a long duration of action. Other adverse effects include hyperglycemia (by inhibition of insulin release), rashes, hyperuricemia, sodium and water retention, flushing, and headaches [11].

Enalaprilat
Enalaprilat is an angiotensin-converting enzyme (ACE) inhibitor that produces vasodilatation and decreases systemic vascular resistance. This agent is particularly effective in lowering BP in patients who have high rennin levels [6]. The onset of action of enalaprilat may take 30 to 60 minutes after intravenous administration, which may limit its use during a true hypertensive emergency [13].

Effects may last for up to 4 to 6 hours. It is primarily eliminated (60% to 80%) via the kidneys, and therefore requires dosing adjustment if the patient has renal impairment. Suggested doses are 5 to 10 µg/kg/dose administered intravenously every 8 to 24 hours [23]. Enalaprilat can cause severe hypotension in patients who are volume depleted.

Its use is contraindicated in patients with bilateral renal artery stenosis [15].

Nifedipine
Much controversy has arisen in the literature over the use of nifedipine in the pediatric population. In adults, reports of adverse cardiac and neurologic sequelae secondary to

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**TABLE I**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Onset of Action</th>
<th>Duration of Action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Nitroprusside</td>
<td>0.3-8 µg/kg/min IV infusion</td>
<td>Seconds</td>
<td>During infusion only</td>
<td>May increase ICP.&lt;br&gt;Risk of cyanide and thiocyanate toxicity.</td>
</tr>
<tr>
<td>Labetalol</td>
<td>0.4-3 mg/kg/hr IV or 0.2-1 mg/kg initial bolus then 0.25 -1.5 mg/kg/hr</td>
<td>2-5 min</td>
<td>2-6 hours</td>
<td>Contraindicated in asthma,&lt;br&gt;chronic lung disease and heart failure.&lt;br&gt;May mask hypoglycemia.</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>0.5-3 mg/kg/min IV infusion</td>
<td>2-5 min</td>
<td>30 min-4 hr</td>
<td>May increase ICP.</td>
</tr>
<tr>
<td>Esmolol</td>
<td>100-500 µg/kg loading then 50-300 µg/kg/min</td>
<td>Immediate</td>
<td>10-30 min</td>
<td>May cause bronchospasm and congestive heart failure.</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>0.1-0.5 mg/kg/dose (max 20 mg/dose)</td>
<td>5-30 min</td>
<td>4-12 hr</td>
<td>Less potent than others.</td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>0.1-2 µg/kg/min</td>
<td>5-40 min</td>
<td>60 min</td>
<td>Limited experience in children.</td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>5-10 µg/kg/dose</td>
<td>Up to 60 min</td>
<td>4-6 hr</td>
<td>Useful for high rennin states.</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>1-3 mg/kg up to 150 mg/dose</td>
<td>1-5 min</td>
<td>3-12 hr</td>
<td>Difficult to titrate.</td>
</tr>
</tbody>
</table>
hypotension from the use of nifedipine have led to a moratorium on its use in the treatment of adult HT. This has led many to question its use in children. Similar sequelae related to hypotension have not been observed in children, however. Instead, case reports have been published detailing rebound HT causing adverse neurological events associated with the use of short acting nifedipine [24].

Nevertheless, many nephrologists continue to use nifedipine for the treatment of moderate to severe HT. Blaszak et al. [25] published a retrospective study of 117 children treated with nifedipine, and found that the drug is safe and effective provided the initial dose is no greater than 0.25 mg/kg. No clinically significant side effects were observed during the study.

Nifedipine can be administered sublingually or orally. For enhanced absorption, the liquid-filled capsule may be bitten and swallowed. Because the smallest dose available is a 10-mg capsule, the liquid within the capsule is often aspirated with a small needle for smaller dosing requirements. Due to the unpredictable nature of the orally administered drug, it is recommended that use of nifedipine be limited to hypertensive urgencies alone. Intravenous medications are better suited to hypertensive emergencies.

SUMMARY
Although relatively uncommon, pediatric hypertensive urgencies and emergencies must be recognized and treated promptly. Treatment goals are to lower the BP in a safe and effective manner, and to recognize and treat any secondary sequelae which may result from the hypertensive crisis. Therapy should be administered, preferably parenterally, with fast-acting medications that have the shortest duration of action. Several medications are available; choice should be based on the cause of the HT and the adverse effect and safety profiles of the medications. Once treatment is started, children should be monitored closely in an intensive care setting with close monitoring of the BP, neurological and clinical examination.

REFERENCES