INTRODUCTION

The evaluation of children with elevated blood pressure (BP) differs somewhat from that of the adult. Because secondary causes for hypertension (HT) are much more common in children, particularly pre-adolescents, clinicians treating children with HT are obligated to look for underlying etiologies. In the most recent guidelines of the National High Blood Pressure Education Program Working Group, the diagnostic approach to the child with HT provides rationale for such a work up, as well as a list of studies and the indication to perform more invasive, and potentially less fruitful studies [1-3]. There are only few studies which provide hard data on the utility of a given test in the hypertensive child [4]. Therefore, the individual clinician’s experience and discretion often direct diagnostic evaluations.

This review will present the concepts for the traditional approach of the authors. In general, three questions must be answered: 1) Is the child truly hypertensive? 2) Why is the child hypertensive? 3) Is there evidence for HT related target organ damage? 

IS THE CHILD TRULY HYPERTENSIVE?

Current definitions for HT have been discussed in another section of the journal. However, this issue cannot be overemphasized given that an extensive evaluation and potentially pharmacologic treatment may be initiated based upon the answer to this first question. Severe HT warrants a more timely evaluation; the current recommendations use a staging approach to assist the clinician with this issue [1].
For those children who have less severe HT, ambulatory BP monitoring (ABPM) is helpful in confirming the presence of abnormal BP pattern. Alternatively, home BP measurement is also an accepted although not equivalent approach to confirming to both the clinician and the family that the BP is increased outside the medical office. ABPM is continuous monitoring of BP usually over a 24-hour period. Typically 2-4 measurements are taken per hour. This method allows for calculation of a 24-hour mean BP, a diurnal mean BP, and a nocturnal mean BP. Specific threshold values for ABP in children are available and differ from the normative values for casual BP. The 95th percentile values for ABPM are based upon height and gender for diurnal and nocturnal periods. The patient’s ABPM mean systolic and diastolic BP levels are compared to available normative values. In addition, the percent of readings which are greater than the 95th percentile threshold values (the BP “load”) are also calculated for day and night. ABPM also allows evaluation for normal nocturnal decline in BP; BP levels usually decrease by 10% or more during sleep when compared to awake values. Furthermore, some of the evidence emerging from 24-hour ABPM studies demonstrates that children without an adequate nocturnal systolic decline are more likely to have renal scarring; this information may be used to direct the evaluation in that direction [5]. Emerging data is beginning to demonstrate that patterns seen in ABPM can aid in differentiating between primary and secondary HT as well as assessing for effectiveness of anti-hypertensive medications and dosage [1, 6]. Most importantly ABPM is extremely useful in ruling out white coat HT in the patient with mild to moderate HT. However, the use of ABPM requires specialized training for application and for interpretation, therefore it is best left in the hands of specialists who are experienced in this tool’s use and in the analysis of the information it provides [1].

**WHY IS THE CHILD HYPERTENSIVE?**

The etiology of HT is discussed in another section of this journal. However, in order to design a staged HT evaluation, one must have a good working knowledge of the potential causes, as well as their relative frequency. It is logical to start the diagnostic evaluation with tests which detect renal and renovascular disease and coarctation of the aorta. If these are ruled out, then search for less common causes may proceed depending upon the patient’s characteristics.

**RENOVASCULAR HYPERTENSION**

Renovascular HT is more often found in the younger child and among older children with more severe HT. Clues from the history include previous umbilical artery catheter, presence of neurofibromatosis or other genetic syndromes such as William’s syndrome, Marfan’s syndrome, or Klippel-Trenaunay-Weber syndrome. A history of systemic vasculitis (including Kawasaki disease) or abdominal irradiation also increases the risk for renovascular HT. On physical examination, the presence of multiple café au lait spots or an abdominal bruit suggests possible renovascular disease. Determination of plasma
renin when the child is ambulatory and prior to initiation of therapy can help identify those children with increased renin levels for further evaluation. However, since many children with proven renovascular HT have normal random plasma renin levels, the presence of a normal renin in a child with severe HT should not prevent further evaluation [9-11]. Most publications describing renovascular HT in children are single-center case series which report only those cases found to have abnormal renal arteries. However, one single center case series encompassing a 15-year period used clinical criteria to determine when to perform angiography in the hypertensive child namely, BP levels exceeding the 99th percentile or failure to control BP with a single anti-hypertensive agent [10]. Of the 28 children who underwent renal angiography, 43% had renovascular abnormalities. Comparison of those with and without renal arterial disease, found that those who had abnormalities had higher peak systolic BP levels (182 ± 11 vs 155 ± 7). Those with renovascular HT tended to be younger and more likely to have abnormal findings on renal ultrasound. Plasma renin levels and nuclear medicine renal scans are not reliable enough to distinguish which children are likely to have renal artery stenosis and should undergo angiography [9-10]. Another center reported 33 children seen over a 20-year period with renovascular disease. A significant percentage of patients demonstrated cerebrovascular disease (21%) or aortic involvement (24%) in addition to renovascular alterations [11]. Almost half of the children in this report had bilateral renal artery involvement and/or intrarenal arterial disease.

There is some emerging data in adult populations that suggest that improved renal Doppler ultrasonography correlates to digital subtraction angiography in patients that meet clinical criteria of resistant, malignant, or severe HT [12]. However, due to current paucity of evidence of adequate sensitivity in the pediatric population and due to the technique driven accuracy of renal Doppler ultrasonography, it is the opinion of the authors that it is not very helpful in the diagnostic evaluation of a child with suspected renal artery stenosis. Reliance on color Doppler imaging in the child for excluding renovascular disease, particularly small vessel disease is a potential pitfall. Particularly in younger children, standard angiography or digital subtraction angiography are the gold standard. The utility of less invasive imaging modalities such as CT angiography or MR angiography in children is still unknown. Issues in children include smaller vessel size, in general, and frequent presence of small vessel disease often not detected by CTA or MRA. Furthermore, angiography also offers a potential therapeutic option in the event that main or branch renal artery stenosis is found as angioplasty or vascular stent placement can occur when the lesion is detected.

COARCTATION OF THE AORTA

Nothing in the history is specific for detection of coarctation of the aorta. On physical examination, diminished femoral or peripheral lower extremity pulses may be found [13]. Blood pressure measured in the lower extremity is typically higher than that in the brachial artery of the arm. The finding of decreased or absent lower extremity BP is highly suggestive of coarctation of the aorta. This prompts imaging of the aorta and referral to cardiology. In addition, a heart murmur is also a common, yet nonspecific finding in children with HT later confirmed to have coarctation of the aorta.

FURTHER DIAGNOSTIC STUDIES

The utility of further diagnostic studies must consider the likelihood of primary HT and the severity of HT and associated symptoms. No comprehensive, prospective studies are available to guide the clinician in this area. Among adolescents with obesity and/or a strong family history of HT, further testing after the more common secondary causes have been ruled out is not likely to be useful. Renal ultrasonography among obese adolescents was found to be of limited use [14]. The presence of flushing, sweating and palpitations should prompt a search for pheochromocytoma. Younger children and those with more severe HT should undergo testing for steroid-mediated HT and pheochromocytoma if no other etiology for HT is found. Urine and/or plasma catecholamine levels, and fractionated metanephrines are recommended to screen for pheochromocytoma. Although primary hyperaldosteronism is exceedingly rare in childhood, we routinely measure aldosterone levels when the renin levels and other blood studies are performed during the initial assessment. Although aldosterone levels are not routinely included as part of the initial work up by many authors, they can be helpful in the diagnostic evaluation if below normal (Liddle’s syndrome, apparent mineralocorticoid excess, and congenital adrenal hyperplasia) or above normal (glucocorticoid-remediable aldosteronism or primary hyperaldosteronism). Low renin HT in the setting of a strong family history of HT, particularly early onset HT suggests monogenic disorders such as Liddle syndrome (low aldosterone), glucocorticoid-remediable aldosteronism (increased aldosterone), or apparent mineralocorticoid excess (low aldosterone) [15].

IS THERE EVIDENCE FOR HYPERTENSION RELATED TARGET ORGAN DAMAGE?

The most commonly found HT associated sequelae detected in children is left ventricular hypertrophy (LVH), reported to be present in 30-40% of unselected children with HT [1]. Echocardiography is recommended in the initial evaluation of children with HT for this reason. The finding of LVH is not exclusively related to HT, since obesity may also be associated with LVH. However, LVH in the setting of HT is a compelling indication for more aggressive antihypertensive therapy. Microalbuminuria is not consistently reported among children with HT and therefore, is not routinely included in the work-up. Testing should also screen for co-morbid con-
ditions such as hyperlipidemia, obstructive sleep apnea and alterations in glucose metabolism.

**SUMMARY**

The first step in evaluation of any child with elevated BP is to confirm whether HT truly exists. Those with severely elevated BP do not require further measurements to confirm HT. Repeat BP by either clinic personnel, in-home monitoring or ABPM should be used to confirm mild to moderate HT.

In those with confirmed HT, the initial work up should be focused on the evaluation for renal parenchymal disease, structural abnormalities or evidence of a renovascular lesion. In children with normal body habitus, strong consideration of renal ultrasound should be given. It is our opinion that Doppler ultrasonography does not conclusively provide helpful data in children sufficient enough to prove or disprove the presence of renovascular lesions and is not a necessary part of ultrasonographic evaluation. In obese children, renal ultrasonography is not likely to yield useful information, and should be ordered only if screening labs demonstrate any clues of renal parenchymal disease. DMSA scan should be performed in children with a history of vesicoureteral reflux, a urinary tract infection prior to the age 5 years, possible occult febrile urinary tract infection, intra-uterine ischemic insult, and/or of family history of vesicoureteral reflux. DMSA scan should be strongly considered even in the absence of one of the aforementioned conditions since renal scarring has been found in otherwise normal children with HT. Consider obtaining a random renin and ± aldosterone levels when the patient is in a euvoletic state with initial labs prior to the start of any anti-hypertensive medications as these levels can become difficult to interpret once a BP medication is started.

Secondary evaluation should be focused on history and clinical findings. Consideration of angiography should be made in children with severe HT and no evidence of renal parenchymal disease, with HT requiring more than a single anti-hypertensive agent to achieve adequate BP control, or with confirmed BP > 99<sup>th</sup> percentile for sex/age/height percentile. Screening for endocrinopathies should be directed by compatible history and findings on physical examination and should not be a portion of a routine initial work up.

In any child diagnosed with HT, attempts should be made to evaluate for end organ disease and co-morbid conditions. Echocardiogram should be obtained to assess for LVH as evidence of chronic HT and evidence of the adequacy of either adequacy of BP control. A fasting lipid profile or at a minimum a total cholesterol should be obtained to evaluate for co-morbid hypercholesterolemia in all children being treated for established HT. If history or physical examination is suggestive of obstructive sleep apnea and/or diabetes, then appropriate evaluation should be pursued. Figure 1 outlines the work up of HT in children.

**REFERENCES**