Guidelines for the management of Hypertension

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DISCLAIMER: These guidelines were produced in good faith by the author(s) in conjunction with the paediatric nephrology team at the University Hospital of Wales, Cardiff reviewing available evidence/opinion. They were designed for use by paediatric nephrologists at the University Hospital of Wales, Cardiff for children under their care. They are neither policies nor protocols but are intended to serve only as guidelines. They are not intended to replace clinical judgment or dictate care of individual patients. Responsibility and decision-making (including checking drug doses) for a specific patient lie with the physician and staff caring for that particular patient.

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August 2018

Summary

These guidelines are aimed at providing the doctors presented with a child with hypertension with information to help identify the underlying problem and to guide treatment.

Introduction

Measurement of blood pressure should be part of the routine assessment of any child seen as an in patient or out patient. Methods of measuring blood pressure are dealt with in a separate guideline.
Hypertension may be secondary to an underlying pathology (usually renal). However with the growing problem of obesity, more children are presenting with primary hypertension.

Definitions

Blood pressure is a continuous variable and the differentiation between normal and abnormal has been defined statistically. There has also been debate about the relative importance of systolic and diastolic hypertension. It is felt that systolic blood pressure is probably of greater relevance and a value > 95th centile for age and height using appropriate centile charts measured on three occasions defines someone as being hypertensive (see appendix 1). Any measurements taken using an automated device should be confirmed manually and if possible ambulatory measurement should be used to confirm mild hypertension.

Severe hypertension is a systolic blood pressure > 95th centile for age and height with symptoms (headache, visual disturbances, neurological disturbances). This requires urgent investigation and management.

Aetiology

Secondary hypertension is more common than primary hypertension in young children. However primary hypertension is now starting to become the dominant cause of hypertension in children older than 6 years of age as a result of the growing problem of obesity.

Underlying causes:

- Renal disease. Renal parenchymal (most common) and renal vascular disease may cause hypertension. Wilms tumours are commonly associated with hypertension
- Coarctation of the aorta should be excluded
- Endocrine causes (Cushings / Conns / Phaeochromocytoma)
- Rare renal tubular single gene disorders (Gordons, Liddles, apparent mineralocorticoid excess (AME) and glucocorticoid remediable aldosteronism (GRA) can cause hypertension (see below).
- Elevated Intracranial pressure
- Pain

Monogenic hypertension

Hypertension in this group of patients is secondary to salt and water retention which is not a result of primary renal disease, but because of dysfunction of a single gene.

Even though rare, these can result in severe hypertension and cause abnormalities in serum potassium levels and alkalosis with suppression of renin and aldosterone. The causes, along with electrolyte and biochemical abnormalities seen in these conditions are listed below:

	Inheritance pattern	Renin	Aldosterone	K^+	HCO_3	FE_{Na}	Diagnostic indicators
AME	AR	↓	↓	↓	↑	↓	Prolonged cortisol half life Urinary cortisol metabolities increased Urinary cortisone metabolities decreased
GRA	AD	↓	↑	↓	↑	↓	Urinary 18-oxotetrahydrocortisol and 18-ydroxycortisol: tetrahydroaldosterone ratio increased Angiotensin II decreased
CAH	AR	↓	↓	↓	↑	↓	Ambiguous genitalia/menorrhoea Virilisation/Precocious puberty
Liddle syndrome	AD	↓	↓	↓	↑	↓	Family history, clinical and lab findings
Gordon syndrome	AD	↓	N or ↓	↑	↓	↓	Family history, clinical and lab findings
FH II	AD	↓	↑	N or ↓			
FGR	AD/AR	↓	↓	N or ↓			
H-P	AD	↓	↓	N or ↓			

AME, syndrome of apparent mineralocorticoid excess; CAH, congenital adrenal hyperplasia; FeNa, fractional excretion of sodium; GRA, glucocorticoid remediable aldosteronism; FGR, familial glucocorticoid resistance; FH II, familial hyperaldosteronism type II; H-P hypertension exacerbated by pregnancy

Investigations

First line:

- History and examination, to include palpation of the femoral pulses, comparison of the right arm and lower limb pulse and fundoscopy. Consider stigmata of underlying causes of hypertension (see appendix 2).
- Urinalysis and early morning urine for protein:creatinine ratio.
- Urea & Electrolytes / Bone profile / Magnesium / Full Blood Count / Glucose / Bicarbonate / Thyroid Function Tests / Lipid profile / Uric acid
- Renin and aldosterone (after 30 minutes supine; ideally before starting treatment). Discuss with biochemistry
- Ultrasound of urinary tract **WITH** doppler imaging of renal vessels
- Consider ambulatory BP monitoring. Interpretation needs comparison with an appropriate reference range. A form for use at UHW can be downloaded by clicking here.
- Further assessment of end organ damage CXR/ECG/ECHO/Ophthalmology

Second Line: (discuss with paediatric nephrologist)

- Urine steroid profile (24 hour collection where practical and random urine if not).

- Metanephrines. These are the current recommendations from the biochemistry lab at UHW:
    - Urine VMA / HVA is not recommended in the exclusion of phaeochromocytoma in paediatric patients. It is only useful for diagnosis and monitoring of patients with neuroblastoma.
    - 24 hr fractionated urine and plasma metanephrines have replaced these urine catecholamine metabolites. Metanephrines have much better sensitivity and specificity for phaeochromocytoma. There is no evidence to suggest use of random/spot urine samples to screen for phaeochromocytoma.
    - Recommended investigations for phaeochromocytoma if there is a strong clinical suspicion or genetic predisposition:
        - 24 hr fractionated urine metanephrine assay. (In house assay). Do not have verified reference ranges for the paediatric population (due to limited sample numbers), but use published paediatric reference ranges as a guide.
        - If the patient has CKD or in whom collection of 24 hr urine is impractical, it is advised to do plasma metanephrines. Samples currently sent to Newcastle for analysis. Specific sample handling requirements: EDTA-purple tube sample should be collected from a <u>supine</u> position after 30 minutes, sample must be sent immediately to the laboratory <u>on ice</u>.
- ASOT/autoimmune profile/complement (C3 & C4) / ANCA
- Random cortisol,
- DMSA scan
- MRA / Captopril MAG 3 / Renal angiography
- MRI / MIBG scan

<u>Management</u>

Emergency management of severe hypertension:
Discuss with paediatric nephrologist

- Patients may require management on PICU or renal ward
- Aim for a slow reduction over 72 hours to avoid a sudden drop in perfusion pressure which may cause catastrophic cerebral ischaemia. Aim for one third of overall desired reduction in the 1st 24 hours. Avoid mydriatics for fundoscopy.
- Site two IV cannulae. One is used to deliver IV antihypertensive agent and the second to deliver a 10ml/kg saline bolus if the blood pressure falls too quickly.
- The choice of IV agent should be one with which the clinician is familiar. The options include labetalol, nicardipine and sodium nitroprusside. Another is hydralazine, but this tends to be used more for treatment of neonates. These agents should be administered using a sliding scale to titrate the dose administered with BP, measured every 15 minutes (usually monitored via arterial line in patients on PICU). An arterial line is mandatory when using sodium nitroprusside.

Dosages:

Labetalol	0.5 - 3 mg/kg/hr
Sodium nitroprusside	0.5 - 8 µg/kg/min. Protect from light and should have an arterial line for bp monitoring. Advantage of very short t½. Need to check cyanide level.
Nicardipine	0.5 - 3 µg/kg/min BNF recommends to infuse at concentration of 0.1mg/ml. Can infuse higher concentrations via a central line. If fluid volume is an issue concentrations up to 0.5mg/ml have been used peripherally [1].

Once control has been established with parenteral agents, convert to oral medications as below.

Asymptomatic patients
It may be possible to achieve gradual blood pressure reduction with oral therapy using a calcium antagonist. Start with a small dose of nifedipine (0.1 mg/kg).

Oral maintenance treatment
Aim to maintain BP <95th centile but preferably the 50th centile in patients with renal disease [2].
Choice of oral agents (also see Specific considerations for treatment of hypertension):

- Angiotensin converting enzyme inhibitors (ACEi; e.g. enalapril / lisinopril) or angiotensin II receptor antagonists (ARB; valsartan, irbesartan)
    - May cause hyperkalaemia. Monitor serum [K^+]; check levels within 7 days of starting or increasing dose
    - Avoid if renal artery stenosis suspected
    - Avoid in the early period after renal transplantation
- Beta blockers: Metoprolol has selective blockade and non-renal excretion. Use if concerns about the possibility of renal artery stenosis or ACE/ARB contraindicated
- Calcium channel blockers: Amlodipine/ nifedipine LA
- Consider diuretics if fluid overload is contributing. First line treatment in acute nephritis.

Once daily dosing schedules should improve compliance.

Non-pharmacological management
Consider the following advice in all children with hypertension

- Sodium restriction
- Weight loss
- Exercise
- Attention to other cardiovascular risk factors: Control of blood lipids, glycaemic control in diabetes

Specific considerations for treatment of hypertension

- Following renal transplantation.

The use of angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists are not generally used in the early post transplant phase due to the

difficulty interpreting elevated creatinine. Calcium channel blockers are a sensible choice and there is evidence that use of these agents in the peri-operative period reduce the incidence of post-transplant acute tubular necrosis [3]. Once stable renal function is achieved there are potential benefits from using an ACEi/ARB.

- Wilms Tumour.

Hypertension in Wilms tumour (WT) patients has been reported to be associated with elevated plasma renin levels in 80% of cases [4]. ACE inhibitors should be considered in WT patients with hypertension prior to nephrectomy.

- Phaeochromocytoma [5, 6].

This is characterised by episodic hypertension/palpitations and sweating. Specific investigations should include: 24 hour urine or plasma metanephrines, abdominal USS, abdominal MRI, MIBG isotope scan. Control of hypertension is required before surgery using alpha and beta blockade. The alpha blocker of choice is phenoxybenzamine and the beta blocker is propanolol. Stop antihypertensives 8-12 before theatre on discussion with the anaesthetist.

- Renovascular disease [7].

This is characterised by very high renin levels and may be secondary to renal artery stenosis or obstruction to vessels by cysts in polycystic kidney disease. In this situation, intra-glomerular pressure depends on efferent arteriolar constriction and therefore ACE inhibitors or angiotensin II receptor antagonists must be used with caution as these agents cause efferent arteriolar dilatation. Investigations may include: MRA/Angiogarphy. Treatment: metoprolol / amlodipine / other.

- Neonatal hypertension [8].

Intravenous agents described in the literature are: labetalol, hydralazine and nicardipine. Oral agents in suspensions used in neonates are: propanolol, hydralazine and captopril. If using an ACEi renal function must be carefully monitored as neonates have a greater reliance on the renin-angiotensin system for maintenance of intraglomerular capillary pressure.

- Rare single gene disorders

Glucocorticoid remedial hyperaldosteronism (GRA), Gordons [9], Liddle syndrome [10] and AME (apparent mineralocorticoid excess) are characterised by hypertension due to interruption of the renin-aldosterone axis. They are often associated with hypo- or hyperkalaemia and diagnosis is with a urine steroid profile. Treatment includes the use of potassium sparing diuretics.

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Appendix 1. Blood pressure centiles based on gender, age, and height

TABLE 3. BP Levels for Boys by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
For research purposes, the SDs in Table B1 allow one to compute BP Z scores and percentiles for boys with height percentiles given in Table 3 (ie, the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z scores given by: 5% = −1.645; 10% = −1.28; 25% = −0.68; 50% = 0; 75% = 0.68; 90% = 1.28; and 95% = 1.645, and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.

TABLE 4. BP Levels for Girls by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

* The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.

For research purposes, the SDs in Table B1 allow one to compute BP *Z* scores and percentiles for girls with height percentiles given in Table 4 (ie, the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height *Z* scores given by: 5% = −1.645; 10% = −1.28; 25% = −0.68; 50% = 0; 75% = 0.68; 90% = 1.28; and 95% = 1.645 and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.

Appendix 2. Examination findings.

	Finding	Possible Aetiology
Vital signs	Tachycardia	Hyperthyroidism, phaeochromocytoma, neuroblastoma, primary hypertension
	Decreased lower extremity pulses; drop in BP from upper to lower extremities	SPARCstation of the aorta
Eyes	Retinal changes	Severe hypertension, more likely to be associated with secondary hypertension
ENT	Adenotonsillar hypertrophy	Suggests association with sleep-disordered breathing (sleep apnoea), snoring
Height / weight	Growth retardation	Chronic renal failure
	Obesity (high BMI)	Primary hypertension
	Truncal obesity	Cushing syndrome, insulin resistance syndrome
Head and neck	Moon facies	Cushing syndrome
	Elfin facies	Williams syndrome
	Webbed neck	Turner syndrome
	Thyromegaly	Hyperthyroidism
Skin	Pallor, flushing, diaphoresis	Pheochromocytoma
	Acne, hirsutism, striae	Cushing syndrome, anabolic steroid abuse
	Café-au-lait spots	Neurofibromatosis
	Adenoma sebaceum	Tuberous sclerosis
	Malar rash	Systemic lupus erythematosus
	Acanthrosis nigricans	Type 2 diabetes
Chest	Widely spaced nipples	Turner syndrome
	Heart murmur	Coarctation of the aorta
	Friction rub	Systemic lupus erythematosus (pericarditis), collagen-vascular disease, end stage renal disease with uremia
	Apical heave	LVH/chronic hypertension
Abdomen	Mass	Wilms tumor, neuroblastoma, phaeochromocytoma
	Epigastric/flank bruit	Renal artery stenosis
	Palpable kidneys	Polycystic kidney disease, hydronephrosis, multicystic-dysplastic kidney, mass (see above)
Genitalia	Ambiguous/virilization	Adrenal hyperplasia
Extremities	Joint swelling	Systemic lupus erythematosus, collagen vascular disease
	Muscle weakness	Hyperaldosteronism, Liddle syndrome

Adapted from Flynn JT. *Prog Pediatr Cardiol.* 2001;12:177–188