

# Wessex Paediatric Oncology Supportive Care Guidelines: Management of Hypertension.

## **Scope**

This guideline applies to all paediatric oncology patients in the region. It does not apply to neonates on neonatal units.

## **Purpose**

Children receiving treatment at the Southampton Paediatric Oncology Principal Treatment Centre (PTC) have open access to the designated Paediatric Oncology Ward at either the PTC or their Paediatric Oncology Shared Care Unit (POSCU). Their parents/carers will be in possession of contact details for these wards and have been instructed to contact them for any medical problems that arise while they are receiving treatment. These Guidelines are intended for the use of the medical teams at the PTC or POSCU. If one of the Paediatric Oncology patients presents to a medical service outside of the PTC or POSCU, please contact the medical teams at the PTC or POSCU for advice.

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# Identification and Management of Hypertension

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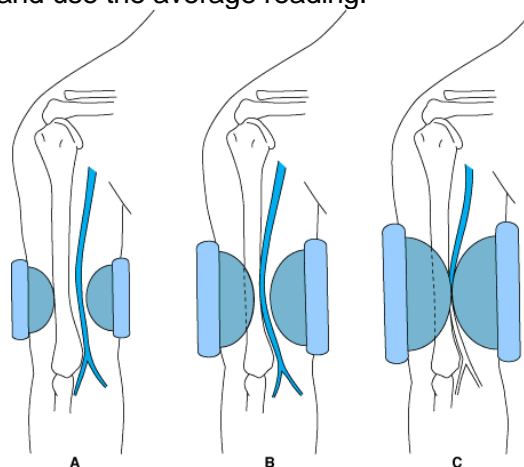
## 1.1 Overview of hypertension management

Hypertension may occur in children with cancer due to the disease itself (e.g. Neuroblastoma, Wilms tumour or tumours causing obstructive uropathy), side effects of treatment (e.g. steroids) or occasionally be related to an underlying disorder (e.g. Neurofibromatosis). It is important to distinguish between “standard” hypertension and an acute hypertensive crisis. Mild-moderate hypertension, if asymptomatic, may be observed over 1-2 days before initiating treatment. Severe hypertension needs repeat monitoring over a period of hours, and immediate discussion with the renal team if confirmed. However, an acute hypertensive crisis is an emergency requiring immediate management.

The medical management of hypertension can be complicated owing to the large number of available drugs. Choice of therapy depends on the severity of the hypertension and its underlying cause. Treatment is often started with a short acting drug and then if needed continued with a more long acting formulation. The main groups to use are calcium channel blockers, diuretics and ACE inhibitors with beta-blockers as third line drugs. Discuss with PTC.

### 1.1.2 Step 1: Check Blood Pressure (BP) reading is accurate and consistent

Accurate and repeated measurement of BP is essential for the diagnosis of hypertension. It is easy to get a false measurement. The cuff used must encircle the upper arm and its width should cover two-thirds of the distance from the shoulder to the elbow (Figure1). A sensible rule is to use the largest cuff which fits comfortably. If an abnormal BP is expected, or detected by automated measurement, this should be confirmed by a manual sphygmomanometer. If the first reading is high, retake the blood pressure a total of three times and use the average reading.



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Figure 1. Illustrating how the wrong size cuff will lead to inaccurate blood pressure results. Using a small cuff, you will overestimate the true blood pressure. C shows correct cuff size.

**1.1.3 Step 2: Check if BP is too high for child, using the Quick Reference Chart. This will help identify if reading may be elevated, then look up height centile and plot BP centile for height.**

The blood pressure should be interpreted using the blood pressure tables published by the Fourth Report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents (child’s height centile is required). The Systolic Blood Pressure (SBP) is more useful than diastolic measurements when determining end organ damage risk. The simplified table below (Table 1) is based on the 90<sup>th</sup> systolic percentile for the 5<sup>th</sup> percentile of height at each age. This will overestimate high blood pressure in taller children and is intended as a prompt to look up the blood pressure on the height centile charts (Table 2). This table is useful for identifying children who require further evaluation of their blood pressure.

**1.1.4 Definitions of hypertension**

Normal BP	=	systolic and diastolic < 90 <sup>th</sup> centile for age and sex
High – Normal BP	=	90-95 <sup>th</sup> centile
Stage 1 Hypertension	=	if > 95 <sup>th</sup> centile on at least 3 separate readings then treatment required
Severe/Stage 2 hypertension	=	symptomatic or > 5mmHg above 99 <sup>th</sup> centile

**Table 1: Simplified Table illustrating 90<sup>th</sup> centile BP**

Age	SBP Boy	SBP Girl		Age	SBP Boy	SBP Girl
1	94	97		10	111	112
2	97	98		11	113	114
3	100	100		12	115	116
4	102	101		13	117	117
5	104	103		14	120	119
6	105	104		15	120	120
7	106	106		16	120	120
8	107	108		17	127	122
9	109	110				

**1.2 Step 3: Medical treatment of hypertension**

***Mild to Severe “Standard” Hypertension***

This often occurs due to fluid overload or high dose steroid use in children with cancer. Amlodipine is safe, well tolerated and requires only once per day dosing. For dosing see Table 3: Paediatric Oncology Antihypertensive drug doses.

For renal tumours and steroid induced hypertension, ACE inhibitors such as captopril/enalapril may be used. **Captopril** is usually the first line treatment for renal tumours as it has a short half-life. Use with caution in bilateral problems: ensure intravascular volume is not depleted. **Enalapril** once per day may be used as maintenance treatment.

For third line treatment in children without contra-indications such as reduced cardiac function on ECHO or asthma, beta blockade with atenolol may be a useful addition. Additional agents such as Hydralazine

or Doxazosin (vasodilators) can be considered in experienced hands if an IV agent is required. Discuss with PTC consultant on call and consultant nephrologists. Steroid induced or tumour associated (i.e. Neuroblastoma or Wilms) hypertension should be treated in the same way. However, it is important to rule out whether there is a major component of fluid overload or not.

### ***Catecholamine Excess Hypertension***

Neuroblastomas/Phaeochromocytomas may be associated with hypertension due to excess release of catecholamines and increased central sympathetic activity. In these cases, alpha blockade with Phenoxybenzamine or Doxazosin should commence first and later the addition of beta blockade with atenolol may also be required. Nifedipine or other calcium channel blockers may also be useful in these cases. It is important to have control of blood pressure using adequate alpha blockade a minimum of a week before any planned surgery.

## **1.3 Hypertensive Crisis/Acute Hypertensive Encephalopathy**

### ***Discuss with Paediatric Haematology/Oncology on-call consultant urgently***

In a hypertensive emergency, there is a severe acute elevation in blood pressure and evidence of life-threatening symptoms or target organ damage. This is often associated with extremely high blood pressure readings. However the absolute value of the blood pressure is far less important than evidence of end organ damage or symptoms (as the same readings may be present in two children with very different effects on the body's organs).

### **Symptoms of hypertensive crisis:**

Hypertensive Encephalopathy: lethargy/coma/seizures Congestive heart failure Pulmonary oedema
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Emergency intervention is necessary in this case to protect the brain, kidneys, eyes and heart. After recognition of this scenario, such children need emergency stabilisation and establishment of IV access and appropriate anti-hypertensives to reduce their BP acutely before safe transfer/retrieval to tertiary high dependency or PICU care at their PTC and discussion with a nephrologist. The aim of treatment is to bring the blood pressure steadily back to normal over about 72 hours, avoiding sudden hypotension. A useful target is to aim to reduce the BP by one third of the total required reduction (from current BP to 95<sup>th</sup> centile) in the first 12 hours of treatment and then by another third in the next 24 hours.

Because of the need to use drugs with rapid action, great care needs to be taken to avoid sudden hypotension. Intravenous (IV) Labetalol and Sodium Nitroprusside are both effective. Refer to SORT guidelines. Hydralazine may be used in milder cases particularly if high dependency care is not available. Good IV access with a running saline infusion is required in case of the need for immediate saline bolus and frequent high dependency nursing observations including pupillary reactions to light and visual acuity are essential. This is due to the risk of optic nerve head infarction with rapid hypotension. Any loss of vision or decrease in pupillary reactivity requires use of saline or plasma bolus to raise the BP and Dexamethasone may be required. Oral/sublingual hypotensive agents or diuretics are contraindicated in the initial management of hypertensive crisis until the blood pressure is safely controlled. If the child is having a convulsion a suitable anticonvulsant (such as Lorazepam) should be administered intravenously in addition to steps being taken to reduce blood pressure.

**Table 3: Paediatric Oncology Antihypertensive drug doses**

Drug	Age	Route	Dosing information
Amlodipine	1 month – 11 years	PO	Initially 100–200 micrograms/kg once daily; increased if necessary up to 400 micrograms/kg once daily, adjusted at intervals of 1–2 weeks; maximum 10 mg per day.
	12 years – 17 years	PO	Initially 5 mg once daily, then increased if necessary up to 10 mg once daily, adjusted at intervals of 1–2 weeks
Atenolol	1 month–11 years	PO	0.5–2 mg/kg once daily, dose may be given in 2 divided doses, doses higher than 50 mg daily are rarely necessary.
	12–17 years	PO	25–50 mg once daily, dose may be given in 2 divided doses, higher doses are rarely necessary.
Captopril	1–11 months	PO	Test dose 100 micrograms/kg (max. per dose 6.25 mg), monitor blood pressure carefully for 1–2 hours; usual dose 100–300 micrograms/kg 2–3 times a day, then increased if necessary up to 4 mg/kg daily in divided doses, ongoing doses should only be given if test dose tolerated.
	1–11 years	PO	Test dose 100 micrograms/kg (max. per dose 6.25 mg), monitor blood pressure carefully for 1–2 hours; usual dose 100–300 micrograms/kg 2–3 times a day, then increased if necessary up to 6 mg/kg daily in divided doses, ongoing doses should only be given if test dose tolerated.
	12–17 years	PO	Test dose 100 micrograms/kg, alternatively test dose 6.25 mg, monitor blood pressure carefully for 1–2 hours; usual dose 12.5–25 mg 2–3 times a day, then increased if necessary up to 150 mg daily in divided doses, ongoing doses should only be given if test dose tolerated
Enalapril	1 month–11 years	PO	Initially 100 micrograms/kg once daily, monitor blood pressure carefully for 1–2 hours, then increased if necessary up to 1 mg/kg daily in 1–2 divided doses.
	12–17 years (body-weight up to 50 kg)	PO	Initially 2.5 mg once daily, monitor blood pressure carefully for 1–2 hours, maintenance 10–20 mg daily in 1–2 divided doses.
	12–17 years (body-weight 50 kg and above)	PO	Initially 2.5 mg once daily, monitor blood pressure carefully for 1–2 hours, maintenance 10–20 mg daily in 1–2 divided doses; maximum 40 mg per day.

Drug	Age	Route	Dosing information
<b>Furosemide</b>	1 month–11 years	PO	0.5–2 mg/kg 2–3 times a day, alternatively 0.5–2 mg/kg every 24 hours, if corrected gestational age of under 31 weeks, higher doses may be required in resistant oedema; maximum 80 mg per day; maximum 12 mg/kg per day.
	12–17 years	PO	20–40 mg daily; increased to 80–120 mg daily, in resistant oedema
	1 month–11 years	Slow IV injection	0.5–1 mg/kg every 8 hours (max. per dose 40 mg every 8 hours) as required; maximum 6 mg/kg per day.
	12–17 years	Slow IV injection	20–40 mg every 8 hours as required, higher doses may be required in resistant cases
	Child	continuous intravenous infusion	0.1–2 mg/kg/hour.
<b>Hydralazine</b>	1 month–11 years	PO	250–500 micrograms/kg every 8–12 hours, increased if necessary to 7.5 mg/kg daily; maximum 200 mg per day.
	12–17 years	PO	25 mg twice daily, increased to 50–100 mg twice daily.
	1 month–11 years	Slow IV injection	100–500 micrograms/kg, dose may be repeated if necessary every 4–6 hours; maximum 3 mg/kg per day; maximum 60 mg per day.
	12–17 years	Slow IV injection	5–10 mg, dose may be repeated if necessary every 4–6 hours.
	1 month–11 years	continuous intravenous infusion	12.5–50 micrograms/kg/hour, continuous intravenous infusion is the preferred route in cardiac patients; maximum 3 mg/kg per day
	12–17 years	continuous intravenous infusion	3–9 mg/hour, continuous intravenous infusion is the preferred route in cardiac patients; maximum 3 mg/kg per day.
<b>Nifedipine</b> *Interacts with vincristine*	1 month–11 years	PO	200–300 micrograms/kg 3 times a day, dose frequency depends on preparation used; maximum 3 mg/kg per day; maximum 90 mg per day
	12–17 years	PO	5–20 mg 3 times a day, dose frequency depends on preparation used; maximum 90 mg per day.
<b>Spirolactone</b>	1 month–11 years	PO	Initially 1–3 mg/kg daily in 1–2 divided doses; increased if necessary up to 9 mg/kg daily, in resistant ascites
	12–17 years	PO	Initially 50–100 mg daily in 1–2 divided doses; increased if necessary up to 9 mg/kg daily, in resistant ascites; maximum 400 mg per day

Table 4: Upper BP centiles, according to gender age and height

Age	BP Percentile	Systolic BP, mm Hg													
		Boys - Height Centile							Girls - Height Centile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	90th	94	95	97	99	100	102	103	97	97	98	100	101	102	103
	95th	98	99	101	103	104	106	106	100	101	102	104	105	106	107
	99th	105	106	108	110	112	113	114	108	108	109	111	112	113	114
2	90th	97	99	100	102	104	105	106	98	99	100	101	103	104	105
	95th	101	102	104	106	108	109	110	102	103	104	105	107	108	109
	99th	109	110	111	113	115	117	117	109	110	111	112	114	115	116
3	90th	100	101	103	105	107	108	109	100	100	102	103	104	106	106
	95th	104	105	107	109	110	112	113	104	104	105	107	108	109	110
	99th	111	112	114	116	118	119	120	111	111	113	114	115	116	117
4	90th	102	103	105	107	109	110	111	101	102	103	104	106	107	108
	95th	106	107	109	111	112	114	115	105	106	107	108	110	111	112
	99th	113	114	116	118	120	121	122	112	113	114	115	117	118	119
5	90th	104	105	106	108	110	111	112	103	103	105	106	107	109	109
	95th	108	109	110	112	114	115	116	107	107	108	110	111	112	113
	99th	115	116	118	120	121	123	123	114	114	116	117	118	120	120
6	90th	105	106	108	110	111	113	113	104	105	106	108	109	110	111
	95th	109	110	112	114	115	117	117	108	109	110	111	113	114	115
	99th	116	117	119	121	123	124	125	115	116	117	119	120	121	122
7	90th	106	107	109	111	113	114	115	106	107	108	109	111	112	113
	95th	110	111	113	115	117	118	119	110	111	112	113	115	116	116
	99th	117	118	120	122	124	125	126	117	118	119	120	122	123	124
8	90th	107	109	110	112	114	115	116	108	109	110	111	113	114	114
	95th	111	112	114	116	118	119	120	112	112	114	115	116	118	118
	99th	119	120	122	123	125	127	127	119	120	121	122	123	125	125
9	90th	109	110	112	114	115	117	118	110	110	112	113	114	116	116
	95th	113	114	116	118	119	121	121	114	114	115	117	118	119	120
	99th	120	121	123	125	127	128	129	121	121	123	124	125	127	127
10	90th	111	112	114	115	117	119	119	112	112	114	115	116	118	118
	95th	115	116	117	119	121	122	123	116	116	117	119	120	121	122
	99th	122	123	125	127	128	130	130	123	123	125	126	127	129	129
11	90th	113	114	115	117	119	120	121	114	114	116	117	118	119	120
	95th	117	118	119	121	123	124	125	118	118	119	121	122	123	124
	99th	124	125	127	129	130	132	132	125	125	126	128	129	130	131
12	90th	115	116	118	120	121	123	123	116	116	117	119	120	121	122
	95th	119	120	122	123	125	127	127	119	120	121	123	124	125	126
	99th	126	127	129	131	133	134	135	127	127	128	130	131	132	133
13	90th	117	118	120	122	124	125	126	117	118	119	121	122	123	124
	95th	121	122	124	126	128	129	130	121	122	123	124	126	127	128
	99th	128	130	131	133	135	136	137	128	129	130	132	133	134	135
14	90th	120	121	123	125	126	128	128	119	120	121	122	124	125	125
	95th	124	125	127	128	130	132	132	123	123	125	126	127	129	129
	99th	131	132	134	136	138	139	140	130	131	132	133	135	136	136
15	90th	122	124	125	127	129	130	131	120	121	122	123	125	126	127
	95th	126	127	129	131	133	134	135	124	125	126	127	129	130	131
	99th	134	135	136	138	140	142	142	131	132	133	134	136	137	138
16	90th	125	126	128	130	131	133	134	121	122	123	124	126	127	128
	95th	129	130	132	134	135	137	137	125	126	127	128	130	131	132
	99th	136	137	139	141	143	144	145	132	133	134	135	137	138	139
17	90th	127	128	130	132	134	135	136	122	122	123	125	126	127	128
	95th	131	132	134	136	138	139	140	125	126	127	129	130	131	132
	99th	139	140	141	143	145	146	147	133	133	134	136	137	138	139



#### 1.4 References & Further Reading

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