

## Hypertension in Paediatric Haematology/Oncology

### Overview and aetiology:

Hypertension is a common problem in Paediatric Haematology and Oncology patients. There are a number of causes, some related to the disease itself or the treatment, For example:

- Wilms tumour – the mass compresses the normal kidney inducing reno-vascular hypertension.
- Neuroblastoma – causes hypertension both by kidney compression but also by excess catecholamines especially around the time of initial biopsy or relapse.
- Pheochromocytoma – hypertension is secondary to adrenaline and noradrenaline release
- Brain tumours can cause hypertension due to raised intracranial pressure
- Therapy induced
  - steroids lead to fluid and salt retention,
  - hyperhydration at induction leading to volume overload
  - cyclosporine (CSA) etc.
- Underlying general paediatric conditions

Identifying the cause of the hypertension is important as it can often direct the management.

### 1.1. Definitions of hypertension

- **Normal BP:** Systolic and diastolic BP < 90th centile for height centile
- **High normal BP:** Systolic and diastolic BP > 90th but < 95th centile for height centile (warrants observation)
- **Hypertension:** Systolic and diastolic BP > 95th centile for height centile on at least 3 occasions (requires further investigation and treatment)

Filename: Hypertension	Page 1 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
Version: 3.0	Agreed by: Chair Network Chemotherapy Group	Review date: 04/09/2017	
Children's Cancer Measure: N/A		Author: Sheila Lane / Shaun Wilson	

Table: 95th percentile of BP for 5th and 95th centile of height for age (abbreviated to show results for children on 5<sup>th</sup> and 95<sup>th</sup> centile height

NOTE: This table is abbreviated and provided for initial guidance only. The full table, which should be consulted if you are concerned about an individual child, is available here: [http://pediatrics.aappublications.org/content/114/Supplement\\_2/555.full.pdf](http://pediatrics.aappublications.org/content/114/Supplement_2/555.full.pdf)

Age	5th centile (ht) Boys	95th centile (ht) Boys	5th centile (ht) Girls	95th centile (ht) Girls
1	98/55	106/59	101/57	107/60
2	101/59	110/63	102/61	109/63
3	104/63	113/67	104/65	110/68
4	106/66	115/71	105/67	111/71
5	108/69	116/74	107/69	113/73
6	109/72	117/76	108/71	114/75
7	110/74	119/78	110/73	116/76
8	111/75	120/80	112/74	118/78
9	113/76	121/81	114/75	120/79
10	114/77	123/82	116/77	122/80
11	116/78	125/83	118/78	124/81
12	120/79	127/83	120/79	126/82
13	121/79	130/84	121/80	128/84
14	124/80	132/85	123/81	130/85
15	127/81	135/86	124/82	131/86
16	129/83	138/87	125/83	132/86
17	132/85	140/89	126/83	132/86

### **Investigations**

Filename: Hypertension	Page 2 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
Version: 3.0	Agreed by: Chair Network Chemotherapy Group	Review date: 04/09/2017	
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In many cases the cause will be obvious – neuroblastoma, steroids, cyclosporine, hyperhydration etc. in which case further investigation may not be not required unless the hypertension does not respond to appropriate treatment. If a clear cause is not apparent then the following base line investigations should be considered:

**First Line Investigation**

- Urinalysis
- Blood/protein/cast/infection
- U&E, creatinine
- Electrolytes (low Na indicates volume depletion and vice versa)
- FBC (HUS) only if acutely unwell and history is suggestive
- Urine Catecholamines (spot urine unless pheochromocytoma suspected)
- X-ray chest
- ECG
- Renal ultrasound
- DMSA
- Urine Cortisol (24 hour)
- Ophthalmology review if hypertension thought to be long standing

**Second Line Investigation**

Further investigations are dependent on the results of the first line investigations and may be indicted in the following:

- Glomerular disease: Glomerulonephritis screen
- VUR or obstructive uropathy: MCUG, MAG3
- Renovascular disease: Discuss/refer
- Coarctation: Cardiac opinion should be sought

**Treatment**

**NB Hypertensive Crisis/Acute Hypertensive Encephalopathy** is a medical emergency and will need to be managed urgently in PICU and management is not part of these guidelines.

**Consider the cause and then direct treatment:**

- **Hyperhydration +/- steroids:** Consider decreasing the IV fluid and stopping steroids if not part of the chemotherapy treatment. Consider a dose of IV furosemide but beware not to reduce blood pressure too precipitously with large amounts of diuretic especially if the patient has already been started on nifedipine or any other anti hypertensive medication.
- **Renal compression** as in Wilms' tumour is known to be associated with elevated plasma renin levels in 80% cases (3) and thus ACE inhibitors could be considered

Filename: Hypertension	Page 3 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
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pre surgery and then stopped after surgery as the hypertension often resolves quickly once the renal compression is removed. **ACE inhibitors** (captopril/enalapril) are the drug of choice in this situation unless there is evidence of renal artery stenosis or bilateral tumours are present. If using ACE Inhibitors ensure intra vascular volume is not depleted prior to starting therapy. Monitor for hyperkalaemia in the first 7 days of starting treatment or if the dose is increased. Captopril is relatively short acting and would be the drug of choice in the first instance, this could be converted to enalapril (once per day) when dose is stable if required long term.

- **Neuroblastoma** In the initial phase prior to treatment there will be both an element of renal compression and raised catecholamines. **Beta +/- alpha blockade** (ie atenolol +/- prazosin) may be required pre – treatment i.e. for biopsy to control the excess catecholamine release (unless contraindicated due to asthma or poor cardiac function). Once treatment is started and catecholamine levels have fallen, the renal compression may be best controlled with an ace inhibitor (3) if investigations have shown no evidence of renal artery stenosis. Note comments above on use of ACE inhibitors.
- **Drugs eg cyclosporine** - Check levels for toxicity and renal function especially serum creatinine, reduce dose of cyclosporine if appropriate or treat hypertension with a short acting agent such as nifedipine until cyclosporine or other drug such as steroids can be discontinued
- **Phaeochromocytoma** – this will require alpha and beta blockade and treatment is complex and needs very careful management by the team involved with surgical treatment

**Medical management (See attached dosing schedule)**

Whilst awaiting investigation or if there is no obvious cause the following medical management is recommended

**First Line: Calcium channel blockers (CCB)**

**Nifedipine** - a calcium channel blocker and thus vasodilator can be started if treatment is required whilst the underlying cause is further investigated. Nifedipine is relatively short acting and can be titrated according to response. **Amlodipine** has the advantage of being a once a day preparation and can be used in conjunction with nifedipine for breakthrough.

**Second Line Therapy** - If nifedipine is inadequate and there is no obvious cause as listed above with specific treatment then second line therapy should be use of a beta blocker such as **atenolol or metoprolol** (unless contraindicated due to asthma or poor cardiac function). **Metoprolol** has selective blockade and non renal excretion. Unless fluid overload is a problem, beware of indiscriminate use of diuretics in the initial phase of treatment as they can cause a precipitous fall in blood pressure when used with beta blockers or calcium channel blockade.

Filename: Hypertension	Page 4 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
Version: 3.0	Agreed by: Chair Network Chemotherapy Group	Review date: 04/09/2017	
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**If hypertension is difficult to control with single agent or there are complications after discuss with the Consultant of the Week and or the patients own Consultant discuss with Dr Janet Craze.**

Filename: Hypertension	Page 5 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
Version: 3.0	Agreed by: Chair Network Chemotherapy Group	Review date: 04/09/2017	
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Drug Dose Table

Drug	Route	Dose Range	doses/day	Maximum Dose
Amlodipine	oral	<b>1 month – 12 yrs</b> 100 – 200 micrograms/kg <b>12yrs – 18yrs</b> 5mg – 10 mg	1  1	10mg 10mg
Atenolol	oral	0.5 – 1.0 mg/kg/dose	1 - 2	100mg/day
Captopril	oral	<b>1 month – 12 yrs</b> Test dose 100microgram/Kg (max 6.25mg) if tolerated give 100 - 300 microgram/kg/day <b>12 yrs – 18 yrs</b> Test dose 100microgram/kg (max 6.25mg). If tolerated 12.5 – 25 mg/day	3  3	6mg/kg/day  150mg/day
Enalapril	oral	<b>1 month – 12 yrs</b> Test dose 100 micrograms/kg. If tolerated 300 – 500 microgram/kg/day <b>12yrs – 18 yrs</b> Test dose 2.5mg . If tolerated 10 – 20mg/day	1  1	1mg/kg  40mg/day
Frusemide	Oral/ IV	0.5mg – 1mg/kg/dose	1 – 6 doses	
Labetalol	Oral  IV	<b>1month – 12yrs</b> 1 - 2mg/kg/dose <b>12yrs – 18 yrs</b> 50 – 100mg/dose <b>1month – 12yrs</b> 250 – 500 micrograms/kg <b>12yrs- 18yrs</b> 50mg	3  2  1  1	2.4grams/d aily 20mg 200mg
Nifedipine	Oral (capsules) Slow release	<b>1 month – 12 yrs</b> 0.25mg/kg/dose <b>12 yrs – 18 yrs</b> 5 – 20mg/dose 0.5mg – 3mg /kg/dose	4 – 6 doses  3  2	3mg/kg/day
Propranolol	oral	<b>1month – 12 yrs</b> 0.25 – 1mg/kg <b>12yrs – 18 yrs</b> 80mg	3  2	5mg/kg daily 160- 320mg/day

Filename: Hypertension	Page 6 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
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## 1.2 Measurement

**Standard BP tables are for measurements on the arm. If measurements are taken on the leg they will be higher unless an appropriate larger size cuff is used.**

- Mercury sphygmomanometer is the gold standard but has been withdrawn for safety reasons. Manual measurement with an aneroid sphygmomanometer is the most commonly used method in outpatients. It is important that the equipment is calibrated regularly: with this proviso, it is a very reliable method.
- Automated digital machines eg Dinamapp are most often used on the wards. They are certainly helpful in monitoring trends but, as they are pre-set to inflate to a higher level than necessary for most children, they can be very painful and some children respond by getting upset and this increases the reading. For this reason, it is important that the measure is repeated manually and not based on a one off automated measurement. Doppler may be helpful in difficult situations.
- Cuff bladder width should be 40% of the arm circumference midway between olecranon and acromion.
- Cuff bladder should cover 80 to 100% of the circumference of the arm
- Several measurements should be taken. In an anxious child, consider 24hr ambulatory BP
- See appendix 1 Appendix 1 for tips on measuring blood pressure.

**In the initial clerking at diagnosis and on each admission for chemotherapy blood pressure should be recorded and compared to the normal value table. If elevated the blood pressure readings must be repeated as above and if consistently elevated discussed with the Consultant of the Week and the patient's own Consultant.**

Filename: Hypertension	Page 7 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
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**Blood pressure tables**

**Blood Pressure Levels for Girls by Age and Height Percentile**

Age (Year)	BP Percentile ↓	Systolic BP (mmHg)								Diastolic BP (mmHg)							
		← 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	

Filename: Hypertension	Page 8 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
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**Blood Pressure Levels for Girls by Age and Height Percentile (Continued)**

Age (Year)	BP Percentile ↓	Systolic BP (mmHg)							Diastolic BP (mmHg)						
		← Percentile of Height →							← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
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

BP, blood pressure

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

For research purposes, the standard deviations in Appendix Table B-1 allow one to compute BP Z-scores and percentiles for girls with height percentiles given in Table 4 (i.e., 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%; 95% = 1.645) and then computed according to the methodology in steps 2-4 described in Appendix B. For children with height percentiles other than these, follow steps 1-4 as described in Appendix B.

Filename: Hypertension	Page 9 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
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		← 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

Filename: Hypertension	Page 10 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
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Age (Year)	BP Percentile ↓	Systolic BP (mmHg)						Diastolic BP (mmHg)							
		← Percentile of Height →						← Percentile of Height →							
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
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

BP, blood pressure

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

For research purposes, the standard deviations in Appendix Table B-1 allow one to compute BP Z-scores and percentiles for boys with height percentiles given in Table 3 (i.e., 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; 95% = 1.645) and then computed according to the methodology in steps 2-4 described in Appendix B. For children with height percentiles other than these, follow steps 1-4 as described in Appendix B.

**References:**

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Filename: Hypertension	Page 11 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
Version: 3.0	Agreed by: Chair Network Chemotherapy Group	Review date: 04/09/2017	
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Dr Sheila Lane, Paed Oncology Consultant	New doc	Not recorded	1.0	Not recorded
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Filename: Hypertension	Page 12 of 12	Date agreed: 04/09/2015	Issue date: 04/09/2015
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