

Wessex Paediatric Oncology Supportive Care Guidelines: Investigation of new patients

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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Assessment and Investigation of New Patients

In addition to the general history taking process, there are some details that are particularly important in paediatric oncology patients either for disease assessment, to measure response to treatment, or to collect trial data.

Please update the patient information card with significant information in the front of the notes.

1.1. History

Note duration of and any recent deterioration in symptoms e.g.: -

- Pallor, lethargy
- Bruising, bleeding, petechiae
- Recent infections
- Bone pain
- Respiratory problems
- Abdominal pain, distension
- Recent weight changes
- Haematuria, dysuria, poor urine output
- Areas of swelling or lymphadenopathy
- Visual problems, gait disturbance, headache, vomiting
- History of menarche, possibility of pregnancy and contraception.

NB Document immunisation history and history of infectious illnesses, chicken pox and measles.

Family history

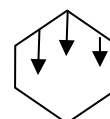
Family tree with parental names, ages, occupations and any other medical conditions.

Ask especially about history of malignancy in extended family.

Document immunisation status of siblings (particularly chicken pox and measles as vaccination may then be advised for siblings see viral infection guideline).

1.2. Examination

- General well-being and nutritional status (document weight, height, BMI and BSA in m² (CCLG chart: see appendix x)
- Fully document observations: respiratory rate, heart rate, saturations, temperature and **blood pressure**
- Anaemia, bruising, petechiae
- Lymphadenopathy (distribution, size, tenderness, hardness)
- Any masses (size, position, texture, tenderness, mobility), rashes or skin lesions
- Hepatosplenomegaly (measure longitudinal distance below the costal margins at xiphisternum, mid-clavicular line and anterior axillary line)
- Any evidence of infection
- Mouth and teeth
- Testes/external genitalia and Tanner pubertal staging
- Full neurological examination including head circumference and fundoscopy (haemorrhages, leukaemic infiltration, papilloedema).





























1.3 Table 1. Essential Diagnostic Blood Tests Reference Guide for Suspected New Leukaemia/Lymphoma. Check individual protocol once diagnosis is confirmed for additional pre-treatment investigations.			
Request on EQUEST and print forms for:	Bottle type	UHS Bottle colour	Specific Instructions
FBC and film comment	EDTA Purple VC or small red if infant		
Coag Screen	Sodium citrate blue (VC) or small green coag bottle if infant		
U&Es, creatinine	SSTII gold or small orange Li Hep if infant		Take by person to lab if high count to avoid cells lysing prior to analysis.
Calcium and Phosphate	SSTII or Li Hep		
LFTs (inc albumin)	SSTII or Li Hep		
LDH and Urate	SSTII or Li Hep		
Blood Cultures if febrile	Culture bottle		
Baseline Viral serology IgG For Varicella/CMV/Measles/EBV/Toxo	2-3mls Red topped plain		prior to any blood component transfusion. State on form if had chicken pox or not.
Immunoglobulins (prior to any blood component transfusion)	2-3mls Red topped plain		
Paper form for Group & Save	Large pink EDTA		BloodTrack system in UHS, barcode onto bottle and onto form, doctor to sign form.
Paper form for TPMT genotype/Equest form in UHS (prior to red cell transfusion)	full purple EDTA tube		In UHS request TPMT on EQUEST. And write "As discussed with Dr Paul Cook TPMT genotype for new acute leukaemia".
In addition in high count leukaemia with presenting counts >50 it may be possible to obtain diagnostic samples on peripheral blood instead of bone marrow. These samples should be hand delivered to the lab by the ward doctor and documented carefully in the notes.			
Cytogenetics	5-10 ml lithium heparin green (LH)		Need to be taken to UHS haematology lab to be sent to Salisbury before 15.00 on working days. Store at room temperature. Send with green page of bone marrow request form (state sample is blood).
Cell markers/ Immunophenotyping	5-10 ml EDTA		Call Dr E Hodges on ext 6976 (lab x6604) when sending. Store sample in fridge carefully labelled out of hours. Send with blue page of bone marrow request form (state sample is blood).
MRD sample	5-10 mls ACD		Not to be stored in the fridge, store at room temperature. In hours give by hand to the leukaemia data manager. Out of hours place in day ward treatment room carefully labelled.

Table 2. Essential Diagnostic Blood Tests Reference Guide for Suspected New Solid/Brain Tumour. Check individual protocol once diagnosis confirmed for additional pre-treatment investigations.			
Request on equest and print forms in usual way	Bottle type	Bottle colour	Specific Instructions

for:			
FBC and film comment	EDTA Purple VC or small red if infant		
Coag Screen	Sodium citrate (VC) or small green coag bottle if infant		
U&Es, creatinine	SSTII or small orange Li Hep if infant		
Calcium & phosphate	SSTII or Li Hep		
LFTS (inc albumin)	SSTII or Li Hep		
LDH & Urate	SSTII or Li Hep		
AFP/bHCG	SSTII or Li Hep		if suspected hepatoblastoma/germ cell tumour.
Ferritin	SSTII or Li Hep		in suspected neuroblastoma.
Blood Cultures if febrile	Culture bottle		on PB stored under sink in drug prep room.
Baseline Viral serology IgG For Varicella/CMV/Measles/EBV/Toxo prior to any blood component transfusion.	2-3mls Red topped plain		State on form if had chicken pox or not.
Immunoglobulins (prior to any blood component transfusion)	2-3mls Red topped plain		
Specific paper forms needed for the following:			
Group & Save	EDTA (purple or pink)		BloodTrack system, barcode onto bottle and onto form, doctor to sign form.

If a patient needs to be transfused at local hospital prior to transfer, please send Virology and Immunology samples locally and send TPMT sample with the patient as well as slides.

If not doing BM, stained slides from peripheral blood to be saved.

1.4 Urinary Samples

- Urine microscopy and culture if renal tumour
- Urinary HMVA & HMMA spot sample, request on equest (not 24hour urine collection) if neuroblastoma is suspected, or renal tumour at diagnosis: **essential prior to nephrectomy** (to exclude intrarenal neuroblastoma). Phone chromatography lab to inform sample is coming and ask for it to be processed urgently (ext. 6264).

1.5 Radiology

NB. Caution pregnant parents or staff unable to accompany children for CT, MIBG or PET scans.

CXR Essential prior to anaesthetic if leukaemia suspected or other condition that may involve mediastinal widening such as lymphoma. Needed if respiratory symptoms, looking for infection or mediastinal disease. Essential if signs of superior vein obstruction. Part of most staging investigations looking for parenchymal disease. If done in POSCU please arrange for digital images to be EXPOAXED to UHS if not on shared server.

Abdominal USS For abdominal masses. Look for ureteric obstruction/renal infiltration in **ALL** with renal impairment/oliguria, abdominal lymphoma prior to induction treatment. Consider in patients with leukaemia & WCC > 100 x 10⁹/l.

USS/CT/MRI scan As indicated - see individual protocols. Arrange with consultant radiologist.

CT scan If performing abdominal CT scan, usually need to give oral contrast medium. Most scans will also need IV access for IV contrast (preferably left sided if mediastinal disease). Scanning of the lungs for parenchymal disease, however, does not require IV contrast. Younger children will need either good sedation or a general anaesthetic for CT scans. Although the faster scan has reduced the need for GA and sedation, some young children manage with intensive play support. GA will affect the quality of lung images due to atelectasis. Therefore CT scans investigating for possible pulmonary metastases are best performed under sedation rather than GA. Ensure patient has had CXR prior to any sedation. **Do not give sedation/anaesthetic to child with respiratory compromise/significant mediastinal mass/SVC obstruction in order to CT scan (or any other reason).** Patient may not even be able to lie flat if airways problem.

Oral contrast Generally start drinking 1½ hours before scan, leaving last amount to take just before scan. In older teenagers the full amount may be taken just before the scan. For pelvic views the radiologist may request that some of the contrast may be taken the night before. Oral contrast should be diluted in water/squash (or milk) but not in carbonated drinks.

Niopam is oral contrast currently in use for CT scanning in Southampton.

Age	Amount of Niopam	Diluted in water/squash	Amount of diluted contrast to give child
1yr	1.75 ml	100 ml	100 – 150 ml
18months-2yrs	4.25ml	200mls	150-200ml
3yr	8.5 ml	400 ml	200-250ml
4yr	8.5 ml	400 ml	300 – 350 ml
5-10yrs	17 ml	800 ml	400 – 800 ml
10ys+	17 ml	800 ml	800 ml

Where a range is given, this allows some flexibility for patient size, but generally more is better.

If having CT under GA then give 15ml/kg finish diluted contrast 2 hours before scan. Contrast must be diluted in clear fluids under these circumstances.

Sedation: Infants less than 6 months do not usually require sedation for CT scanning: if fed and swaddled this should be sufficient. Older children can often be supported to tolerate imaging with early involvement of our play specialists, consider referral early in the diagnostic work-up for appropriate children before they become frightened. If sedation needed, use chloral hydrate (for up to 15 kg) or midazolam.

Chloral hydrate: 1 month – 12 years: 30 – 50 mg/kg (max. 1g) 45–60 minutes before procedure. Doses up to 100 mg/kg (max. 2 g) may be used with respiratory monitoring.

Midazolam: 1 month – 18 years: 0.5 mg/kg orally 15-30 minutes before scan (maximum dose 20 mg). Generally for over 4 years, rather than chloral.

Please record effectiveness (or otherwise) of sedation used for future reference and scanning. Some children become hyperactive with sedation and may be better not sedated in future, particularly when they are more used to having procedures and have had more play prep.

Heavily sedated children need close observation and monitoring: aiming for child to lie still rather than being deeply sedated with above drugs so as to AVOID respiratory or cardiovascular compromise. Continually monitor & document depth of sedation, respiratory rate and depth, arterial oxygen saturation, heart rate, BP, pain, coping & distress.

If procedure performed as outpatient, ensure vital signs & conscious levels returned to baseline prior to discharge.

MRI scan Brain/spine arrange with neuro-radiology. Other CT scans with paediatric consultant radiologist. GA needed for younger children to ensure they stay still for required length of time.

MIBG scans For neuroblastoma: arrange with nuclear medicine (X 6204). Give as much warning as possible: the MIBG usually needs to be ordered by Wednesday for the following week. Need IV access before injection, & be able to take/tolerate oral iodine (1 dose which nuclear medicine will administer) then scanned over next 1-2 days.

PET scan Protocols are increasingly suggesting PET CT scan evaluation of disease at diagnosis and for response assessment. PET referrals are made by printing a form from the UHS staffnet process current provider is Alliance complete and take to UHS nuclear medicine department as well as an equest request. Children <8 years who require GA are currently having their PET scans under GA in St Thomas's Hospital in London. Children > 8yrs may have PET in UHS or Portsmouth.

Other common investigations: -

GFR	As a baseline prior to chemotherapy as per protocol. Request on EQUEST, nuclear med tab, select "CR51 EDTA GFR". Please state height and weight on request and what type of access child has (if any). Arrange with nuclear medicine (X 6627/6115). Blood is sampled 2, 3 & 4 hours after injection from a site or lumen different to that of the injection. If bone scan also needed, do GFR first, or you will need to allow sufficient time (days) between bone scan & GFR. Children with a single lumen line will require a cannula for injection of isotope.
Bone scan	To look for bony metastases in Ewing's, osteosarcoma, rhabdomyosarcoma and neuroblastoma (if mIBG negative). Nuclear medicine X 6204. Request on EQUEST. See also individual protocols.
Audiology	Pre Cisplatin and Carboplatin. Audiology department, RSH (or local hospital where possible).
Echocardiogram	Routinely prior to Anthracyclines and thereafter dependent on dose. See individual protocols for exact timings, as a general rule need to re-echo more often after cumulative dose of 240 mg/m ² . Request on EQUEST as "Paeds Cong TTE". Fill in the "intended investigation date" as current date, and type in date you really want the test done in the clinical information bit. The requests only get printed out on the "intended investigation date" and so will only be sorted from then. Then phone X 6404 and ask dayward HCA to chase date and time. Currently changed to have 6 slots on a Thursday morning.
Lumbar puncture	Diagnostic LPs are not recommended in leukaemia unless giving intrathecal chemotherapy at the same time. If diagnosis of leukaemia not confirmed on peripheral blood, do not perform diagnostic LP with first bone marrow. Only perform LP after diagnosis of leukaemia is confirmed, and then administer chemotherapy with first LP. On first diagnostic tap collect 30 drops for cytopsin analysis: ask haematology lab to send for cell markers if cells present and 6 drops for MC&S. On subsequent cytopsin collect 20 drops unless CNS disease suspected. If first cytopsin positive, must send further sample on all subsequent lumbar punctures. For neuro-oncology patients sample needs to go to neuropathology and usually need at least 5 mls. All intrathecal chemotherapy drugs will be supplied in Luer-Lock syringes, and compatible Luer-Lock lumbar puncture needles must be used for all intrathecal procedures.

1.4 Bone marrow Aspirates & Trephine Biopsy

Bone marrow examination is routine for assessment of the patient with leukaemia, unless the white cell count is so high that bone marrow is not needed for diagnosis. If patient is not fit for a general anaesthetic, can almost always do under local anaesthetic. In UHS there are routine general anaesthetic lists on a Tuesday and Friday morning for Bone Marrow Aspirates and Lumbar Punctures.

FASTING INSTRUCTIONS

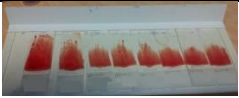





- no food or milky drinks for 6 hours (breast feeding 4 hours) before the procedure
- should be encouraged to have clear fluids until 2 hours pre-anaesthetic.


Patients having a bone marrow aspirate should have paracetamol before or with the procedure. For inpatients, a dose of oral paracetamol may be given with their last drink before the procedure. For outpatients, a dose of PR or IV paracetamol may be given with procedure. All patients having a trephine under GA will also have a long acting local anaesthetic (bupivacaine) infiltrated at the time of the procedure. If done under local, use lidocaine for quicker onset of action.

For local infiltration for BM/LP

Bupivacaine	Max 2 mg/kg (0.8 ml/kg of 0.25%).	
Lidocaine (1% = 10 mg/ml)	Aged 1 month – 12 yrs	3 mg/kg (0.3 ml/kg of 1% solution)
	12-18 yrs	up to 200 mg

Marrow aspirates are sent for morphology ± cell markers, cytogenetics, MRD, other as dictated by diagnosis. Trephines needed in certain circumstances. Send white copy of consent form with BMA form. (see folder in treatment room).

Table 3. Bone Marrow Aspirate & Trepine Sample details			
Morphology	Spread Slides x 9		Take to haem lab, white page of bone marrow request form and white copy of patients consent form for the aspirate. Request "MGG x 2". Fe stain only in certain circumstances (usually by haematologist's request). If not doing diagnostic marrow in high count leukaemia, ask for 4 blood film slides (2 stained, 2 unstained) to be made & kept.
Direct Prep for Cytogenetics	Put 3 drops in KCH medium (stored in bottom drawer PB tx room) and take directly to haematology lab (give prior notice on X 3863)		All new or relapsed patients with leukaemia should have standard and "direct prep" cytogenetics done. Also for diagnostic samples in staging of solid tumours except Hodgkin's. Follow up leukaemias may need follow up samples – if they do a standard culture bottle is usually sufficient.
Cytogenetics Culture	1 ml in cell culture medium		Need to be taken to UHS haematology lab to be sent to Salisbury before 15.00 on working days. Store at room temperature. Send with green page bone marrow request form. If unable to get marrow send peripheral blood see Table 1.
Cell markers/ Immunophenotyping/Flow	1-2 ml EDTA		Call Dr E Hodges on ext 6976 (lab x6604) when sending. Store sample in fridge carefully labelled out of hours. Send with blue page of bone marrow request form. If unable to get marrow send peripheral blood see table 1.
MRD sample	2 - 5 ml aspirate in yellow topped ACD bottle for ALL. AML & others: EDTA check current protocol and if unsure of diagnosis take both samples.	 	Send at diagnosis & specified times in protocol. If unable to get any aspirate at diagnosis but WCC > 20 x 10 ⁹ /l then send 5 ml blood in ACD. For follow up samples always need bone marrow. Sample to Bristol in all cases. Do not contaminate with heparin. Reposition during MRD sampling. If completely dry tap, send trephine in ACD tube for MRD. Ideally follow up samples for MRD should have N ≥ 0.5 x 10 ⁹ /l and platelets ≥ 50 x 10 ⁹ /l. Not to be stored in the fridge, store at room temperature. In hours give by hand to the leukaemia data manager. Out of hours place in day ward treatment room carefully labelled.

Bone marrow trephines	Sent in formalin for histology		H&E, reticulin and Giesma staining. For neuroblastoma request PGP 9.5, NB 84, NSE. If the initial aspirate has been "dry" do touch preps from the trephine sample prior to putting in formalin. Send with yellow page of bone marrow request form.
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1.4.1 Indications for trephine

Leukaemia: trephine needed if aspirate difficult, sample aparticle at diagnosis and no blasts or few blasts on peripheral film, or if aparticle aspirate for assessment of remission. Aspiration may be difficult in a new patient: do a trephine roll if dry tap prior to putting sample in formalin. D8 and 15 marrows in ALL will usually be aparticle and routine trephines are not needed. If diagnostic marrow aparticle but aspirates easily and numerous blasts have been seen on peripheral film trephine is not usually needed. Remember trephine for MRD if suspect aspirate will be insufficient.

Other haematological conditions: aplastic anaemia: confirmed, or in differential of leukaemia (cytopenia with no blasts on peripheral blood film) - trephine essential for determination of cellularity), myelodysplasia, other aplasias

Solid tumour: bilateral aspirates and trephines for staging of most solid tumours – see individual protocols.

14.1.2 Bone marrows other than routine list

At times, bone marrows will need to be performed outside the morning list. This may be with a biopsy or at the same time as a line is inserted in main theatres if prearranged with the surgeon: if this is the case all the necessary equipment and bottles need to be taken down to theatre from the ward. Contact theatre co-ordinator to arrange. Remember to give prior warning to the lab on X 3863 as early as possible for direct prep and slides.

14.1.3 Analgesia for bone marrows

If need to perform bone marrow other than under GA use local anaesthetic + other analgesia, including paracetamol ± morphine. Entonox can be effective for procedural pain but should not be used for lumbar punctures with intrathecal methotrexate. Consider midazolam as alternative: 2 trained healthcare professionals should be available during sedation. Monitor depth of sedation, respiratory rate, arterial oxygen saturation, heart rate, pain, coping & distress. Flumazenil (antagonist to Midazolam) should be available. If patient is not fit for GA, then probably not fit for sedation for bone marrow. **Do not sedate if there is evidence of a significant mediastinal mass or SVC obstruction.**

Midazolam:

IV: Give IV in increments of 25 microgram/kg waiting 2 minutes for effect to be seen.

Dilute to 10 ml with 5% glucose or 0.9% saline.

1 mth – 6 yrs: 25 – 50 microgram/kg initially, inc. if necessary in small steps (max. 6 mg)

6yrs – 12 yrs: 25 - 50 microgram/kg initially, inc. if necessary in small steps (max. 10 mg)

12yr – 18 yrs: 25 - 50 microgram/kg initially, inc. if necessary in small steps (max. 7.5 mg)

Oral: 500 microgram/kg (max 20 mg) 30 – 60 minutes before procedure.

14.1.4 Entonox

Although entonox has been used for older children/TYA for lumbar punctures, there is evidence to suggest an increase in methotrexate toxicity when given in association with nitrous oxide due to an additive effect of impedance to the folate pathway. **Therefore should not be routinely used for intrathecal.**

Entonox is used as an adjunct to a multi-modal pain relief strategy (see UHS guideline). Research has found it to be a safe option for procedural sedation. The safety and efficacy of Entonox is dependant on careful clinical management and observations. This compressed medical gas is a mixture containing 50% nitrous Oxide and 50% oxygen. Entonox combines the analgesic effect of nitrous oxide while preventing hypoxia with the addition of supplemental oxygen. In this sub-anaesthetic concentration it has powerful analgesic and anxiolytic properties. It is of rapid onset when inhaled (3-5 minutes) and of short duration (effects wear off after 3-5 minutes). It should be prescribed by a doctor and administered

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by a nurse trained in the procedure. The dose is self-regulated by a demand valve. Nitrous oxide is highly diffusible and will move more rapidly into an air pocket than the nitrogen will move out. The air pocket will expand in volume, or if in a confined space, pressure will increase.

Side-effects: Mildly sedating. Risk of emesis very low: child does not need to be fasted unless other sedatives/analgesics have been used. Drowsiness, nausea, giddiness indicate excessive nitrous oxide intake, muscle rigidity indicates hyperventilation effect.

There are a number of conditions where Entonox should not be used including situations where air may be trapped within the body and situations where there is an impaired conscious level.

14.1.5 Contraindications to entonox

- Head injuries with impaired consciousness
- Pneumothorax
- Air embolism
- Gross abdominal distension
- Maxillofacial injuries
- Intoxication
- Intrathecal Methotrexate.

1.5 Follow up/out patient investigations

Ensure day ward has a record of any investigations requested such as GFRs, Echos and Scans and ensure date for next appointment is put onto Aria by the day ward nurses.

1.6 References & Further Reading:

- *Sedation in children & young people. NICE Dec 2010.*
- *Guidelines for the use of PET-CT in Children, Second Edition. The Royal College of Radiologists, 2014.*
- *U. Lobel, MD ,1 J. Trah, MD ,2 and G. Escherich MD. Severe Neurotoxicity Following Intrathecal Methotrexate With Nitrous Oxide Sedation in a Child With Acute Lymphoblastic Leukemia
Blood Cancer 2015;62:539–541.*
- *Ueland PM, Refsum H, Wesenberg F, Kvinnisland S. Methotrexate therapy and nitrous oxide anaesthesia. New England Journal of Medicine 1986; 314: 1514.*
- *Entonox reference UHS guidelines. Children: The Policy for the Administration of 50% Nitrous Oxide & 50% Oxygen (Entonox®)*
<http://staffnet/TrustDocsMedia/DeptDivSpecific/DivC/ChildHealth/ChildHealthGuidelines/ChildHealthPainManagementServices/Entonox-Policy/Entonox-Policy.pdf>