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PAEDIATRIC ONCOLOGY MANUALv. 6

MOI TEACHING AND REFERRAL HOSPITAL

ELDORET, KENYA

INDEX PAEDIATRIC ONCOLOGY MANUAL

A. Preparation of patient prior to chemotherapy

B. Care of the patient during chemotherapy

C. Supportive care during and after chemotherapy

D. Specific diseases and protocols used in MTRH

WORK PROCEDURE WHEN MALIGNANCY IN A CHILD IS SUSPECTED

Document history: Duration, progression, presence of pain, fever, bleeding, weight loss, any co-morbidity ; HIV, prior transfusions, medication, hospitalization, surgery, alternative treatment.

Documentfindings: e.g. Lymphadenopathy (site and size important!)
Presence of palpable liver or spleen with measurements
Presence of bleeding tendency in skin, sclera, gums etc
Description and measurements of any masses with drawing in file

Investigate to getcytological / histological by:
Peripheral blood film (PBF) for haematological malignancies
Fine needle aspirate (FNA)
Bone marrow aspiration
Biopsy - Biopsy is preferred above FNA in solid tumors, take a whole node if possible.
(Put an imprint of the cut specimen on a slide and contact the PATHOLOGIST if a pediatric tumor is suspected for speedy review of tissue specimen.
If needed do ultrasound guided core biopsy

Get supportive biochemical evidence:
β-CG (in Embryonal tumors)
VMA / HVA in Neuroblastoma
LDH in Leukemia and Lymphoma
Alfa1-Feto Protein in Hepatoblastoma and Embryonal tumors
Carcino embryonic antigen (CEA) (+ve in Colon cancer, sometimes in embryonal tumors)

Determine stageby: Bone marrow in Non Hodgkin Lymphoma, Neuroblastoma, Retinoblastoma, Rhabdomyosarcoma, extensive Hodgkin, Ewing and Osteosarcoma.
CXR in Nephroblastoma, Hodgkin and Hodgkin Lymphoma, Leukemia, Sarcoma's and Abdominal ultrasoundin Hodgkin or Non Hodgkin Lymphoma, and all abdominal tumors
CSF in Leukemia, Non Hodgkin Lymphoma (when platelets $20x10^9$/dl or >50 in case of circulating blasts), give IT cytotoxics in same session. Use good technique and an experienced physician to avoid haemorrhagic tap.
CT Scan chest or abdomen where indicated and for brain tumors

Do Baseline investigationsto prepare for chemotherapy:
Full haemogram with differentials
Creatinine and full U/E if tumor burden is high
ALT and full LFT's if any suspicion of liver disease or liver metastases
Uric Acid in high tumor load eg in Leukemia or Non Hodgkin Lymphoma
ALL patients with a malignancy should have HIV serology confirmed prior to starting treatment.

Stabilize patient by treating any infection, bleeding, deworm, improve hydration and improve nutritional status. Correct anaemia till Hb $\geq$ 10 g/dl unless WBC count is very high.

Counsel: parent(s) / caretaker during process of investigations to make them part of your suspicion
and ensure their cooperation.
Definitive counseling is done after confirmation of diagnosis.
Also children need counseling according to their level of understanding.

Consult: oncologist always before giving chemotherapy and if guidance needed at any of the previous stages.

Calculate surface area: in m^2 with formula $\sqrt{\frac{\text{Height (in cm)} \times \text{Weight (in kg)}}{3600}}$

COUNSELING

Counseling plays integral part of the overall management of children with cancer. It should start from the time a diagnosis of cancer is suspected up to the time of follow up after end of treatment or the time of death. Various medical personnel have a role to play in the counseling process. These include the doctors, the nurses, the medical social worker and the psychological counselors. The doctor is the team leader though the psychological counselor is bound to spend more time with the families. The counseling should be done in a language that the parents/child best understand.

The parents as well as the child especially if they are of an age where they can understand should be fully involved and kept aware of the various aspects of management of the disease to optimize the outcome. The young children should be informed in a way that they can understand that they are suffering from a chronic condition that requires long term treatment. Continued discussions with the families and even repeating and re-emphasizing previously discussed aspects is very paramount

When a diagnosis of cancer is suspected it is important to let the family be aware and involve them through the process of investigations. This should be done preferably by the doctor and should be done in such a way that is not discouraging to the family.

Once the diagnosis is confirmed a lot of issues need to be discussed.
The doctor should be the one to disclose the diagnosis but the other aspects are handled by the whole team together. The issues to be addressed include:

- Disclosure of the diagnosis to the parents and to the child if the age allows. Allow the parents/child to express what they understand about the disease and then proceed on to explain what is understood medically about the disease.
- Explain the cause/risk factors if they are known
- The course of the disease with and without treatment and the expected outcomes/prognosis.
- The treatment options that can be used and what is available in our set-up. The phases and duration of treatment also should be explained in detail.
- The adverse effects of the various modes of therapy.
- Long term effects of therapy
- Will the treatment be done on an inpatient or out - patient setting?
- Importance of keeping return appointments and the need to contact the hospital in case of any medical problems while at home
- The costs of various modes of treatment and how they can handle them (cash payment vs health insurance[NHIF])
- Need for screening other children in case of hereditary conditions
- The role that the parents, other siblings and the rest of the family can play in offering psychological support to the child

Once the treatment has been started keep the family continually updated about the progress. Any changes in terms of treatment should constantly be communicated. Any questions arising from the family need to be adequately addressed.

Regular follow up after the end of treatment should be emphasized.

Whenever death is anticipated in the course of treatment the psychological counselor should counsel the parents about the same and prepare them adequately for the eventuality. Palliative care team should be involved early and during end of life period.
In case of death the family should be helped through the grieving process
All medical workers who are in contact with children with cancer need to be aware of their condition and should always handle them appropriately.

PAIN MANAGEMENT

Pain is one of the most common symptom in children with cancer. Its management is very critical in the treatment of cancer.
The main causes of pain in children with cancer include: The disease itself, procedures done on the patient and the treatment modalities.

ASSESSMENT OF PAIN

The assessment of pain is critical as it impacts on the treatment to be given. Important factors to be considered include the location, duration, intensity, quality of pain and any known relieving or aggravating factors. The severity of pain can be assessed using various scales:
For children older than three years the faces pain rating scale can be used.
The numeric scale can be used in children older than 5 years. It's represented by a line with a scale from 0-10 with 0 representing no pain and 10 representing the worst pain imaginable.

MANAGEMENT

The management of pain in children with cancer involves a multidisplinary approach. The Doctor, nurses, child life specialist, physiotherapist, pharmacists and also the parents and the family all have a role to play.
There are both pharmacological and non-pharmacological therapies that can be utilized.
The WHO approach for pain is recommended, where 4 levels of pain management are recognized:

1) Mild pain: non opioid analgesics and non pharmacological methods.
2) Moderate pain: weak opiods +/- adjuvants and non pharmacological methods
3) Severe pain : Strong opiods adjuvants+ non pharmacological methods
4) Intractable pain: Strong opiod+ adjuvants + invasive techniques+ non pharmacological means.

In children its recommended you move from level one to three without using weak opioids.

Non opioid analgesics that we use are: Paracetamol given orally at 15mg/kg/dose every 6-8 hours, Ibuprofen orally 10mg/kg/dose every 8 hours
Other NSAIDs can be used as alternatives
Weak opioids that are available include oral dihydrocodeine (0.5-1mg/kg/dose every 4 hours)
Strong opioids: We use morphine P.O (0.3mg/kg/dose every 4 hours)

ADJUVANT DRUGS include the following

Anxiolytics e.g lorazepam 0.03 to 0.1mg/kg every 4-6 hours
Antidepressants e.g amitriptyline 0.2-0.5 mg/kg per day
Anticonvulsants e.g carbamazepie 2.5 -5 mg/kg initially, then increase up to 20 mg/kg/day BD
Corticosteroids e.g dexamethasone 0.1mg/kg/dose every 12 hours
Barbiturates e.g phenobarbitone 3-5 mg/kg/day

NON PHARMACOLOGICAL TECHNIQUES

Always consult a child life specialist when managing children with moderate to severe pain and procedural pain. They are useful in providing the non-pharmacological interventions.
The techniques that are used include:

Explaining the procedure to the child who understands
Parental presence
Physical (massage, heat and cold stimulation, acupuncture e.t.c)
Behavioral (exercise, relaxation, art and play therapy)
Cognitive (distraction, imagery, music therapy)

For **PROCEDURAL PAIN** use topical anaesthetics, conscious sedation as per the protocol or general anaesthesia

Modalities that are available for INTRACTABLE PAIN include: Palliative chemotherapy, nerve and epidural blocks. The nerve and epidural blocks are done by the anaethesiologists.

It is important to keep assessing pain and to change the treatment accordingly. If the child seems to continue having pain move up on the WHO ladder and give the appropriate treatment.
The goal in paediatric oncology is to make sure our patients are pain free as much as possible.

PEDIATRIC SEDATION PROTOCOL FOR CHILDREN ≥ 3 YEARS

AIMS OF THE PROTOCOL

1. To facilitate the performance of minor procedures (e.g. intrathecal drug administration, bone marrow aspirates/biopsies and lymph node biopsies) in the ward procedure room.
2. To minimize the potential risks of cardiorespiratory complications of sedo-analgesia.

**For children under the age of 3 years consult the anaesthesiologist*.

PREPARATIONFOR SEDO-ANALGESIA

1) Equipment.		Suction machine with catheter & tubings.
		Bag Valve Mask – Ambu bag.
		Oxygen source.
		Face masks – Various sizes.
		IV canulae – G 24, 22.
		Needles – G 21, 23.
		Syringes – 2, 3, & 10 cc.
		Oral airway-various sizes
2)	Drugs	Atropine 1 mg/mL.
		Adrenaline 1mg/mL.
		Ketamine 50 mg/mL.
		Midazolam (Dormicum) 1mg/mL.
		Lidocaine 2%
3)	IV Fluids	Normal Saline
		Ringer's lactate
4)	Personnel	The Doctor performing the procedure Doctor/Qualified nurse/clinical officer responsible for monitoring cardiorespiratory function during procedure.

DILUTION OF DRUGS

1. Ketamine – Draw 1 cc (50 mg) in a 10 cc syringe and add 9 cc of Normal Saline to make 10 cc. The final concentration will be 5mg/mL.
2. Midazolam (Dormicum)– Draw 5cc (5 mg) in a 10 cc syringe and add 5 cc of Normal Saline to make 10 cc. The final concentration will be 0.5 mg/mL.
3. Atropine – Draw 1 cc (1mg) in a 10 cc syringe and add 9 cc of Normal saline to make 10 cc. The final concentration will be 0.1 mg/mL.
4. Adrenaline (1:1000) – Draw 1 cc (1mg) in a 10 cc syringe and add 9 cc of Normal saline to make 10 cc. The final concentration will be 0.1 mg/mL.
5. Lidocaine – Draw 5cc (100 mg) in a 10 cc syringe and add 5 cc Normal saline to make 10 c.c. The final concentration will be 10 mg/mL.

PROCEDURE FOR SEDATION

1. Confirm that the patient has fasted for at least 6 hours.
2. Get patient's ACTUAL WEIGHT and work out the maximum dosage for each drug
3. Ensure that the patient has an obviously patent intravenous canula with some appropriate intravenous fluid infusing.
4. Ensure that the drugs are diluted appropriately and the necessary equipment is available and in good working condition.
5. Delegate the responsibility of continual basic cardio respiratory monitoring (respiration and pulse) to a nurse or doctor.
6. Premedicate the child with atropine 0.02mg/Kg IV (0.2ml/kg) 15 to 30 minutes before the beginning of the procedure.
7. Administer Ketamine 1 mg/Kg (0.2ml/kg) bolus and administer oxygen by mask at 5L/min.
8. Within 2 min, the child should be well sedated at which point consideration should be given to additional sedation if necessary with midazolam 0.05 mg/Kg (0.1ml/kg).
9. Where possible, infiltrate the operative site with lidocaine to a maximum of 4 mg/Kg(0.4ml/kg)

MANAGEMENT OFCOMPLICATIONS

1. Bradycardia – Atropine 0.02 mg/Kg (0.2ml/kg) and repeat as necessary.
2. Cardiac arrest – Immediate CPR with chest compressions and Bag Valve Mask (Ambu bag) ventilation. Administer adrenaline 0.1 mg/Kg IV (0.1ml/kg).
3. Inadequate sedation – Incrementally administer Ketamine boluses at 0.5 mg/Kg.(0.1ml/kg)

   NB: Use of Local Anesthetics greatly reduces Ketamine/benzodiazepine requirements.
4. Excessive sedation – Ensure that the patient has a clear patent airway and is breathing well. Assist ventilation with a Bag Valve Mask bag if necessary. Monitor the pulse and Blood pressure every 5 minutes.
5. Convulsions – These will usually be due to local anesthetic toxicity. Manage with Midazolam at 0.15mg/kg (0.3ml/kg).

POST SEDATION CARE

1. Place the child in a lateral position and confirm adequate ventilation.
2. Administer oxygen by mask until the child is awake.
3. Neuropsychiatric manifestations may be managed with IV midazolam 0.05 mg/Kg.
4. Remember that the child will experience post operative pain and prevent it if necessary.
5. Allowthe child to feed once he/she is fully awake.
6. In case of intrathecally administered drugs let the patient be flat for (2-)4 hours

NUTRITION IN ONCOLOGY

Effects of cancer on nutritional status

Changed metabolism leading to increased lipolysis, reduced protein synthesis, hypermetabolism
Anorexia.
The result is progressive wasting as part of natural progression of the disease.

Effects of chemotherapy on nutritional status

Anorexia, early satiety
Nausea and vomiting
Taste and smell changes
Depression and anxiety

Local effects of tumor mass on food intake and digestion

Difficulty in feeding and swallowing
Tumor mass effect on digestion, bowel movements
Intestinal obstruction

Effects of nutritional status on outcome

Cachexia contributes to sepsis, malabsorption,
Higher incidence and increased severity of chemotherapy side effects
Reduction of quality of life
Contributes to reduced chances of survival

Recognition and detection of malnutrition

Height, weight, LUMAC, BMI
Assessment of food intake

Aim of nutrition care

Should be part of quality of care in oncology in order to
Maintain or improve body weight and nutrition stores.
It protects cancer patients to the impact and side effects of chemo and radiotherapy.
Improves outcome

Mode of nutrition care

Higher caloric intake,
High protein and vitamin containing diet,
More meals per day,
NG tube feeding

To get amount per feed (mls) to achieve desired kilocalories use:

$$\text{Mls} = \frac{\text{Kcl X Wt (kg)}}{\text{No of meals X 1.0}}$$

Ratio of 1.0 is when using F100 (in case of breast milk, 0.67)

Kcl = desired kilocalories in 24 hours, No of meals usually 8 or 6 in 24 hours.

TRANSFUSION MANAGEMENT

RED BLOOD CELL TRANSFUSION

General indication for blood transfusions is symptomatic deficit in oxygen carrying capacity, and tissue hypoxia due to inadequate circulating blood cell mass. Other anaemias that can be corrected by non transfusion therapy should get the alternative treatment in the form of iron and /or folate supplementation.
This rule should not apply to children with cancer. Here iron supplementation works too slow, and the bone marrow is often inactive. So blood transfusions should be given regularly.

Chemotherapy often depresses bone marrow production, including red cell production, irrespective of available iron stores. To maintain good oxygen carrying capacity the haemoglobin level needs to be maintained at least above 8 g/dl and preferably above 10 g/dl till end of chemotherapy or radiotherapy.
Only in a new diagnosed leukemia patient with a WBC count above 100,000 the maximum Hb should be 8 g/dl.

Preference is given to packed red cells, dosage 10-15 ml/kg, to raise the Hb level with 1-3 g/dl. If the deficit is large, the following formula can be used: **deficit in g/dl x3x Body weight** in kg is required volume. If the patient is in failure this amount needs to be spread over several days.

There is no need to warm the blood except in neonates. The blood should not be kept longer than 1 hour outside the fridge before start of transfusion and transfusion should not take longer than 4 hours. Lasix should not be given as routine, only when circulation overload exists.

Fresh blood (less than 72 hours) should be given when there is anaemia *and* thrombocytopenia.
Whole blood should be reserved for patients with acute blood loss.

PLATELET TRANSFUSION

INDICATIONS

If thrombocyte count $<10x10^9/L$
In active bleeding with any low thrombocyte count
Pre-procedure e.g. lumbar puncture, lymph node biopsy etc.

Many procedures can be done despite minimal platelet count, eg bone marrow can be done despite low counts. Patients with leukemia undergoing diagnostic lumbar puncture should have a platelet count > 50 x 10^9/l due to possibility of seeding CNS with tumor due to micro bleeding. When circulating blasts are absent, then the cut off level for lumbar puncture is 20 x10^9/l.

CONTRA INDICATIONS for platelet transfusions include

Irreversible bone marrow failure
Thrombocytopenia due to platelet destruction by antibodies (e.g. ITP) unlesssevere bleeding
Prophylactic transfusion

DOSAGE in Paediatrics: 1-2 x 10^9 cells/kg or 1-2 units per 10kg body weight.

COMPLICATIONS: Transmission of infectious agents like CMV. HIV
Inducement of platelet antibodies

VENOUS ACCESS PRESERVATION IN PAEDIATRIC ONCOLOGY

WHY

Maintaining reliable venous access is not only important for the administration of chemotherapy but also for the supportive care as antibiotics, blood products, hydration, parenteral nutrition etc.

WHERE

Use veins in hands and arms whenever possible. Start with the most distal veins and avoid using the same vein repeatedly. **Remove canula** after finishing the antibiotic or cytotoxic treatment. Use foot veins only when a suitable upper extremity vein cannot be found.

IV LINES

For cytotoxics use a freshly placed branula or a scalp vein needle.
Wash your hands between patients and always use aseptic techniques.
Use spirit to clean the skin and do not touch the needle or the tip of the infusion set.
If a vein does not become prominent enough after applying the tourniquet, try the following maneuvers: Hang arms down, ask patient to open and close the fists repeatedly. While the arm is still down, apply tourniquet. Then bring the arm up to normal position OR soak the arms for five minutes in a basin of warm water.
Insert the needle into the skin with the bevel of the needle up. Once under the skin, go into the vein, and then secure the needle with a piece of tape.
Start with **normal saline** infusion, or push 5 - 10 ml saline to be certain that the canula is patent while it helps the vein to open up.

DRUG PREPARATION

Use gloves and mask when preparing drugs. Use a gown if available.
Dissolve the drugs after obtaining a patent line and use the appropriate solvents, eg

Water for injection for Adriamycin, Cyclophosphamide and Cytarabin, (not NS!)
Normal saline for Vincristine.
Water for injection without preservative for Dactinomycin.

Make sure there are no air bubbles or undissolved particles in the drug solution.
Calculate accurately the amount needed for the patient and draw up each drug in a separate syringe. Do not spray excess drugs in the air, but push excess back into the bottle.
Label the syringes if necessary.

DRUG ADMINISTRATION

After the vein is clearly found to be patent, begin infusion of the drugs. This can be done with the syringe directly attached to the needle, or via the infusion tube. Adriamycin should be given in infusion of one hour duration to reduce the chance of cardiotoxicity. Also Cyclophosphamide should be given in infusion during 30 – 60 minutes. After Vincristine always flush the vein with at least 20 ml normal saline (not water for injection).

AVOID EXTRAVASATION

Chemotherapy extravasations are best avoided. Therefore:

- Do not attempt to give an intravenous drug unless you are confident of accessing and maintaining the vein.
- Do not make more than three attempts at inserting a butterfly or canula.
- Do not use the antecubital veins for cytotoxics , only for withdrawing of blood.
  Extravasation at this site can be catastrophic.
- Do not give drugs in a peripheral vein after you have punctured proximal veins in search for a line.
- Avoid giving cytotoxics after 5.30 PM, before 8.30 AM and over the weekend.

CHARACTERISTICS OF CYTOTOXIC AGENTS

ACTINOMYCIN-D

Generic name	Brand name	Presentation	Strength
DACTINOMYCIN-D	Actinomycin-D Cosmegen	Powder	0.5 mg
Reconstitution	Add 1 ml sterile water to give a final concentration of 500µg/ml or 0.5 mg/ml. Use preservative free water to avoid formation of a precipitate.		

Dilution	The reconstituted drug can be further diluted in 5% dextrose or normal saline for intravenous infusion or bolus.
Administration	IV push or infusion. Max dose 2 mg
Stability after reconstitution	
Toxicity	Myelosuppresion (dose-limiting and severe), liver toxicity including veno occlusive disease, nausea and vomiting, mucositis, hyperpigmentation of skin, hypersensitivity to sunlight, and alopecia.
Remarks	It's a potent vesicant hence should be infused over 15 minutes to avoid extravasation.

ASPARAGINASE

Generic name	Brand name	Presentation	Strength
ASPARAGINASE	L-asparaginase, Elspar		10,000 IU
Reconstitution	For IM use, 2 ml of normal saline should be added to the vial. For IV use 5 ml of normal saline should be added to the vial.		

Dilution	The drug for IV use can further be diluted with normal saline.
Administration	IM, IV 1 hour infusion.
Stability after reconstitution	Refrigerate and use within 8 hours of preparation.
Toxicity	Hypersensitivity reaction (occurs in 25% of patients). Pancreatitis, neurotoxicity, Diabetes Mellitus, hypertriglyceridemia.
Remarks	Patient should be observed for several hours after administration for possible reactions, Asparaginase is a contact irritant. Contraindicated in patients with active pancreatitis or a history of pancreatitis.

BLEOMYCIN

Generic name	Brand name	Presentation	Strength
BLEOMYCIN	Blenoxane	powder	15, 30 units
Reconstitution	Dilute in normal saline or sterile water. Do not reconstitute in dextrose containing solutions.		

Dilution	
Administration	Give as an IV push. Can also be administered IM,SC or intracavitary.
Stability	Stable for 24 hours after reconstitution.
Toxicity	Pulmonary toxicity is dose limiting. Usually presents as pneumonitis. It is dose and age related. Cumulative doses greater than 400 units and age greater than 70 years are associated with increased incidence of this complication. 1% of the patients may progress to fibrosis. Skin reactions and hypersensitivity reactions also occur.
Remarks	

CARBOPLATIN

Generic name	Brand name	Presentation	Strength
CARBOPLATIN	Paraplatin	Vials aqueous solution	150 mg/15 ml 450 mg/45 ml
Reconstitution	Reconstitute with saline to a final concentration of 10 mg/ml		

Dilution	Can be diluted further with 5 % dextrose or normal saline to concentration of 0.3, 0.5 and 2 mg/ml
Administration	Intravenous infusion
Stability after reconstitution	Store protected from light. Diluted solutions between 15-25^{0}C are stable for 24 hours. If refrigerated solution stability is 48 hours.
Toxicity	Dose limiting toxicity is myelosuppression, especially thrombocytopenia. Myelosuppression is closely related to renal function and prior chemotherapy.
Remarks	Dose can be according to renal function rather than body surface area.

CISPLATINUM

Generic name	Brand name	Presentation	Strength
CISPLATINUM	Platinol, Platinex	Powder Solution	10 mg, 50 mg 1 mg/ml
Reconstitution	Add sterile water to give a final concentration of 1 mg/ml .		

Dilution	Dilute further with Normal saline. Never mix with dextrose as it leads to formation of precipitate.
Administration	Give as an IV infusion over 6 hours.
Stability after reconstitution	Stable for 24 hours at room temperature. DO NOT refrigerate the reconstituted solution.
Toxicity	Nephrotoxicity (dose-limiting), Neurotoxicity (peripheral sensory neuropathy), Nausea and vomiting (acute and delayed), myelosuppression and ototoxicity.
Remarks	Avoid use of any aluminium containing equipment. Ensure adequate hydration before, during and at least 24 hours post drug administration (urine output should be > 1.5cc/kg/hr). Highly emetogenic. Manage with 5-HT_3 antagonist and dexamethasone. Protect from direct sunlight during administration.

CYCLOPHOSPHAMIDE

Generic name	Brand name	Presentation	Strength
CYCLOPHOSPHAMIDE	Endoxan Cytoxan	Powder for dilution Tablets	100 , 200 , 500 mg , 1 and 2 gm 25 mg, 50 mg
Reconstitution	Dissolve in water for injection al follows: 100 mg in 5 ml 500 mg in 25 ml 200 mg in 10 ml 1000 mg in 50 ml.		

Dilution	Can be diluted further in Normal Saline or 5% Dextrose.
Administration	Mostly IV, (Also oral, Intrapleural). IV push or with doses > 500 mg in 30 - 60 min infusion, diluted in Normal Saline or 5% Dextrose. Continue hydration initial IV and later oral for 24-48 hours.
Stability after reconstitution	Use preferably within 3 hours after dissolving. Solution is stable 24 hours at room temperature, 6 days with refrigeration (2-8 ^{0}C).
Toxicity	Haemorrhagic cystitis, myelosuppression (nadir 8 – 14 days), nausea, vomiting , alopecia, secondary malignancy, testicular or ovarian failure.
Remarks	Solubility can be improved by warming solution to max 60^{0}C or by leaving it on the bench for few minutes.

	Ensure sufficient fluid intake IV or oral to prevent haemorrhagic cystitis, encourage patient to empty their bladder frequently, and / or give a concurrent (repeated) dose of MESNA (Urumitexan) especially with dose > 500 – 1000 mg/m^2. Encourage patients to empty the bladder two hourly. High dose cyclophosphamide is cardiotoxic (rare).

CYTOSINE ARABINOSIDE

Generic name	Brand name	Presentation	Strength
CYTOSINE ARABINOSIDE	ARA-C, Cytosar	Powder	100 mg, 500 mg, 1000 mg, 2000 mg
Reconstitution	Dilute in sterile water. For I.T. administration use preservative free diluent(Normal saline).		

Dilution	You can further dilute with normal saline or 5% dextrose.
Administration	Give as an IV infusion over 3 hours or subcutaneously if dose is low.
Stability after reconstitution	The drug diluted with preservative free diluent should be used immediately after reconstitution and any unused drug discarded. Any drug reconstituted with preservative containing diluent is stable for 48 hours at room temperature and for seven days upon refrigeration.
Toxicity	Myelosuppression (nadir 7-10 days), neurotoxicity (cerebellar ataxia ,lethargy and confusion), mucositis. Ara-C syndrome (fever, myalgia, malaise, bone pain, maculopapular rash, conjunctivitis). Seizures, alterations in mental status and fever may be observed within the first 24 hours after IT administration.
Remarks	Conjuctivitis is observed with high doses as the drug is excreted in tears.

DACARBAZINE

Generic name	Brand name	Presentation	S.trength
DACARBAZINE		Powder	100 mg, 200 mg
Reconstitution	100 mg in 9.9 ml water for injection, 200 mg in 19.7 ml water for injection.		

Dilution	Can be diluted further in Normal Saline or 5% Dextrose.
Administration	IV infusion over 30-60 minutes.
Stability after reconstitution	Administration preferably within 8 hours after reconstitution. Solution is stable 24 hours at room temperature, 96 hours with refrigeration. Always protect from light.
Toxicity	Neutropenia, thrombocytopenia (nadir at 2-3 weeks) , severe nausea and vomiting for up to 12 hours, anorexia, alopecia, rash, flu-like syndrome, hypotension, hypersensitivity reaction, photosensitivity, hepatic dysfunction.
Remarks	Can cause burning pain at the injection site and along the course of the vein. Reduce this by reducing infusion rate of increasing volume of diluent. Protect solution from light, pink solution indicates decomposition. Reduce doses for patients with poor renal function.

DOXORUBICIN

Generic name	Brand name	Presentation	Strength
DOXORUBICIN	Adriamycin, Adriablastine.	Powder	10 mg, 50 mg
Reconstitution	Dissolve in water for injection 10 mg drug in 5 ml, 50 mg drug in 25 ml.		

Dilution	Can be diluted further in Normal Saline or 5% Dextrose (preferred for children)
Administration	Preferably in 100 ml infusion over 60 min, piggy back in Normal Saline, or (in adults only) use IV push over 3-5 minutes followed by Normal Saline flush.
Stability after reconstitution	Administration preferable immediately after reconstitution. Solution is stable 7 days at room temperature and 15 days if refrigerated and protected from light.
Toxicity	Myelosuppression (nadir 1-2 weeks), nausea, vomiting, alopecia, mucositis, cardiotoxicity, arrhythmia, photosensitivity.
Remarks	Doxorubicin is a vesicant. For extravasation check separate protocol. Cardiotoxicity: Do not exceed a lifetime cumulative dose of 550 mg/m^2 or 450 mg/ m^2 if concomitant use of Cyclophosphamide, or 350 mg/m^2 in children. Measurement of ejection fraction is advised with doses above 250 mg/m^2 Drug may turn urine red. Reduce dose in impaired hepatic function.

ETOPOSIDE

Generic name	Brand name	Presentation	Strength
ETOPOSIDE	Vepesid	Capsules IV solution	50 and 100mg capsules 100 mg vials
Reconstitution	Reconstitute to 20 mg/ml or 10 mg/ml using either normal saline, 5% dextrose		

Dilution	Can be further reconstituted with normal saline or 5% dextrose to a final concentration of 0.1 mg/ml.
Administration	Administer over 30-60 minutes.
Stability after reconstitution	Do not refrigerate solution. Stable for 48 hours at a concentration of 0.4ml/ml and for 96 hours at a concentration of 0.2 mg/ml.
Toxicity	Nausea and vomiting, myelosuppression, hypersensitivity reaction, mucositis, metallic taste during infusion of drug.
Remarks	Give as an infusion to avoid risks of hypotension, monitor for anaphylaxis.

5 FLUORO URACIL

Generic name	Brand name	Presentation	Strength
5-FU	Adrucil Fluradecyl	IV solution	Vials 50 mg/ml Vials:5ml,10ml,20ml, 50ml,100ml
Reconstitution	Not Applicable		

Dilution	Normal saline
Administration	IV infusion
Stability after reconstitution	7 days at room temperature (shorter is safer)
Toxicity	Mucositis, skin pigmentation changes, conjuctivitis
Remarks	

HYDROXYUREA

Generic name	Brand name	Presentation	Strength
HYDROXY UREA	Hydrea	capsules	500 mg
Reconstitution	N/A		

Dilution	N/A
Administration	Oral / enteral
Stability after reconstitution	N/A
Toxicity	Myelosuppression (onset7-10days), Maculopapular rash.
Remarks	Monitor CBC weekly while on therapy. Withhold treatment if the WBC falls to < 2500/mm^3.

IMATINIB

Generic name	Brand name	Presentation	Strength
Imatinib	Gleevec/Glivec	Tablets, unbreakable	100, 400 mg
Reconstitution	N/A		

Dilution	N/A
Administration	Orally
Stability after reconstitution	N/A
Toxicity	Bone marrow suppression
Remarks	*Long-term use: growth failure, cardiac failure*

MERCAPTOPURINE

Generic name	Brand name	Presentation	Strength
MERCAPTOPURINE	6-MP, Purinethol.	Tablets	50 mg
Reconstitution	N/A		

Dilution	N/A
Administration	Oral, enteral
Stability after reconstitution	N/A
Toxicity	Myelosuppression, mucositis, hepatotoxicity.
Remarks	Reduce dose by 50-75 % in patients who are concurrently receiving allopurinol. Administer on an empty stomach to facilitate absorption. *Give nocte for better activity.*

METHOTREXATE

Generic name	Brand name	Presentation	Strength
METHOTREXATE	MTX, Amethoprin		50 mg, 100 mg, 200 mg, 1000 mg
Reconstitution	For IT administration avoid preservatives		

Dilution	Dilute with Normal saline.
Administration	Can be given IV, IM or IT.
Stability after reconstitution	Reconstituted solution is stable for 24 in room temperature. However, for IT administration always prepare freshly
Toxicity	Myelosuppression, mucositis, acute renal failure, hepatotoxicity incl raised transaminases.
Remarks	Avoid folic acid supplements during therapy, but folinic acid can be given as rescue after higher dose MTX, and urine alkalinisation is required for HD-MTX.

VINBLASTINE

Generic name	Brand name	Presentation	Strength
VINBLASTINE	Velban	Powder Solution	10mg
Reconstitution	Add normal saline to make a solution of 1 mg/ml.		

Dilution	Can be further diluted with normal saline if necesary
Administration	IV push over 1 minute
Stability after reconstitution	
Toxicity	Myelosuppression (nadir 4-6 days), mucositis and stomatitis, neurotoxicity.
Remarks	It's a vesicant, avoid extravasation. If it occurs discontinue infusion, flush with sterile water, elevate the limb. Local cold application is advised. Fatal if given intrathecally

VINCRISTINE

Generic name	Brand name	Presentation	Strength
VINCRISTINE, VCR	Oncovin	Powder	1 mg, 2 mg, 5 mg.
Reconstitution	Dissolve in 10 ml diluent (normal saline + preservative).		

Dilution	Can be diluted further in 100 ml normal saline or 5% glucose.
Administration	IV push over 1 minute followed by N/S, or infusion of 100 ml in 15 – 30 min
Stability after reconstitution	Administration preferably within 24 hours. Dissolved drug is stable for 2 days at room temperature and 2 weeks refrigerated at 4^0C.
Toxicity	Peripheral neuropathy , alopecia, constipation, paralytic ileus, jaw pain, foot drop.
Remarks	Maximum dose 2.5 mg. Vincristine is a vesicant. For extravasation check separate protocol Neurotoxicity is cumulative but often reversible, withhold dose if severe paraesthesia or motor weakness. Reduce dose in the presence of significant liver disease. Stool softeners can be given to prevent constipation. Drug is fatal if given intrathecally. Wash skin / eye thoroughly if accidental contact occurs.

CHEMOTHERAPY EXTRAVASATION

Some chemotherapy drugs are vesicants, so they are notorious for serious consequences of extravasation of the drug, leading to ulcers and even necrosis of the area affected by extravasation.
These drugs are Vincristine
Actinomycin D
Adriamycin
Daunorubicin

Chemotherapy extravasations are best avoided. Therefore:-

- Always give cytotoxics in a freshly placed butterfly or canula.
- Always check patency of IV lines by flushing with 5 -10 mls of normal saline prior to administering cytotoxics.
- Do not attempt to give an intravenous drug unless you are confident of accessing and maintaining the vein.
- Do not make more than three attempts at inserting a butterfly or canula. With failure consult a senior colleague. Ensure that you don't spoil all the sites!
- Try not to use the antecubital veins: extravasation at this site can be catastrophic. Always start with the most peripheral veins and start from peripheral to proximal – Never the reverse.
- Avoid giving cytotoxics after 5.30 p.m. and before 8.30 a.m.
- Be prepared and ready to give cytotoxics and do not look forward to a `quick job'.
- Always have an assistant and be ready to counteract extravasation.

Should extravasation occur or is suspected, then:

1. Stop infusing the drug
2. Alert the nurse and your assistant
3. Remove the needle or canula being used
4. Apply silver sulfadiazine cream (SSD) if available (usually kept in the fridge) generously and immediately, or apply a cold pack
5. Cover with dry dressing
6. Complete chemotherapy drug infusion at another site
7. Repeat SSD or cold application twice daily for at least 5 days, irrespective of absence of local reaction
8. Put information down in records about extravasation so that appropriate follow-up is arranged

INTRATHECAL ADMINISTRATION OF CYTOTOXIC DRUGS

Contraindications

Platelets < 20.000 x 10^9/L

Platelets < 50.000 x 10^9/L in presence of circulating blasts. Transfuse platelets if that is required to raise the platelet count.

Preparation of drugs:

1. Prepare sterile trolley as for lumbar puncture
2. Wash hands and wear sterile gloves and mask to prepare drugs. Use a gown if available.
3. Make use of an assistant to keep all syringes sterile.
4. Use only Methotrexate with the specification "for IT use". Fill a 5 ml syringe with 4 ml normal saline and add accurately the required amount of drug (0.1 ml = 2.5 mg).
5. Dilute Cytosine Arabinoside in 5 ml normal saline or water for injection without preservative, and don't use the solution prepacked with the drug, since this contains preservatives. Accurately measure the drug in a 5 ml syringe (1 ml = 20 mg).
6. Dilute entire Hydrocortisone vial (100 mg) in 4 ml preservative free water for injection and withdraw only the required amount (0.1 ml = 2.5 mg).
7. Put all the drugs on the trolley

Dosages:

Methotrexate:	<1 yr = 6mg	1yr = 7.5mg	2 yrs = 10mg	>3 yrs = 12.5 mg
Cytosar:	<1yr =15mg	1 yr = 20mg	2 yrs = 25mg	3-4 yrs = 30mg> 5yrs = 40mg
Hydrocortisone	<1 yr = 6mg	1yr = 7.5mg	2 yrs = 10mg	>3 yrs = 12.5 mg

For CNS prophylaxis use either single MTX (in ALL), or combined with Cytosar (in AML and NHL) combined with Hydrocortisone. In CNS disease, combine all three drugs

Administration of drugs:

1. Use conscious sedation as per protocol or use anaesthetic patch or spray on the lumbar area.
2. The aide should then position the patient as for lumbar puncture. Clean with spirit or iodine, then drape the site of operation, usually L4/L5 or L5/S1.
3. Do a lumbar puncture in the usual way by using G21 (green) needle, or the stylet of a G21 branula (pink).
4. Always allow 3 – 5 ml of CSF to flow out, or put the CSF into plain specimen bottles for cytology and for biochemistry.
5. Cautiously but firmly attach the drug-containing syringe onto the lumbar puncture needle. Aspirate the CSF into the syringe to ascertain that the needle is still in position. If there is free flow of CSF, then slowly push the drug.
6. Repeat this if more than one drug used.

First use the Methotrexate, then Cytosar, and finally Hydrocortison.

7. On finishing, quickly withdraw the needle to avoid tracking back by the drug and apply sterile dressing on the puncture site.

Bed rest

It is advisable that the patient remains horizontal for 2 – 4 hours after the procedure to promote distribution of the drug(s) to the intracranial area and to prevent headaches.

Register

IT procedure and administration of drugs should be noted in the file with signature

MANAGEMENT OF NAUSEA AND VOMITING DURING CHEMOTHERAPY

There are three main categories of nausea and vomiting:

1. Anticipatory nausea and vomiting that occurs before giving chemotherapy due to fear, anxiety and previous experience. It should be avoided by adequate anti-emetics before the very first chemotherapy dose.
2. Nausea and vomiting occurring acutely within 24 hours after chemo therapy.
   Anti emetics are given once before chemotherapy, repeated PRN after 4-6 hours.
3. Severe vomiting and delayed-onset nausea and vomiting occurs 24 hours or more after treatment especially with Cisplatin therapy. Combination anti emetics should be given frequently and anticipatory for prolonged period up to one week.

Emetogenicity of cytotoxic drugsdepends on type of drug used

None	Vincristine, 6-Mercaptopurin, Cytosine Arabinoside <50mg/m^2, L-Asparaginase	No anti-emetics
Low	IT treatment, Bleomycin, Etoposide, Cytosine arabinoside 50-1000mg/m^2, Cyclophosphamide <500mg/m^2 , Vinblastine	Anti-emetics group C $\pm$ B, repeat PRN after 4-6 hours
High	Actinomycin D, Anthracyclines, Carboplatinum, Dacarbazine, Cyclophosphamide > 500 mg/m^2, Ifosfamide, Lomustine, Procarbazine,	Anti-emetics group A$\pm$ B, repeat 6-8 hourly day 1, then PRN day 2-3. In severe vomiting add drugs of group D.
Very high	Cisplatinum	Anti-emetics group A + B $\pm$ D, repeat 6-8 hourly day 1,2 then PRN day 3 – 7.

Level of emetogenesis and choice of anti-emetic drugs

	GROUP	NAME	DOSAGE per administration
High risk	A. 5- HT_3 ANTAGONISTS	Granisetron (Kytril) Ondansetron (Zofran)	3 mg/m^2 5 mg/m^2
	B. CORTICOSTEROIDS	Hydrocortisone Dexamethason *	2 mg/kg 0.1 mg/kg
Low risk	C. DOPAMINE ANTAGONISTS	Metoclopramide (Plasil)	2-3 mg/kg
Anticipatory or severe persistent vomiting	D. SEDATION	Lorazepam (Temesta) Chlorpromazine (Largactil) Chlorpheniramine (Piriton)	0.05 mg/kg/dose 0.5-1 mg/kg/dose 0.35 mg/kg/dose

- Avoid dexamethasone as much as possible in AML because of potential stimulating effect on the AML blasts by dexamethasone.

TUMOR LYSIS SYNDROME (TLS)

DEFINITION

Syndrome that is caused by rapid tumor cell turnover after start of chemotherapy especially occurring with large tumor load as in ALL, NHL, Neuroblastoma in the first 5 -7 days

LABORATORY features

- Hyperuricaemia
- Hyperkalaemia
- Hyperphosphataemia
- Hypocalcaemia
- High LDH
- Elevated Creatinine

SYMPTOMS

Nausea and vomiting, shortness of breath, irregular heartbeat, clouding of urine, lethargy, and / or joint discomfort

If TLS is untreated, its progression may cause acute renal failure, cardiac arrhythmias, seizures, loss of muscle control, and death.

PREVENTION

1. Hyperhydration resulting in adequate urine output; use furosemide if necessary for that
2. Medication: Allopurinol
3. Rasburicase (in stead of allopurinol for patients with high risk of TLS)

MONITORING

- Electrolytes daily for 2-3 days
- Fluid status (urine output, weight)
- Vital signs

HYDRATION

- To start 12-24 h before chemotherapy, make sure adequate urine output is achieved before chemotherapy is started; if necessary, use furosemide for forced diuresis
- 3000 ml/m^2/day (oral, NG tube, IV)
- Monitor input/output, weight
- Consider use of lasix (With Cisplatinum don't use lasix but use mannitol)
- Continue hydration at least first 24 hours up to 5-7 days if risk of TLS is high

CONTROL HYPERURICAEMIA

ALLOPURINOL for 1-2 weeks

- Inhibits production of uric acid
- To start 24 hr before chemotherapy
- Dose 10 mg/kg/day in 2 or 3 divided doses

INFECTION PREVENTION DURING CHEMOTHERAPY

WARD	Patient should be in isolation area (away from acute infections) Only one patient per bed In severe neutropenia one patient per cubicle
STAFF	Strict hand washing / hand sanitizer in between patients In severe neutropenia handling of the patients should be as little as possible fresh linen should be provided daily
FOOD	Only use safe foods (no salads, raw eggs, left over foods)
VISITORS	Allow only limited visitation, without respiratory infections Visitors should wash hands before entering patients room
PERSONAL	Regular hand washing Oral hygiene: Cleaning of mouth with water after every meal (with assistance if needed) Use of soft tooth brush twice daily Betadine mouth wash in severe neutropenia
DRUGS	Pneumocystis carinii prophylaxis in all patients on chemotherapy: Use Cotrimoxazole 15+3 mg/kg OD Continue till end of maintenance

MANAGEMENT OF FEBRILE NEUTROPENIA

DEFINITIONS

NEUTROPENIA Absolute neutrophil count = ANC (% neutrophils x total WBC)

Mild: ANC < 1000/mcL

Severe: ANC < 500/mcL

FEVER

Single axillary temperature $\geq 38.5^0$ C

Or temperature of $>38.0^0$ C in 2 readings 1 hour apart

EVALUATION OF FEBRILE NEUTROPENIA

History

Time since last chemotherapy
Recent antibiotic therapy / prophylaxis
HIV status
Exposure to sick persons

Examination

Site of branula
Skin
Lungs
Alimentary canal (mouth, pharynx)
Perivaginal / perirectal

Laboratory

Bloodslide for malaria parasites
CBC including differentials
CXR if respiratory symptoms
Blood culture
Urine culture if symptoms or catheter
Or if severe neutropenia
Stool culture if diarrhea

NOTE Nadir after administration of drugs is generally 7-14 days

INITIAL THERAPY FOR FEVER AND NEUTROPENIA

Re-emphasize infection prevention measures

Choice of antibiotics should be tailored to findings on history and physical exam
IV antibiotics should be used, covering gram +ve and gram –ve organisms
Monotherapy: Cefepime, Ceftazidime or Meropenem are the best. In MTRH: use reliable ceftriaxone or combination drugs: Aminoglycoside + antipseudomonal penicillin + beta lactamase inhibitor

If in 48 h no response: Add AB covering anaerobes (IV Metronidazole)
If in 72 h no response: Add antifungal (Amfotericine-B, Fluconazoleif amfo-B is unavailable)

Low risk patient (and outpatient Rx):

Oral antibiotic allowed: Ciprofloxacin or Amoxicillin/Clavulanic acid
Mouth care with antiseptic
Close observation, and review by a clinician within 72 hours

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

In the western world ALL is the most common childhood cancer, representing 23% of cancer diagnoses. ALL is the second most common cancer in children under 15 year after Non Hodgkin Lymphoma in East Africa. The worldwide incidence is 1:25,000 in the white population; in the black race incidence is 2-3x less. Kenya should have over 250 children with ALL per year, the majority probably not reaching treatment centers. The peak age is 4 years, 85% of the patients is diagnosed between ages 2 and 10 years.

ALL results from uncontrolled proliferation of immature lymphocytes. Its cause is unknown, genetic factors, exposure to radiation and chemicals may play a role. Children with *Down syndrome* have increased risk for developing both ALL and acute myeloid leukemia. Increased occurrence of ALL is associated with certain genetic conditions, including *neurofibromatosis*, *Shwachman* syndrome, *Bloom's* syndrome, and *ataxia telangiectasia*.

Before the use chemotherapy this disease was fatal, usually within several months. Currently cure rates in the western world reach over 75% and remission rates more than 95%. In developing countries like Kenya there are generally low survival rates, largely because of limitations in the existing health care systems. Cancer treatment is no priority in any country when major childhood mortality is due to infectious diseases as malaria, pneumonia and diarrhea. Poverty plays an important role in cancer co-morbidities as malnutrition and infections, leading to poorer outcomes and treatment related deaths.

Signs and symptoms are pallor, petechiae, purpura, bone pains, hepatosplenomegaly, and lymphadenopathy. Haemogram shows combination of anemia, thrombocytopenia, leucopenia or leucocytosis, and often lymphoblasts in the peripheral blood smear. Diagnosis is confirmed by bone marrow with presence of more than 25% lymphoblasts. Histochemical stains help distinguish ALL from AML. Immunophenotyping of ALL blasts by flow cytometry helps distinguish precursor B-cell ALL from T cell ALL or AML. About 5 % of patients present with CNS leukemia, which is defined as cerebrospinal fluid WBC count > 5/µL with blasts present on cytocentrifuged specimen.

Differential diagnosis include chronic infections as Epstein Barr Virus (EBV) or cytomegalovirus (CMV); Immune thrombocytopenic purpura (ITP), auto immune haemolytic anemia, aplastic anaemia, and juvenile rheumatoid arthritis (JRA).

Further investigations necessary are CXR which may show mediastinal widening or anterior mediastinal mass and tracheal compression due to lymphadenopathy or thymic infiltration especially in T-cell ALL. Abdominal ultrasound may show kidney enlargement from leukemic infiltration or uric acid nephropathy, as well as intra-abdominal adenopathy. Before chemotherapy baseline investigations for liver and renal function including uric acid and LDH assessment need to be done.

Intensity of treatment is determined by specific prognostic features present at diagnosis or early in treatment. There are protocols for standard and high risk disease. High risk stratification includes patients not in 2-9 age group, WBC count >50.000/µL or CNS disease on diagnosis and presence or absence of specific chromosomal abnormalities*Philadelphia chromosome confers a poor prognost*ic outcome. Prognosis also depends on response to treatment, and minimal residual disease at end of induction.

General strategy of chemotherapy of acute leukemia include:

- Remission induction with maximum supportive care, for disease eradication or disease reduction
- CNS prophylaxis (or treatment)during all phases of treatment
- Consolidation with different drugs to eradicate disease in the sanctuary sites and obtain more cures with continued CNS prophylaxis / treatment
- M-Phase, with use of methotrexate, to amplify CNS disease prevention
- Re-induction
- Maintenance. Optimal duration unknown, mostly 2 years (from start of treatment)

ACUTE LYMPHOBLASTIC LEUKEMIA &LYMPHOBLASTIC LYMPHOMA MANAGEMENT

Name……IP No…….

Disease characteristics(tick appropriately/ make notes)

Subtype	B-cell	T-cell
Wide mediastinum (chest x-ray)	Present	Absent
CNS disease	Positive	Negative
WBC count at diagnosis		

- ✓Do CXR, diagnostic bone marrow. Thrombocytopenia is no contra indication!
- ✓Stabilize as indicated with packed cells till Hb >10 mg/dl unless WBC > 50.000, then aim at Hb 8 mg/dl. Platelets transfusion if platelets < 10 x 10^9 or if bleeding. Treat infections
- ✓Do baseline investigations as HIV, creatinine, electrolytes, uric acid, ALT, BS for MP's, stool O/C
- ✓Do diagnostic lumbar puncture once platelets >20x10^9, give IT methotrexate and hydrocortisone.This should not happen beyond the 2nd week of induction chemotherapy. If necessary do LP after platelet transfusion. Use sedation and good LP technique to prevent leukaemic spread. Start PO Allopurinol 10mg/kg in TID ideally 12-24 hours before start of prednisone / chemotherapy
- ✓Start PO Prednisone 60mg/m^2 in TID (lower with WBC >50.000 x 10^6: Start 10mg/m^2, increase daily with 10 mg/m^2 tilldose of 60 mg/m^2 is reached at day 6.
- ✓Hydrate 24 hours before and after cytotoxics, 3000 ml/m^2 ; furosemide if urine output is not adeqaute;
- ✓ Start septrin for PCP prophylaxis

CHEMOTHERAPY Ht cm Wt kg SA **XXX = do not give**

INDUCTION	DATE / DOSE	**Wk 0**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 5**	**Wk 6**	
IV Vincristine 2 mg/m^2 (max 2.5 mg)		XXX						XXX	BONE MARROW
IM L-Asparaginase 6000U/m^2 (3 doses per wk during week 2, 3 and 4 on day 1, 3 and 5)		XXX	XXX	1 3 5	1 3 5	1 3 5	XXX	XXX	
IT Methotrexate / Hydrocortisone			XXX		XXX		XXX		
In CNS disease ** 3 drugs weekly IT Methotrexate / Hydrocortisone and Cytosar		XXX	*	*	*	*	*	*	
PO *Prednisone 60mg/m^2 in TID week 0,1,2 and 4, 5					XXX			XXX	
Signature									
Name									

Response evaluation	Day 8 PBF(note change in WBC and blasts)	
	Week 6 bone marrow(blast count)	
	Chest xray (with initial mediastinal widening)	

- Do weekly haemogram with peripheral blood film. Do bone marrow to check for remission in week 6.
- Low WBC count is no contra indication to continue with IV Vincristine, l-asparaginase and prednisone!!

If no CNS diseases give IT alternate weeks as per schedule.

In CNS disease**: combine IT Cytosar, Hydrocortisone and Methotrexate and give weekly till end of induction or for minimum of four weeks.*for prednisone note **start** and **stop** dates on both the chart and Treatment sheet.

Intrathecal drug dosages(Diluent should not contain preservatives !)

DRUG \ AGE	< 1 year	1-2 years	2-3 years	3-4 years	≥5 years
Methotrexate	6 mg	8mg	10 mg	12 mg	12 mg
Cytosar	15 mg	20 mg	25 mg	30 mg	40 mg
Hydrocortisone	6 mg	8mg	10 mg	12 mg	12 G

If no circulating blasts, IT can be given if platelets are >20 $x10^9$/L

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** **m^2**

**Criteria to start consolidation: good clinical condition, ANC > 1000, Ptl >150, otherwise start in week 7or 8*

Consolidation	DOSE	Week 6*					Week 7*			
		Day1	2	3	4		Day 8	9	10	11
IV Cyclophosphamide 1000mg/m^2 Infusion over 1 hours			XX	XX	XX	Do haemogram day 7, if ANC < 500 omit week 7	XXX	XX	XX	XX
IV Cytosar 75mg/m^2 OD IV push or SC day 1-4, 8-11										
PO 6-Mercaptopurine 50 mg/m^2 nocte x 2 wks										
IT Methotrexate / Hydrocortisone day 1,8 (plus Cytosar in CNS disease)			XX	XX	XX			XX	XX	XX
Signature										
Name										
Major events:										

* **Omit** week 7 if ANC < 500 and restart treatment with M-phase at week 9. Document.

Criteria to start M phase: Good clinical condition, WBC > 2000; ANC > 1000; Ptl > 50* ***stopSeptrin*

M-Phase	**DOSE**	WEEK 9	WEEK 11	WEEK 13	Week 15
		Date	Date	Date	Date
Methotrexate 1500 mg/m^2 start with bolus of 10% in 30 min, then infusion over 24hrs Then continue hydration					
Folinic acid 30 mg/m^2 IV or PO		42, 48 and 54 hrs after start of MTX	42, 48 and 54 hrs after start of MTX	42, 48 and 54 hrs after start of MTX	42, 48 and 54 hrs after start of MTX
6-Mercaptopurin 50mg/m^2/day PO nocte x8 weeks					
IT Methotrexate, IT Hydrocortisone(plus cytosar in CNS disease)					
Signature					
Name					
Major events:					

REQUIREMENTS FOR METHOTREXATE INFUSIONS

Hyperhydration and alkalinisation (both to reduce risk of MTX-nephropathy)

Folinic acid ***has*** *to be present* before starting MTX infusion and needs to be given **strictly *at the indicated hours*** after the infusion

Hydrate with 3000 ml/m^2 24 hours before start of chemotherapy

Continue hydration for 48 hours after chemotherapy, or till last folinic acid dose.

** Criteria to start re-induction: good clinical condition, ANC > 1000, WBC > 2000, Ptl > 50*

Reinduction	**DOSE**	**Wk 18**	**Wk 19**	**Week 20**
		DATE:	**DATE:**	date
iV Vincristine 2 mg/m^2 (max 2.5 mg)				
IV Adriamycin 25 mg/m^2 (infusion four hours)				XXXXX
IM Asparaginase 6000IU/ m^2		1 3 5	1 3 5	XXXXX
IT Methotrexate / hydrocortisone IT Cytosar if CNS disease			XXXXX	XXXXX
PO Dexamethasone 6 mg/m^2 in TID for 2 weeks(week 18,19)				XXXXX
Signature				
Name				
Major events:				

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

ALL MAINTENANCE 1ST YEAR - 9 cycles			**Wk 21**	**Wk 25**	**Wk 29**	**Wk 33**	**Wk 37**	**Wk 41**
		DATE						
		DOSE						
IV DRUGS	VINCRISTINE 2mg/m², max 2.5 mg							
PO DRUGS	6-MERCAPTOPURIN50mg /m²/day nocte		Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks
	METHOTREXATE 20mg/m² once weekly		Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks
		Maintain WBC count between 2 -3 x 10^9 /L by Increasing (by 25%) or reducing (by 50%) dosages of both 6-MP and Methotrexate. Omit drugs x 2 weeks if WBC < 1x 10^9 /L or platelets < 50 x 10^9 /L.						
	*DEXAMETHASONE 6 mg/m² in tid x 7days							
	SEPTRIN							
IT DRUGS (alternate months x 5)	METHOTREXATE according to age			XXXXXXXX		XXXXXXXX		XXXXXXXX
	HYDROCORTISONE			XXXXXXXX		XXXXXXXX		XXXXXXXX
	CYTOSAR if CNS ds			XXXXXXXX		XXXXXXXX		XXXXXXXX
INVESTIGATIONS	BLOOD	WBC						
		ANC						
		HB						
		MCV						
		PTL						
	Name /Signature							
	BOOKING DATE							
Significant events/ Response during Maintainance Phase.								

**Dexamethasone – make clear orders on when to start and stop steroids,document clearly on Treatment sheet and on prescription order when discharging home.*

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

ALL MAINTENANCE 1ST YEAR - 9 cycles			**Wk 45**	**Wk 49**	**Wk 53**	**Wk 57**	**Wk 61**	**Wk 65**
		DATE						
		DOSE						
IV DRUGS	VINCRISTINE 2mg/m², max 2.5 mg						XXXXXX	XXXXXX
PO DRUGS	6-MERCAPTOPURIN50mg /m²/day nocte		Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks	Daily X 4 weeks
	METHOTREXATE 20mg/m² once weekly		Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks	Weekly X 4 weeks
		Maintain WBC count between 2 - 3 x 10^9 /L by Increasing (by 25%) or reducing (by 50%) dosages of both 6-MP and Methotrexate. Omit drugs x 2 weeks if WBC < 1x 10^9 /L or platelets < 50 x 10^9 /L.						
	*DEXAMETHASONE 6 mg/m² in tid x 7days						XXXX	XXXXXX
	SEPTRIN							
IT DRUGS (alternate months x 5)	METHOTREXATE according to age			XXXX		XXXX	XXXX	XXXXXXXX
	HYDROCORTISONE			XXXX		XXXX	XXXX	XXXXXXXX
	CYTOSAR if CNS ds			XXXX		XXXX	XXXX	XXXXXXXX
INVESTIGATIONS	BLOOD	WBC						
		ANC						
		HB						
		MCV						
		PTL						
	Name /Signature							
	BOOKING DATE							
Significant events/ Response during Maintainance Phase.								

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

ALL MAINTENANCE			**Wk 69**	**Wk 73**	**Wk 77**	**Wk 81**	**Wk 85**	**Wk 89**	**Wk 93**	**Wk 97**	**Wk 101**
		DATE									
		DOSE									
PO DRUGS	6-MERCAPTO PURIN50mg/m^2/day nocte		Daily X 4wks	Daily X 4wks	Daily X 4wks	Daily X 4wks	Daily X 4wks	Daily X 4wks	Daily X 4wks	Daily X 4wks	Daily X 4wks
	METHOTREXATE 20mg/m^2 once weekly		Weekly X 4wks	Weekly X 4wks	Weekly X 4wks	Weekly X 4wks	Weekly X 4wks	Weekly X 4wks	Weekly X 4wks	Weekly X 4wks	Weekly X 4wks
		Maintain WBC count between 2 -3 x 10^9/L by Increasing (by 25%) or reducing (by 50%) dosages of both 6-MP and Methotrexate. Omit drugs x 2 weeks if WBC <1 x 10^9/L or platelets < 50 x 10^9/L.									
	SEPTRIN										
INVESTIGATIONS	BLOOD	WBC									
		ANC									
		HB									
		MCV									
		PTL									
	Name /Signature										
	BOOKING DATE										
Comment Response / Significant events during Maintaince.											

FOLLOW UP: Start follow up one month after last dose send home with a Hemogram request. Review monthly X 3 visits, 3 monthly X 3 visits, 6 monthly for 2 years then yearly thereafter. Do physical exam, check hemogram, evaluate for late effects of chemotherapy.Request PBF if indicated,consult oncologist.

ACUTE MYELOID LEUKAEMIA

It's a clonal disease characterized by a maturation arrest during the differentiation of normal myeloid blood cells.

Epidemiology: Globally has an incidence of 1-3 per 100,000 persons per year, 15% of all childhood leukemia's.

Risk factors
Genetic: Trisomy 21, Fanconi Anaemia, Bloom Syndrome, Diamond-Blackfan anaemia, Noonans syndrome e.t.c
Environmental: Treatment with alkylating agents, radiation exposure.

Classification: There are two main classification systems that are in use: The French-American-British (FAB) and the World health Organization (WHO).

FAB classification	M0	Undifferentiated blasts with no maturation of cells
	M1	Undifferentiated blasts with minimal maturation
	M2	Blasts with some maturation (some granules in cytoplasm)
	M3	Promyelocytic leukemia, many granules in cytoplasm
	M4	Acute Myelomonocytic leukemia
	M5	Acute Monoblastic leukemia
	M6	Erythroleukemia
	M7	Acute Megakaryoblastic leukemia

Clinical features
Fever,anaemia, petechiae, ecchymosis, gingival hypertrophy, chloroma's

Investigations
CBC and PBF, bone marrow aspirate, UECs, LFTs, Immunophenotyping and cytogenetics

Prognosis
The outcome in our setup has been poor though the survival rates in the western world are currently about 50%.The prognostic factors are both patient and disease related.

Patient characteristics:

1. Age: Older age has consistently been noted to be a poor prognostic factor. Adolescents have a poorer outcome compared to younger children
2. Race/ethnicity: Caucasians have a better overall survival compared to African Americans (In the USA)
3. Patients with Down Syndrome have a better prognosis
4. BMI: A BMI of >95 percentile confers a poor prognosis

Clinical characteristics

1. WBC count: A high count confers a poorer prognosis
2. FAB subtype: M0 is associated with poor outcome
3. Response to therapy: Early response which is usually assessed after the first course confers a good prognosis
4. Cytogenetic/Molecular characteristics: Favourable; t(8:21), inv(16), t(15:17) (the latter only if ATRA and/or ATO is used) Unfavourable (Monosomy 7)

Name……IP No…….

Subtype…….

✓ Do CXR, diagnostic bone marrow. Thrombocytopenia is no contra indication!

✓ Stabilize as indicated with packed cells till Hb >10 mg/dl unless WBC > 50.000, then aim at Hb 8 mg/dl Platelets transfusion if platelets < 10 x 10^9 or if bleeding. Treat infections

✓ Do baseline investigations as HIV, creatinine, electrolytes, uric acid, ALT

✓ Do diagnostic lumbar puncture at the beginning of Induction course 1 and give triple intrathecal medication . If there is positive CNS disease give Triple intrathecal twice weekly till the CSF is negative and then two more doses.Consider CNS radiation only for those whose CSF does not turn negative.

✓ Start PO Allopurinol 10mg/kg in TID ideally 24 hours before start of chemotherapy

✓ Hydrate 24 hours before and after cytotoxics, 3000 ml/m^2 as long as tumor load is high. Aim is adequate urine output, which must be achieved before chemotherapy is started

✓ Give good supportive care

✓ No maintenance chemotherapy is given

PREPHASE 1

		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date								
Etoposide 50 mg/m2 IV infusion over 1 hour	Dose							

- Do CBC at 0, 3, 7 days

The prephase cycle may be repeated once after one week if the clinical condition remains poor, otherwise proceed to Induction phase.

PREPHASE 2

		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date								
Etoposide 50 mg/m2 IV infusion over 1 hour	Dose							

Start induction phase immediately which consists of two cycles.

INDUCTION PHASE

CYCLE 1

		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date								
Cytosar 100mg/m2 12 hourly IV push	Dose							
Doxorubicin 50 mg/m2 infusion over 4 hours								
IT Methotrexate IT Cytosar IT hydrocortisone								
Name								
Sign								
Date for next cycle								

CYCLE 2

This should begin on day 28 or later after the start of cycle 1. This should be administered only after recovery of neutrophils to more than 1.0 x 10^9/l and platelets to more than 75×10^9/l. The start of cycle 2 should not be delayed beyond day 42.

		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date								
Cytosar 100mg/m2 12 hourly IV push	Dose							
Doxorubicin 50 mg/m2 infusion over 4 hours								
IT Methotrexate IT Cytosar IT hydrocortisone								
Name								
Sign								
Date for next cycle								

CONSOLIDATION PHASE

Consolidation phase consists of two cycles.

Bone marrow examination should be done on day 28 or later after the start of induction cycle 2.

Ensure that the neutrophils and platelets have recovered before doing the bone marrow examination. This should however not be delayed beyond day 42. Non recovery of the neutrophils and platelets by day 42 may indicate failure to achieve remission.

The patient should receive steroid eye drops(prednisolone or dexamethasone) from the beginning of the cytarabine infusion up to 2 days after the last dose every 2 hours, as prophylaxis for conjunctivitis.

CYCLE 1

		Day 1	Day 2	Day 3
Date				
Cytosar 3gm/m2 4-hour infusion 12 hourly(100mg/kg for those less than 12 months or <10kg)	Dose			
IT Methotrexate IT Cytosar IT hydrocortisone				
Name				
Sign				
Date for next cycle				

CYCLE 2

This should start on day 28 or later after start of cycle 1. Start on cell count recovery (neutrophil count >1.0 x 10^9/l and platelet count >75 x 10^9/l) and when the patient is clinically well, but not later than after 42 days.

		Day 1	Day 2	Day 3
Date				
Cytosar 3gm/m2 4-hour infusion 12 hourly(100mg/kg for those less than 12 months or <10kg)	Dose			
IT Methotrexate IT Cytosar IT hydrocortisone				
Name				
Sign				

Start follow up one month after last dose send home with a haemogram request. Review monthly X 3 visits, 3 monthly X 3 visits, 6 monthly for 2 years then yearly thereafter. Do physical exam, check haemogram, evaluate for late effects of chemotherapy. Request PBF if indicated, consult oncologist

ACUTE PROMYELOCYTIC LEUKAEMIA

Name……IP No…….

Primary site…….. Stage……

Do NOT do LP for IT chemo during course 1 due to increased risk of bleeding. Provide supportive care with platelets, cryo, or FFP as needed for clinical bleeding and/or DIC (which is very likely in APML)

Induction Ht (cm) Wt (kg) SA (m^2)

DRUG	Day 1		Day 2		Day 3		Continuation of ATRA for 30 days	
DATE							Start date	Stop date
Adriamycin 50mg/m^2 in 1 hour iv			XXXXX				XXXXXXX	
ATRA (all-trans retinoic acid) 25mg/m^2/day divided BID or 13-cis-retinoic acid (if ATRA is not available) 160mg/m^2/day divided BID	AM	PM	AM	PM	AM	PM	AM daily	PM daily
Name/Signature								
Next course planned								

Consolidation I Ht (cm) Wt (kg) SA (m^2)

Begin Consolidation I upon recovery of the ANC 1.0 x 10e9/l and the platelet count to 100 x 10e9/l, but <u>not earlier than 7 days after stopping ATRA</u>. No BMA until after Consolidation III unless blasts increase during consolidation.

DRUG	Week 1							Continuation of ATRA for 14 days	
DATE								Start date	Stop date
Adriamycin 50mg/m^2 in 1 hour iv	Day 1 only							XXXXXXX	
Cytosar 100mg/m^2/day in 1 hour iv								XXXXXXX	
ATRA (all-trans retinoic acid) 25mg/m2 day divided BID or 13-cis-retinoic acid (if ATRA is not available) 160mg/m^2/day divided BID	AM					PM		AM daily	PM daily
Triple IT (Ara-C, HC and MTX) for <u>all</u> patients regardless of CNS status	Day 1 only							XXXXXXX	
Name/Signature									
Next course planned									

Intrathecal Dosages

DRUG / **AGE**	< 1 year	1-2 years	2-3 years	3-4 years	≥5 years
Methotrexate	6 mg	8mg	10 mg	12 mg	12 mg
Cytosar	15 mg	20 mg	25 mg	30 mg	40 mg
Hydrocortisone	6 mg	8mg	10 mg	12 mg	12mg

Consolidation II **Ht** (**cm**) **Wt** (**kg**) **SA** (**m**^{2})

Begin Consolidation II upon recovery of the ANC 1.0 x 10e9/l and the platelet count to 100 x 10e9/l, but not earlier than 7 days after stopping ATRA. No BMA until after Consolidation III unless blasts increasing.

DRUG	**Week 1**		**Continuation of ATRA for 14 days**	
DATE			Start date	Stop date
Adriamycin 50mg/m^2 in 1 hour iv	Day 1 only		XXXXXXX	
ATRA (all-trans retinoic acid) 25mg/m^2/ day divided BID or 13-cis-retinoic acid (if ATRA is not available) 160mg/m^2/day divided BID	AM	PM	AM daily	PM daily
Triple IT (Ara-C, HC and MTX) for all patients regardless of CNS status	Day 1 only		XXXXXXX	
Name/Signature				
Next course planned				

Consolidation III **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

Begin Consolidation III upon recovery of the ANC 1.0 x 10e9/l and the platelet count to 100 x 10e9/l, but <u>not earlier than 7 days after stopping ATRA</u>. No BMA until after Consolidation III unless blasts increasing.

DRUG	**Week 1**	**Continuation of ATRA for 14 days**
DATE		Start date / Stop date
Adriamycin 50mg/m^2 in 1 hour iv	Day 1 only	XXXXXXX
Cytosar 100mg/m^2/day in 1 hour iv		XXXXXXX
ATRA (all-trans retinoic acid) 25mg/m^2/ day divided BID or 13-cis-retinoic acid (if ATRA is not available) 160mg/m^2/day divided BID	AM / PM	AM daily / PM daily
Triple IT (Ara-C, HC and MTX) for <u>all</u> patients regardless of CNS status	Day 1 only	XXXXXXX
Name/Signature		
Next course planned		

BMA to be done upon count recovery from Consolidation III (be aware of the possibility of normal regenerating blasts)

BMA Result: _____

_____

_____

Maintenance therapy (protocol continued on next page):

Begin Maintenance upon recovery of the ANC 1.0 x 10e9/l and the platelet count to 100 x 10e9/l, but <u>not earlier than 7 days after stopping ATRA in Consolidation III</u>. Maintenance cycles are **12 weeks in duration** with ATRA/13-cisretinoic acid given only for the first 2 weeks of every cycle and LP with IT triples given on cycle 1 only. Adjust oral 6MP and MTX in the same manner as ALL maintenance therapy.

Maintenance **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

AMPL Maintenance **(Cycles given every 12 weeks)**			**Cycle 1**	**Cycle 2**	**Cycle 3**	**Cycle 4**	**Cycle 5**	**Cycle 6**
		DATE						
		DOSE						
PO DRUGS	ATRA (all-trans retinoic acid) 25mg/m^2/ day divided BID or 13-cis-retinoic acid (if ATRA is not available) 160mg/m^2/day divided BID **For <u>14 days</u> at the start of each cycle**		14 days only	14 days only	14 days only	14 days only	14 days only	14 days only
	6-MERCAPTOPURIN50mg/ m^2/day nocte		Daily X 12 weeks	Daily X 12 weeks	Daily X 12 weeks	Daily X 12 weeks	Daily X 12 weeks	Daily X 12 weeks
	METHOTREXATE 25mg/m^2 once weekly		Weekly X 12 weeks	Weekly X 12 weeks	Weekly x 12 weeks	Weekly X 12 weeks	Weekly X 12 weeks	Weekly X 12 weeks
		Maintain WBC count between 2 - 4 x 10^9 /L by Increasing (by 25%) or reducing (by 50%) dosages of both 6-MP and Methotrexate. Omit drugs x 2 weeks if WBC < 1x 10^9 /L or platelets < 50 x 10^9 /L.						
	SEPTRIN							
IT DRUGS (Cycle 1 only)	METHOTREXATE according to age		Cycle 1 only	XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
	HYDROCORTISONE according to age		Cycle 1 only	XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
	CYTOSAR according to age		Cycle 1 only	XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
INVESTIGATIONS	BLOOD	WBC						
		ANC						
		HB						
		MCV						
		PTL						
	Name /Signature							
	BOOKING DATE							

Maintenance (continued) **Ht(cm) Wt (kg) SA (m^2)**

AMPL Maintenance (cycles given every 12 wks)			**Cycle 7**	**Cycle 8**	**Cycle 9**	
		DATE				
		DOSE				
PO DRUGS	ATRA (all-trans retinoic acid) 25mg/m^2/ day divided BID or 13-cis-retinoic acid (if ATRA is not available) 160mg/m^2/day divided BID **For 14 days at the start of each 12-week cycle**		14 days only	14 days only	14 days only	
	6-MERCAPTOPURIN50mg/m^2/ day nocte		Daily X 12 weeks	Daily X 12 weeks	Daily X 12 weeks	
	METHOTREXATE 25mg/m^2 once weekly		Weekly X 12 weeks	Weekly X 12 weeks	Weekly x 12 weeks	
		Maintain WBC count between 2 - 4 x 10^9 /L by Increasing (by 25%) or reducing (by 50%) dosages of both 6-MP and Methotrexate. Omit drugs x 2 weeks if WBC < 1x 10^9 /L or platelets < 50 x 10^9 /L.				
	SEPTRIN					
IT DRUGS (Cycle 1 only)	METHOTREXATE according to age		Cycle 1 only	XXXXX	XXXXX	
	HYDROCORTISONE according to age		Cycle 1 only	XXXXX	XXXXX	
	CYTOSAR according to age		Cycle 1 only	XXXXX	XXXXX	
INVESTIGATIONS	BLOOD	WBC				
		ANC				
		HB				
		MCV				
		PTL				
	Name /Signature					

CHRONIC MYELOCYTIC LEUKEMIA (CML)

DEFINITION: CML is a clonal hematopoietic disorder due to acquired genetic defect in the pluripotent stem cell. It results in gradual replacement of the normal haematopoiesis by an increasing population of differentiated cells with the characteristic expression of myeloid cells.
In 1660 the Philadelphia Chromosome was discovered in CML cells, which is now recognized as a consistent genetic marker of a balanced translocation involving chromosome 9 and 22. In 1980 the BCR-ABL chimeric gene was recognized as a result of this translocation, which encodes a protein with tyrosine kinase activity.

EPIDEMIOLOGY: In USA >600 cases /year, which is 6-15 % of adult leukaemias. It occurs in all decades of life, median age of onset is 50 years. In childhood it comprises of 2-5 % of childhood leukaemias. The childhood form can present as the adult form, or as a separate entity, the juvenile CML, which is Philadelphia Chromosome negative, and has distinct clinical, laboratory and cytogenetic characteristics.

Course of (adult type) Chronic Myelocytic Leukemia is in 3 phases:

Indolent chronic phase, mostly 3-6 years
Accelerated phase of 3-6 month duration
Blastic phase, 2/3 myeloblasts with survival 2-6 months,
1/3 lymphoblasts, with survival up to 12 month

Differences between "adult" type and juvenile type of CML

	Adult type CML	Juvenile CML
Age	> 4 yrs	< 4 yrs
Lymphadenopathy	Unusual	Common
Initial WBC count > 100,000x10^9/L	Common	Unusual
Monocytosis	Unusual	Common
Percentage of Hb F	Normal	Increased
Philadelphia Chromosome	> 90%	Absent
BCR-ABL fusion	Present	Absent
Leukocyte Alkaline Phosphatase (LAP score)	Decreased	Variable
Median survival time	4-6 years	1-2 years
Blastic phase	Common	Unusual

LABORATORY FEATURES
Leucocytosis with increased numbers of granulocytes in mature and immature forms ('left shift') and small percentage of blasts. Frequent thrombocytaemia.
Bone marrow hypercellular with increased number of megakaryocytes and increased granulopoiesis.
(Demonstration of Philadelphia Chromosome in red cell, white cell and platelet precursor cells)

DIFFERENTIAL DIAGNOSIS
Leukemoid reaction, especially in patients with severe infection, congenital heart disease and metastatic cancer, (but normal LAP score, and rarely blasts in PBF).

TREATMENT
Juvenile type frequently does not respond to chemotherapy, needs much supportive care. Some patients respond to cis-retinoic acid or interferon alpha. Cured by allogeneic stem cell transplantation
Adult type: Busulphan or Hydroxyurea. HU better if planning for BM transplant.

- Interferon-α: Eradicates Philadelphia Chromosome but does not cure, delays onset of accelerated phase.
  Has anti proliferative and antiviral properties. Many side effects limiting use.
- Imatinib is a tyrosine kinase inhibitor. Has good cytogenetic and molecular response with cure. Very costly, although is available in Nairobi for free if patients can pay to get BCR-Abl testing done and have the written laboratory result confirming positivity got bcr-abl and/or t(9;22).
  Newer drugs for refractory cases are dasatinib and nilotinib, although these are not available in Kenya.

CML TREATMENT

The aim of therapy for the relatively unaggressive chronic phase is symptom control. Since the inceptionof bone marrow transplantation, it is now possible to get lasting cures for those transplanted in the stable chronic phase. In pediatric patients who have access to TKI (imatinib), this may provide durable cure as well, probably only when used for at least two years. Interferon alpha ($5x10^6$ U/M^2/day) has led to 40-80% hematological responsein adult patients but experience in children is so far limited. Spleenectomy and radiotherapy of the spleenare not beneficial and could be detrimental.

TREATMENT

Chronic Phase

BUSULPHAN 0.06-0.1mg/kg/day (max 4-6mg daily) PO, OD (expect a lag period of 10-30 days before counts drop).
Major side effects include Addisonian-like syndrome, prolonged myelosuppression, hypogonadism and bone-marrow & pulmonary fibrosis. It is long acting, so

- Decrease dose by 50% if WBC count < $30x10^9$/L, and
- Stop treatment if WBC count < $20x1^{09}$/L, continue monitoring blood counts weekly.

OR

HYDROXYUREA 2-10mg daily orally (0.5 – 1.5 g/m^2/day)

Monitor WBC count closely to maintain at 10-$15x10^9$/L. Unlike busulphan, HU has more rapidaction onset, preserves residual normal marrow and pulmonary structures through significantly more expensive. Median survival is similar to those on busulphan.

WITH

Oral **ALLOPURINOL** at 10mg/kg with maximum of 200mg TID as long as counts are high.

Watch out for leucostasis and tumor lysis syndrome with WBC counts above $100x10^9$/L

OTHER TREATMENT OPTIONS:

INTERFERON – α5 MU m^2/day subcutaneous 3x/week,can be increased to daily doses if tolerated.

IMATINIB **THIS IS THE PREFERRED DRUG IF AVAILABLE**
375 mg/m^2 OD
Monitor blood counts regularly
Increase dose after 2 months if non-responder
Decrease the dose if toxicity, mainly thrombocytopenia

Myeloblastic Crisis

- AML like regimens may be tried though not shown to have lasting benefit. If reversion to chronic phase attained, switch back to hydroxyurea or busulphan.

Lymphoblastic Crisis

- Use ALL like regimens

NON HODGKINS LYMPHOMA

Lymphomas are malignant proliferations of lymphoid cells at various stages of differentiation and activation.There are from B or T cell lineage.

Epidemiology: 3rd commonest childhood malignancy worldwide but the commonest in East Africa.
It has a peak incidence of 7 years (range 5-16 years) of age and it has a male predominance. Incidence: 10 cases per 1,000,000people per year in western world, but 1:10,000 in equatorial Africa.

Risk factors: HIV infection, malaria/EBV co-infection, congenital immunodeficiencies e.g. Wiskott-Aldrich syndrome and severe combined immunodeficiency (SCID).
BL has a characteristic chromosomal translocation involving the C-Myc proto-oncogene on chromosome 8q24 and the gene of an immunoglobulin chain on chromosome 14 (most common), 2 or 22. It is thought to be a result of early infection by Epstein Barr virus, resulting in transformation and immortalization of B lymphocytes, and malaria, giving suppression of T cell function. If translocation occurs it may result in uncontrolled proliferation of B-cells.
Cellular classification:
Majority of the NHL in children are high grade, in adults the major type is intermediate or low grade lymphoma.
There are three main histological sub-types in children (figures are of western world).

1. Mature B-cell lymphoma 35-50%
   (Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) and diffuse large B-cell lymphoma (DLBCL)
2. Lymphoblastic lymphoma (30-40%)
3. Anaplastic Large Cell lymphoma (10-25%)

In Equatorial Africa the percentages are quite different with > 80% Burkitts Lymphoma, described as small non-cleaved cell lymphoma. It is the most common malignancy in childhood. It can present in three clinical varieties: majority is endemic type, but also sporadic and immunodeficiency associated varieties exist.

Clinical: The commonest presentation of Burkitts lymphoma is a rapidly growing painless mass of the jaw, or progressive abdominal swelling. CNS involvement is often present, with cranial nerve palsies or paraplegia.

Staging: The St. Jude's staging system:

Stage I	A single tumor (extranodal) or single anatomical area (nodal), not mediastinum or abdomen.
Stage II	Single tumor (extranodal) with regional node involvement, Two or more nodal areas on the same side of the diaphragm, A primary GIT tumor with or without involvement of mesenteric nodes,
Stage III	Two single tumors or nodal areas on opposite sides of the diaphragm, Primary intrathoracic tumors, extensive intra-abdominal disease, and all paraspinal or epidural tumors.
Stage IV	Any of the above with initial CNS and/or bone marrow involvement.

Since BL is a fast growing malignancy, it should be handled as an oncological emergency with prompt confirmation of diagnosis and staging before start of treatment. There is no advantage in performing extensive surgery or debulking, since tumor re-growth is fast and surgery delays and may complicate chemotherapy. Recognized prognostic factors are stage, LDH level, bone marrow involvement and CNS involvement.

Diagnostic work-up: For diagnosis: Histology (preferred) /cytology.
For staging: CXR, abdominal ultrasound, BMA, CSF cytology.
Laboratory: HIV (CD4%), CBC, LDH, LFTs, uric acid, UEC.

Treatment: Useful drugs are Cyclophosphamide, high dose Methotrexate and Cytosine Arabinoside.CNS directed therapy is essential. Supportive treatment is important to manage acute treatment related toxicity including tumor lysis syndrome. Relapses occur early within the first year after diagnosis. When a patient remains in complete remission for one year, he can be considered cured.

MANAGEMENT OF BURKITT LYMPHOMA AND OTHER MATURE B-CELL LYMPHOMAS EXCLUDING LYMPHOBLASTIC LYMPHOMAS

Name……IP No…….

Primary site……..CD20……..... Stage……

Chest X-ray.....CSF.....

Abdominal ultrasound.....

Physical exam Document size of masses, special attention for abdomen and CNS

Investigations Histology of tumor, flow cytometry and IHC if indicated
Haemogram, creatinine, electrolytes, uric acid
ALT or full LFT if indicated, LDH HIV serology important
Bone marrow (if pancytopenia) CSF cytology (and give 1st IT drugs)
CXR Abdominal ultrasound

Aim to give treatment within a few days to a week from admission date
Start allopurinol 10 mg/kg in TDS on diagnosis, at least 1 day before chemotherapy
Start hyper hydration 12-24 hours before cytotoxics with 3000 ml/m^2/day - N/S till 48 hours after chemotherapy, and then continue hydration at maintenance level. Initial aim is adequate urine output which must be achieved before start of chemotherapy
Daily weight; Creatinine and electrolytes at 24 and 48 hrs

Document: S*tart and stop dates for prednisone on chart and treatment sheet*.

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

Pre-phase		**DOSE**	**ROUTE**	**DURATION**	**TICK**
Cyclophosphamide	**300 mg**/m^2		IV	Infusion over one hour	
Vincristine	**2 mg**/m^2 max 2.5 mg		IV	IV push	
Methotrexate	Per age group		IT		
Hydrocortisone	Per age group		IT		
(Cytosar if CNS disease	Per age group)		IT		
Prednisone*	60 mg/m^2/day	TDS	PO	7 days	
Date given		Name and signature			
Comment response/ significant events prephase i.e TLS					

*NOTE: If weight <12 kg use 2/3 of dosages.*Prednisone–Document Start andStop dates on Chart and treatment sheet.*

Closely monitor the patient during and after chemotherapy; Continue hydration the first week after chemotherapy.

INTRATHECAL DRUGS DOSING: (**Diluents Without preservatives, so dissolve in normal saline**)

Drug /Age	**< 1 yr**	**1-2 yrs**	**2-3 yrs**	**3-4 yrs**	**≥ 4 yrs**
Methotrexate	6 mg	8mg	10 mg	12 mg	12 mg
Cytosar	15 mg	20 mg	25 mg	30 mg	40 mg
Hydrocortisone	6 mg	8mg	10 mg	12 mg	12 mg

Course 1 follows immediately the pre-phase, if the clinical condition is acceptable irrespective of blood counts. So start hyper-hydrating on day 7, and give the drugs on day 8, continue hydration till last folinic acid dose.
Rituximab is to be given to all patients whose tumour is CD20 positive(if unknown and histology confirms its Burkitt Lymphoma assume CD20 +ve) during courses 1 to 4. It is given on the day prior to the start of the other chemotherapeutic agents. Premedicate with IV Chropheniramine 0.35mg/kg and IV Paracetamol 15 mg/kg 30-60 minutes before start of Rituximab

REQUIREMENTS FOR METHOTREXATE INFUSION (course 1 and 5)

Hyperhydration and alkalinisation (both to reduce risk of MTX-nephropathy)

Folinic acid ***<u>has</u>*** *to be present* before starting MTX infusion and needs to be given **strictly *at the indicated hours*** after the infusion

Hydrate with 3000 ml/m^2 12-24 hours before chemotherapy

Continue hydration for 48 hours after chemotherapy, or till last folinic acid dose.

Do serum creatinine

Course 1

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administation Mode	Day 1	Day 2
		Date:	Date:
Rituximab	**375mg/m^2** IV Infusion over 2 hour		
Methotrexate	**1500 mg/m^2** IV Infusion over 4 hours		
Cyclophosphamide	**1000 mg/m^2** IV Infusion over 1 hour		
*Folinic acid	**30 mg/m^2** PO or IV 42,48, 54 hours after start MTX		
Methotrexate	IT Per age group		
Hydrocortisone	IT Per age group		
(Cytosar if CNS disease	IT Per age group)		
Prednisone	60 mg/m^2/day TDS for 7 days then stop		
Name and signature			

*Prescribe folinic acid (dose & time) on the Treatment sheet, give a prescription order with day,date,time and dose to mother/guardian if discharging home,

Next course planned for: Date.. .. ..

Give the following seven courses every 3 - 4 weeks if patient is in good clinical condition

And if haemogram shows :WBC > 2000 x 10^6/L, ANC> 1000 x 10^6/L, Platelets > 150 x 10^6/L

Give all courses with hydration before and after the chemotherapy

Course 2

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administation Mode	Day 1	Day 2
		Date:	Date:
Rituximab	**375mg/m^2** IV Infusion over 2 hour		
Adriamycin	**50 mg/m^2** IV Infusion over 4 hours		
Cytosar	**100 mg/m^2** IVInfusion over 1 hour		
Vincristine	**2 mg/m^2 max 2.5** IV push		
Methotrexate	IT Per age group		
Hydrocortisone	IT Per age group		
(Cytosar if CNS disease	IT Per age group)		
Prednisone	60 mg/m^2/day TDS for 7 days then stop		
Name and signature			

Next course planned for: Date.. .. ..

Give3rd course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L

Give course with hydration before and after the chemotherapy

Course 3

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administation Mode Date	Day 1	Day 2	Day3	Day 4	Day 5	Day 6
Rituximab	**375mg/m²** IV Infusion over 2 hour						
Cytosar	**100 mg/m²**/day IV Infusion over 1 hour/day or SC, for 5 days						
Cyclophosphamide	**1500 mg/m²** IV Infusion over 4 hours						
Vincristine	**2 mg/m² max 2.5** IV push						
Methotrexate	IT Per age group						
Hydrocortisone	IT Per age group						
(Cytosar if CNS disease	IT Per age group)						
Prednisone	60 mg/m^2/day TDS for 7 days then stop						
Name and signature							

Next course planned for: Date.. .. ..

Evaluate the patient after the 3rd course: clinically and imaging of initial site (s).

Findings: - Size if applicable:…….

Give 4th course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L

Give course with hydration before and after the chemotherapy.

Course 4

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administration Mode	Day 1	Day 2
		Date:	
Rituximab	**375mg/m²** IV Infusion over 2 hour		
Adriamycin	**50 mg/m²** IV Infusion over 4 hours		
Cytosar	**100 mg/m²** IV Infusion over 1 hour		
Vincristine	**2 mg/m² max 2.5** IV push		
Methotrexate	IT as Per age group		
Hydrocortisone	IT as Per age group		
(Cytosar if CNS disease	IT as Per age group)		
*Prednisone	60 mg/m^2/day TDS7 days then stop		
Name and signature			

Next course planned for: Date.. .. ..

REQUIREMENTS FOR METHOTREXATE INFUSION (course 1 and 5)

Hyperhydration and alkalinisation (both to reduce risk of MTX-nephropathy)

Folinic acid ***has*** *to be present* before starting MTX infusion and needs to be given **strictly *at the indicated hours*** after the infusion

Hydrate with 3000 ml/m^2 12-24 hours before chemotherapy

Continue hydration for 48 hours after chemotherapy, or till last folinic acid dose.

Do serum creatinine

Course 5

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administation Mode	Date:
Methotrexate	**1500 mg/m^2** IV Infusion over 4 hours	
Cyclophosphamide	**1000 mg/m^2** IV Infusion over 1 hour	
*Folinic acid	**30 mg/m^2** PO or IV 42,48, 54 hours after start MTX	
Methotrexate	IT Per age group	
Hydrocortisone	IT Per age group	
(Cytosar if CNS disease	IT Per age group)	
Prednisone	60 mg/m^2/day TDS for 7 days then stop	
Name and signature		

*Prescribe folinic acid (dose & time) on the Treatment sheet, give a prescription order with day,date,time and dose to mother/guardian if discharging home,

Next course planned for: Date.. .. ..

Give 6th course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L

Give course with hydration before and after the chemotherapy

Course 6

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administation Mode	Date:
Adriamycin	**50 mg/m^2** IV Infusion over 4 hours	
Cytosar	**100 mg/m^2** IVInfusion over 1 hour	
Vincristine	**2 mg/m^2 max 2.5** IV push	
Methotrexate	IT Per age group	
Hydrocortisone	IT Per age group	
(Cytosar if CNS disease	IT Per age group)	
Prednisone	60 mg/m^2/day TDS for 7 days then stop	
Name and signature		

Next course planned for: Date.. .. ..

Give 7th course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L
Give course with hydration before and after the chemotherapy

Course 7

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administation Mode	Day 1	Day2	Day 3	Day 4	Day 5
Cytosar	**100 mg/m^2**/day IV Infusion over 1 hour/day or SC, for 5 days					
Cyclophosphamide	**1500 mg/m^2** IV Infusion over 4 hours					
Vincristine	**2 mg/m^2 max 2.5** IV push					
Methotrexate	IT Per age group					
Hydrocortisone	IT Per age group					
(Cytosar if CNS disease	IT Per age group)					
Prednisone	60 mg/m^2/day TDS for 7 days then stop					
Name and signature						

Next course planned for: Date.. .. ..

Give 8th course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L
Give course with hydration before and after the chemotherapy

Course 8

Ht (cm) Wt (kg) BSA (m^2)

Drug	Dose/Administation Mode	Date:
Adriamycin	**50 mg/m^2** IV Infusion over 4 hours	
Cytosar	**100 mg/m^2** IVInfusion over 1 hour	
Vincristine	**2 mg/m^2 max 2.5** IV push	
Methotrexate	IT as Per age group	
Hydrocortisone	IT as Per age group	
(Cytosar if CNS disease	IT as Per age group)	
*Prednisone	60 mg/m^2/day TDS7 days then stop	
Name and signature		

EVALUATE the patient after the 8th course: clinically and imaging of initial site(s)

FOLLOW UP after chemotherapy:

Monthly for 3 months

	Month 1	**Month 2**	**Month 3**
Complaints			
Clinical			

Then 3-monthly for 1 year

	Month 6	**Month 9**	**Month 12**	**Month 15**
Complaints				
Clinical				

Then 6 monthly for 2 years - Clinical exam only, more if indicated, then yearly thereafter.

ANAPLASTIC LARGE CELL LYMPHOMA TREATMENT PROTOCOL

Name……IP No…….

Primary site……. Stage……

Chest X-ray.....

Abdominal ultrasound.....

.....

CSF.....

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

Pre-phase		**DOSE**	**ROUTE**	**DURATION**	**TICK**	
Cyclophosphamide	200mg/m2 for 2 days		IV	Infusion over one hour	Day1	Day 2
Methotrexate	Per age group		IT			
Hydrocortisone	Per age group		IT			
(Cytosar if CNS disease	Per age group)		IT			
Dexamethasone	10mg/m2	BD	PO	5 days		
Date given		Name and signature				
Comment response / significant events prephase i.e TLS						

NOTE: If weight <10 kg use 2/3 of dosages. Dexamethasone–Document Start and Stop dates on Chart and treatment sheet.*

Closely monitor the patient during and after chemotherapy;

Course 1 starts on day 6 of treatment while the subsequent ones are every 21 days.

Wt (**kg**) **SA** (**m²**)

Course 1		**DOSE**	**ROUTE**	**MODE**	TICK	
Methotrexate	1000mg/m^2		IV	24 hour infusion		
Cyclophosphamide	200mg/m2 for 5 days		IV	Infusion over 1 hour		
*Folinic acid	15mg/m^2		PO/IV	42,48, 54 hours after start MTX		
Cytosar	150mg/m^2 twice daily on day 4 and 5		IV	1 hour infusion	Day4	Day5
Etoposide	100mg/m^2		IV	2 hour infusion	Day4	Day 5
Methotrexate	Per age group		IT			
Hydrocortisone	Per age group		IT			
(Cytosar if CNS disease	Per age group)		IT			
Dexamethasone	10mg/m2	BD	PO	5 days		
Date given		Name and signature				
Comment response/ significant events						

*Prescribe folinic acid (dose & time) on the Treatment sheet, give a prescription order with day,date,time and dose to mother/guardian if discharging home,

Next course planned for .. ..

INTRATHECAL DRUGS DOSING: (**DiluentsWithout preservatives, so dissolve in normal saline**)

Drug /Age	**< 1 yr**	**1-2 yrs**	**2-3 yrs**	**3-4 yrs**	**≥ 4 yrs**
Methotrexate	6 mg	8mg	10 mg	12 mg	12 mg
Cytosar	15 mg	20 mg	25 mg	30 mg	40 mg
Hydrocortisone	6 mg	8mg	10 mg	12 mg	12 mg

REQUIREMENTS FOR METHOTREXATE INFUSION
Hyperhydration and alkalinisation (both to reduce risk of MTX-nephropathy)
Folinic acid: ***has*** *to be present* before starting MTX infusion and needs to be given **strictly *at the indicated hours***after the infusion
Hydrate with 3000 ml/m^2 12-24 hours before chemotherapy
Continue hydration for 48 hours after chemotherapy, or till last folinic acid dose.

Give the following courses every 3 weeks , if patient is in good clinical condition
And if haemogram shows :WBC > 2000 x 10^6/L, ANC > 1000 x 10^6/L, Platelets > 150 x 10^6/L
Give all courses with hydration before and after the chemotherapy

Wt (kg) Surface Area m^2

Course 2		DOSE	ROUTE	DURATION	TICK				
Cyclophosphamide	200mg/m2 day1-5		IV	Infusion over 1 hour					
Methotrexate	1000 mg/m^2 day 1		IV	Infusion over 24 hours					
*Folinic acid	15mg/m^2		PO/IV	42,48, 54 hours after start MTX					
Adriamycin	25mg/m^2 day 4,5		IV	IV infusion over 4 hours	Day4		Day5		
Methotrexate	Per age group		IT						
Hydrocortisone	Per age group		IT						
(Cytosar if CNS disease	Per age group)		IT						
Dexamethasone	10 mg/m^2/day	BD	PO	5 days					
Date given		Name and signature							

Next course planned for .. ..

Give3rd course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L
Give course with hydration before and after the chemotherapy

Course 3		DOSE	ROUTE	MODE	TICK
Methotrexate	1000mg/m^2		IV	24 hour infusion	
Cyclophosphamide	200mg/m2 for 5 days		IV	Infusion over 1 hour	
*Folinic acid	15mg/m^2		PO/IV	42,48, 54 hours after start MTX	
Cytosar	150mg/m^2 twice daily on day 4 and 5			1 hour infusion	Day4 Day5
Etoposide	100mg/m^2		IV	2 hour infusion	Day4 Day 5
Methotrexate	Per age group		IT		
Hydrocortisone	Per age group		IT		
(Cytosar if CNS disease	Per age group)		IT		
Dexamethasone	10mg/m2	BD	PO	5 days	
Date given		Name and signature			
Comment response/ significant events					

*Prescribe folinic acid (dose & time) on the Treatment sheet, give a prescription order with day,date,time and dose to mother/guardian if discharging home,
Next course planned for .. ..

Course 4		DOSE	ROUTE	DURATION	TICK
Cyclophosphamide	200mg/m2 day1-5		IV	Infusion over 1 hour	
Methotrexate	1000 mg/m^2 day 1		IV	Infusion over 24 hours	
*Folinic acid	15mg/m^2		PO/IV	42,48, 54 hours after start MTX	
Adriamycin	25mg/m^2 day 4,5		IV	IV infusion over 4 hours	Day4 Day5
Methotrexate	Per age group		IT		
Hydrocortisone	Per age group		IT		
(Cytosar if CNS disease	Per age group)		IT		
Dexamethasone	10 mg/m^2/day	BD	PO	5 days	
Date given		Name and signature			

Next course planned for .. ..

Givenext course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L
Give course with hydration before and after the chemotherapy

Course 5		DOSE	ROUTE	MODE	TICK
Methotrexate	1000mg/m^2		IV	24 hour infusion	
Cyclophosphamide	200mg/m2 for 5 days		IV	Infusion over 1 hour	
*Folinic acid	15mg/m^2		PO/IV	42,48, 54 hours after start MTX	
Cytosar	150mg/m^2 twice daily on day 4 and 5		IV	1 hour infusion	Day4 Day5
Etoposide	100mg/m^2		IV	2 hour infusion	Day4 Day 5
Methotrexate	Per age group		IT		
Hydrocortisone	Per age group		IT		
(Cytosar if CNS disease	Per age group)		IT		
Dexamethasone	10mg/m2	BD	PO	5 days	
Date given		Name and signature			
Comment response/ significant events					

*Prescribe folinic acid (dose & time) on the Treatment sheet, give a prescription order with day,date,time and dose to mother/guardian if discharging home,
Next course planned for .. ..

Course 6		DOSE	ROUTE	DURATION	TICK
Cyclophosphamide	200mg/m2 day1-5		IV	Infusion over 1 hour	
Methotrexate	1000 mg/m^2 day 1		IV	Infusion over 24 hours	
*Folinic acid	15mg/m^2		PO/IV	42,48, 54 hours after start MTX	
Adriamycin	25mg/m^2 day 4,5		IV	IV infusion over 4 hours	Day4 Day5
Methotrexate	Per age group		IT		
Hydrocortisone	Per age group		IT		
(Cytosar if CNS disease	Per age group)		IT		
Dexamethasone	10 mg/m^2/day	BD	PO	5 days	
Date given		Name and signature			

HODGKIN'S LYMPHOMA (HL)

DEFINITION. HL is a malignant disease in lymphoid tissue, with the presence of mononucleated Hodgkin's cells and their polynucleotide derivatives, the Reed Sternberg (RS) cells on histoloyg. RS cells are not pathognomonic, since they also can be present in reactive processes, infectious mononucleosis, graft versus host disease and even Non Hodgkin Lymphoma.

EPIDEMIOLOGY.
There is marked variation from country to country, ranging from 3-7 per million populations. The age specific incidence curve is bimodal, with one peak in young adults aged 15-30, and a second peak at age 45-55 years. The disease is rare before 5 years of age. In undeveloped countries the incidence among children younger than 10 years is higher than in the western world.

AETIOLOGY is unknown. There might be chronic antigen stimulation with some involvement of EBV virus. Environmental or infectious agents are suggested by clustering among relatives of a patient or student groups. Reed Sternberg cells harbor often the EBV genome.

Histopathological CLASSIFICATION according to Rye:

Lymphocyte predominant	10-15%	(The frequency of subtypes varies in different studies)
Nodular sclerosis	30-70%	
Mixed cellularity	20-40%	
Lymphocyte depleted	5-15 %	

CLINICAL PRESENTATION
There is superficial painless lymphadenopathy in over 80% of cases, mostly cervical. Concomitant mediastinal adenopathy is present in 50%. Exclusive mediastinal involvement is rare.

STAGING should be done with each patient, both clinically and assisted with imaging procedures (CXR, abdominal ultrasound or CT scan). Absence or presence of B symptoms as fever, night sweats, weight loss (10 % of weight over 6 months) is marked as A or B.

Ann Arbor staging classification:

Stage I	Involvement of a single lymph node region (I), or single extra lymphatic organ of site (I_E)
Stage II	Involvement of two or more lymph node regions on the same side of the diaphragm (II), or localized involvement of a single extra lymphatic organ or site and of one or more lymph node regions on the same side of the diaphragm (II_E)
Stage III	Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of extra lymphatic organ or site (III_E), or by involvement of the spleen (III_S) or both (III_{SE})
Stage IV	Diffuse or disseminated involvement of one or more extra lymphatic organs or tissue with or without associated lymph node enlargement.

TREATMENT
Cure should be achieved with minimal long term sequelae of radiotherapy and chemotherapy. The late effects of radiotherapy on the growing child, on thyroid function, with late cardiac and pulmonary involvement and secondary malignancies should be avoided. Late effects of chemotherapy are especially gonadal injury, pulmonary and cardiotoxicity, and secondary malignancies (solid tumors and leukemias). There are ongoing studies on the best mode of treatment for limited and extensive disease. ABVD might be a good choice.
At MTRH, we shall give six courses for all stages (stage I to IV) of disease followed by low dose regional radiotherapy in case of residual active disease. Often residual masses contain nonactive, fibrotic diease only not requiring additional therapy.

HODGKIN'S LYMPHOMA MANAGEMENT

Name……IP No…….

Primary site…….. Stage……

History Duration, presence of B symptoms (fever, weight loss, night sweats)

Physical exam Document size and site of masses, and adjacent lymphnode areas

Investigations
- Histology of tumor
- Haemogram
- Creatinine, or full U/E if indicated
- ALT or full LFT if indicated
- HIV serology
- Bone marrow (if pancytopenic/suspicion of BM disease)
- CXR
- Abdominal ultrasound
- Echocardiogram at baseline and if cumulative adriamycin dose>250 mg/m^2

Stage: Size tumor

CHEMOTHERAPY. HODGKINS LYMPHOMA II – Protocol.

All stages: Give 6 cycles ABVD every 4 weeks, and consider radiotherapy after finishing in case of residual active disease; often a residual mass contains non-active fibrotic tissue, not requiring additional therapy.
Repeat cycles every 4wks subject to acceptability of CBC

Give each course if patient is in good clinical condition, WBC > 2000 x 10^6/L; ANC > 1000 x 10^6/L; Platelets > 150 x 10^6/L. The usual interval between cycles is 4 weeks.
Give course with hydration before and after the chemotherapy

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

ABVD Date	DOSE	Cycle 1		Cycle 2		Cycle 3		response /size
		Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	
IV Adriamycin 25 mg/m^2 infusion over 4 hours								
IV Bleomycin 7.5 mg/m^2								
IV Vinblastine 6 mg/m^2 if N/A use vincristine 2mg/m^2, max 2.5 mg								
IV Dacarbazine 375 mg/m^2								
Sign								
Name								
Next appointment								

ABVD Date	DOSE	Cycle 4		Cycle 5		Cycle 6		Response /size
		Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	
IV Adriamycin 25 mg/m^2 infusion over 4 hours								
IV Bleomycin 7.5 mg/m^2								
IV Vinblastine 6 mg/m^2 if N/A use vincristine 2mg/m^2, max 2.5 mg								
IV Dacarbazine 375 mg/m^2								
Sign								
Name								
Next appointment								

NEUROBLASTOMA

Neuroblastoma, ganglioneuroblastoma and ganglioneuroma are embryonal tumors of the sympathetic nervous system derived from the primitive neural crest. The clinical manifestations are diverse, some might regress spontaneously, some are chemo-curable, and others are resistant to intensive chemotherapy. Metastatic neuroblastoma in children above 1 year of age has very poor prognosis. Majority of children have initial response to chemotherapy, relapse, and are then chemo-resistant. Consider palliative care in these patients.

EPIDEMIOLOGY. Annual incidence is 10.5 per million children aged < 15 years. No racial differences. Slightly more males. Peak age between 0 and 4 years, median 23 months. Infants presenting at less than 18 months of age with localized disease have good prognosis with favourable molecular features. Older children often have extensive disease andunfavorable genetic features.

LABORATORY FEATURES. The typical histological appearance of an undiffertiated neuroblastoma is 'a small round blue cell tumor' .The cells are of uniform size and contain dense hyperchromatic nuclei and scant cytoplasm and form pseudorosettes. They may be calcified. With more differentiation ganglion cells and Schwann cells may be seen.
The N-*myc*genes is present in 25-35% of neuroblastomas and is associated with aggressive behaviour of the tumor and unfavorable outcome. Together also loss of chromosome 1p, increased serum ferritin and serum lactate dehydrogenase (LDH) are found.
CLINICAL manifestation is varied, depending on the site of the primary tumor coinciding with normal sympathetic nervous system structures, such as adrenals, the sympathic chain or abdominal paraganglia. 25% is found in neck or thorax, 70% in the abdomen and 5% in the pelvis. Tumors can extend into the neural foramina and compress nerve filaments and the spinal cord, resulting in pain, paraplegia and bowel and bladder symptoms. Metastatic sites are bone, lymph nodes and bone marrow, more rarely skin, liver, lung and central nervous system. Often the child may present with metastases e.g. in the bone with pain, in the bone marrow with anaemia or retro-orbital with proptosis and peri-orbital ecchymoses. Infants with stage IVs can have massive enlarged liver leading to respiratory distress, and skin manifestations with non tender blue tinged subcutaneous nodules.
INVESTIGATIONS: Imaging of the primary tumor with ultrasound and/or CT scan.
Urinary catecholamine in urine (elevated in 90% of patients).
Serum concentration of LDH, ferritin and neuron-specific enolase (NSE) are useful prognostic markers.
Diagnosis is confirmed with tissue biopsy. Bone marrow aspiration should be done from 2 different sites.

International Neuroblastoma Staging System (INSS):

Stage I	Localized, complete gross excision, lymph nodes negative
Stage II	Localized, incomplete gross excision, non adherent lymph nodes negative(IIa) or positive (IIb)
Stage III	Unresectable unilateral tumor infiltrating across the midline with or without regional lymphnodes Or localized unilateral tumor with contra-lateral regional lymph node involvement Or midline tumor with bilateral extension by infiltration (unresectable) or lymph node involvement
Stage IV	Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs, except as defined in stage 4s Stage IV-S : Localized primary tumor with dissemination into skin, liver and/or bone marrow (limited to infants < 1year)

TREATMENT depends on stage and N-*myc* amplification.
In stage 1 and 2 the tumor should be resected with no chemotherapy or radiotherapy.
Stage 2 with amplification of N-*myc* gene and stage 3 should receive surgery if possible, then chemotherapy and/ or radiotherapy,
Stage 3 with amplification of N-*myc* gene and stage 4 should receive chemotherapy ± surgery, than high dose chemo/radio therapy with autologous stem cell transplant in high-income countries. Also monoclonal antibodies may be of use.

NEUROBLASTOMA

Name……IP No…….

Primary site……. Stage……

History Duration of symptoms, presence of fever, weight loss, diarrhea, palpitations

Physical exam Document size and site of masses, and adjacent lymphnode areas

Investigations

Histology of tumor	Haemogram
Creatinine, or full U/E if indicated	ALT or full LFT if indicated
HIV serology	Bone marrow
Urine for VMA	Immunohistochemistry
CXR	Abdominal ultrasound

Audiometry baseline and repeat if hearing loss is suspected

PRE-OPERATIVE CHEMOTHERAPY

Cisplatinum frequently causes severe electrolyte imbalance and requires special precautions on fluid and electrolyte replacement before, during and after its infusion which is briefly as follows:

- Start IV fluids with D/saline solution at 3000 ml/m^2 /day 4 hours before cis-platinum and continue
- for 24 hours after infusion.
- Add KCL at 40mEq/L infusion by adding 10 ml KCL 20% to every 500 ml bottle
- Use Mannitol (20%) 8gm/m^2 over 15 minutes before cis-platinum then 30gm/m^2 over 6 hours Piggy-back during cis-platinum.
- Ensure urine output is >100mls/m^2/hr during cis-platinum infusion.
- Give magnesium sulphate orally (or IV) at 0.25 mmol/kg/day for 7 days after cisplatin infusion
- (magnesium sulfate ampoule 50% has 2mmol magnesium/ml = 500 mg $MgSO_4$/ml)

Cisplatinum is very emetogenic, ondansetron ½ hour before cytotoxics, continue every 6-8 hours as required.

qCRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl >150, except weekly Vincristine.

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

DRUG	**Dose**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 8**	**Wk 12**	**Re evaluate with appropriate imaging**
DATE								
Vincristine 2mg/m^2 (max 2.5mg) IV push								
Etoposide 100 mg/m^2 Infusion over 1 hour			XXXXX	XXXXX				
Cyclophosphamide 500mg/m^2/day infusion over 1 hour, day 1 and 2			XXXXX	XXXXX				
Cisplatinum 100 mg/m^2 infusion over three hours			XXXXX	XXXXXX				
*Prednisone 40 mg/m^2 in advanced disease when in pain	TDS 7 days		XXXXX	XXXXX	XXXXX	XXXXX	XXXXX	
Signature								
Name								

NOTE: If weight <12 kg use 2/3 of dosages. Document start and stop days for prednisone on chart and T-sheet.*

LOCAL TREATMENT Consider radiotherapy on remaining tumor, followed by surgery. Plan for pediatric surgeon to review patient and clinically evaluate patient when they come for week 12of treatment. If surgery is delayed for whatever reason for more than 1-2 weeks, consider to administer additional chemotherapy.

NOTE: Document summary of Intraoperative and Pathology findings including IHC.

Intraop:_____
_____
_____
_____
_____

Histology._____
_____
_____
_____
_____

POST-OPERATIVE CHEMOTHERAPY (6 courses q 3-4 wks)

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl 150

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

DRUG	**Dose**	**Wk 16**	**Wk 20**	**Wk24**	**Evaluation with ultrasound/CT Scan**	**Wk 28**	**Wk 32**	**Wk 36**
DATE								
Vincristine 2mg/m^2 (max 2.5mg) IV push								
Etoposide 100 mg/m^2 infusion over one hour								
Cyclophosphamide 500mg/m^2 infusion over 1 hour, day 1 and 2								
Cisplatinum 100 mg/m^2 infusion over three hours								
Signature								
Name								
Planning date of next course								
Comment Response / significant events post op.								

NOTE: If weight <12 kg use 2/3 of dosages.

FOLLOW UP. Start one month after last dose. Review monthly X 3 visits, three monthly X 3 visits, six monthly for 2 years then yearly. Focus on clinical exam, imaging if indicated and check for late effects of chemotherapy.

NEPHROBLASTOMA

It's the commonest genitourinary malignancy of childhood.

Epidemiology
Peak incidence is between 2 and 6 years. The annual incidence is about 8/million children. It occurs with an equal frequency in boys and girls.

Clinical features
The presenting feature mostly is a painless abdominal mass. Other features may include pain, fever, haematuria and hypertension. Always examine for stigmata of other conditions that may be associated with wilms tumor e.g. hemihypertrphy, genital abnormalities and aniridia.

Work up/Investigations
Aims: confirm diagnosis, delineate the extent of the tumor, determine whether the contralateral kidney is affected, discover any metastasis and ensure the child is fit for surgery.

CBC- may show anaemia or thrombocytosis
Urinalysis
Serum urea, electrolytes and creatinine
Urinary catecholamines to exclude neuroblastoma
Abdominal ultrasound or CT / MRI of the abdomen
Chest radiographs (PA and lateral views)
Bone Marrow

Staging
The National Wilms Tumor (NWT) study staging system:

Stage I	Tumor within renal capsule completely excised
Stage II	Tumor extends beyond the kidney but is completely resected
Stage III	Gross or microscopic residual tumor remains post-operatively, spillage of tumor preoperatively or intraoperatively, regional lymph node metastasis
Stage IV	Haematogenous metastasis or lymph node metastasis outside the abdomen
Stage V	Bilateral tumors

Prognostic features
Tumor size
Histology: Anaplasia confers a poor prognosis
Older age is associated with a worse outcome.
Lymph node involvement is a predictor of treatment failure

Treatment
Surgery is the mainstay of treatment**.**
Pre-operative chemotherapy is always given. Postoperative chemotherapy is also always given, duration depends on the stage. Radiotherapy to tumor bed is often done after chemotherapy. All new patients will start on three-drug preoperative chemotherapy.. Postoperatively, they are placed in either high risk or standard risk depending on risk stratification after nephrectomy and histology.

NEPHROBLASTOMA Protocol

(Stage I to IV – All newly diagnosed patients irrespective of stage)

Name……IP No…….

Primary site……. Stage……

PRE-OPERATIVE CHEMOTHERAPY

Ht (cm) Wt (kg) SA (m^2)

DRUGS / **DATE**	**DOSE**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 5**	**Wk 6**	**Evaluate and plan for Surgery**
IV Vincristine 2mg/m^2 max 2.5 mg								
IV Actinomycin D 1.4mg/m^2 Max 2 mg			xxxxxx		xxxxxx		xxxxxx	
IV Adriamycin 50 mg/m^2 (infusion over 4 hours)			xxxxxx	xxxxxx	xxxxxx		xxxxxx	
Sign								
Name								
Response / Significant events								

**Give 2/3 of dosage if weight < 12 kg*

SURGERY Surgery should be done at Wk 7. Staging is done during surgery. Plan for pediatric surgeon to review patient and clinically evaluate patient when they come for week 6 of treatment.If surgery is delayed for whatever reason for more than 1-2 weeks, administer additional chemotherapy with vincristine and actinomycin-D.

Document summary of intraoperative and Pathology findings here:

Intraop:_____

_____

_____

_____

_____

_____

Histology:_____

_____

_____

_____

_____

POST- OPERATIVE (starts first week post-operative when bowel sounds are back):

Name……IP No…….

Primary site…….. Stage……

A. Low Risk disease (Stage 1): only 4 weeks treatment post operative

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl >150

Wt (kg) SA (m^2)

DRUG **DATE**	**DOSE**	**Week 8**	**Week 9**	**Week 10**	**Week 11**	**Evaluate clinically,and with abd U/sound.**
IV Vincristine 2.0 mg/m^2 max 2.5 mg						
IV Actinomycin D 1.4 mg/m^2 max 2mg		XXXXXX		XXXXXX		
Sign						
Name						
Response/ Significant events.						

**Give 2/3 of dosage if weight < 12 kg*

Document Post chemo evaluation:,……

FOLLOW UP. Start 1month after last dose. Review monthly X 3 visits, three monthly X 3 visits, six monthly for 2 years then yearly. Focus on clinical exam, image if indicated and check for late effects . Document each visit.

B. Standard Risk disease (stage 2 and 3 withfavourable histology) 6 months treatment with VCR and Act-D

Surface Area m^2

DRUG **DATE**	**WEEKS**	**8**	**9**	**10**	**11**	**12**	**14**	**17**	**Evaluation with ultrasound**	**20**	**23**	**26**
	DOSE											
Vincristine 2mg/m^2 max 2.5mg												
Actinomycin D 1.4 mg/m^2 max 2 mg		xxx		xxx	xxx							
Sign												
Name												
Planned date for next visit												
Response /Significant Events												

**Give 2/3 of dosage if weight < 12 kg*

Document response at end of week 11:

……

……

……

C. High Risk disease(stage 4 or post-operative pathology with anaplasia or extensive residual blastemal elements). Patients with clear cell sarcoma of the kidney should move to the Rhaddomyosarcoma treatment protocol

Name……IP No…….

Primary site…….. Stage……

POST-OPERATIVE (starts first week post-operative when bowel sounds are back):

Surface Area **m^2**

DRUG / **DATE**	**WEEKS**	**8**	**9**	**10**	**11**	**12**	**15**		**18**	**21**	**24**	**26**
	DOSE							**Evaluation with ultrasound**				
Vincristine 2 mg/m^2 max 2.5mg												
Actinomycin D 1.4 mg/m^2 max 2 mg		xxx		xxx	xxx							
Adriamycin 50mg/m^2 (infusion over 4 hours)		xxx		xxx	xxx	xxx			xxx		xxx	
Sign												
Name												
Planned date for next visit												

**Give 2/3 of dosage if weight < 12 kg*

Cumulative Adriamycin dose is 300 mg/m^2

NOTE If Actinomycin D is not available, replace it with Cyclophosphamide 450 mg/m^2

RADIOTHERAPY **10 Gy to tumor bed if lymphnodes positive or capsule not intact**

FOLLOW UP. Start one month after last dose. Review monthly X 3 visits, three monthly X 3 visits, six monthly for 2 years then yearly. Focus on clinical exam, image if indicated and check for late effects of chemotherapy. Document findings of each visit.

POST-OPERATIVE CHEMOTHERAPY FOR CLEAR CELL SARCOMA

Name……IP No……..

Primary site…….. Stage……

History Duration

Physical exam Document size and site of masses, and adjacent lymph node areas

Investigations Histology of tumor and IHC Haemogram
Creatinine, or full U/E if indicated ALT or full LFT if indicated
HIV serology Bone marrow
CXR Abdominal ultrasound
Echocardiogram at baseline and if cumulative Adriamycin dose >250 mg/m^2

CHEMOTHERAPY

PRE-OPERATIVE CHEMOTHERAPY (given per nephroblastoma protocol) until week 6.

BEGIN POST_OPERATIVE CHEMOTHERAPY AT WEEK 8 BELOW.

*CRITERIA for chemotherapy: good clinical condition, Hb> 9, ANC > 1000, Ptl>150, except weekly Vincristine***.**

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

DRUG	**Dose**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 8**	**Wk 12**	
DATE								
Vincristine 2mg/m^2 (max 2.5mg) IV push								**RE – EVALUATE WITH appropriate imaging**
Adriamycin 30mg/m^2 (infusion over 1 hour)			XXXXX	XXXXX	XXXXX			
Cyclophosphamide 500mg/m^2day infusion over 1 hour, day 1 and 2			XXXXX	XXXXX				
Signature / Name								
Planned next course								
Comment response / significant event pre – operative.								

NOTE: If weight <12 kg use 2/3 of dosages.

LOCAL TREATMENT Surgery done, radiotherapy when able to arrange.

Note: Document Intraoperative and Pathology findings .

CONTINUED POST-OPERATIVE CHEMOTHERAPY

Name……IP No……..

Primary site…….. Stage……

Four to Six cycles every 4 weeks. *CRITERIA to give chemotherapy: good clinical condition, Hb> 9, ANC > 1000, Ptl 150,*

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

DRUG	**Dose**	**Wk 16**	**Wk 20**	**Wk24**		**Wk 28**	**Wk 32**	**Wk 36**
DATE					**Evaluation with ultrasound**			
Vincristine 2mg/m^2 (max 2.5mg) IV push								
Adriamycin 30mg/m^2 (infusion over 1 hour)								
Cyclophosphamide 500mg/m^2day infusion over 1 hour, day 1 and 2								
Signature / Name								
Planning date of next course								
Comment response/ significantevents post op.								

NOTE: If weight <12 kg use 2/3 of dosages.

FOLLOW UP. Start one month after last dose. Review monthly X 3 visits, three monthly X 3 visits, six monthly for 2 years then yearly. Focus on clinical exam, image if indicated and check for late effects of chemotherapy.

RHABDOMYOSARCOMA AND OTHER MESENCHYMAL TUMORS

Definition Malignant growth of primitive mesenchymal cells
Presentation Rhabdomyosarcoma is the most common soft tissue tumor in childhood and adolescence.
Incidence 10 – 12 % of malignant solid tumors in childhood
10 per million white children in USA, less in black children
Host factors Sex ratio 1.1 M / 1 F Mean age 6 years
Genetic factors More RMS with congenital abnormalities, or other malignancies in relatives as in Li-Fraumeni syndrome and neurofibromatosis type 1

PATHOLOGICAL CLASSIFICATION

Embryonal	57%
Alveolar	18%
Botryoid	7 %
Pleomorphic	2 %
Undifferentiated	16%

Methods of differentiation apart from microscopy should include immunocyto chemistry, cytogenetics, oncogene expression etc

The botyroid type characteristically involves hollow body organs like vagina, nasal cavity and bladder. The botyroid and embryonal subtypes are LOW GRADE and respond well to treatment while the alveolar, anaplastic, pleomorphic and mixed types are HIGH GRADE and tend to perform poorly. It is often difficult to differentiate RMS from other small round cell tumors from a fine needle aspirate.

Rhabdomyosarcoma may arise anywhere in the body where mesenchymal tissue is present:

10%	Orbital	
30%	Head and neck	+/- Parameningeal
20%	Genitourinary tract	Bladder and prostate
		Vagina, vulva, uterus, paratesticular
20%	Extremities	
20%	Other	Truncal (10%), intrathoracic, intra-abdominal, pelvic, perineum and paravertebral

RMS is an aggressive tumor, infiltrating along fascial planes and disseminating along lymphatic and haematogenous routes. 20% of patients present with distant metastases at diagnosis, mainly lung, lymphnodes, bone and bone marrow, rarely liver and brain.

Classification according to SIOP clinical staging

Stage 1	Tumor confined to organ or tissue of origin, size< 5 cm, no nodes, no metastases
Stage 2	Tumors involving one or more contiguous organs or tissues, or with effusion, or multiple tumors in one organ, no nodes, no metastases
Stage 3	Lymphnode infiltration
Stage 4	Distant metastases

Prognostic factors are :Stage,
Histology: good prognosis in botryoid and spindle cell RMS, intermediate in embryonal RMS and poor in alveolar RMS.
Primary site (orbital and genito- urinary site better prognosis)

Mainstay of treatment for solid tumors is surgery, combined with chemotherapy ± radiotherapy.
Primary surgery only if tumor can be excised in toto, or secondary excision after chemotherapy
Chemotherapy with good response with Vincristine, Cyclophosphamide, Adriamycin and Actinomycin.
Radiotherapy gives good local control but with severe long term morbidity.

MANAGEMENT OF RHABDOMYOSARCOMA (RMMT) ANDNON-RHABDOMYOSARCOMA MALIGNANT MESENCHYMAL TUMORS (NRMMT)

Name……IP No…….

Primary site…… Stage……

History Duration

Physical exam Document size and site of masses, and adjacent lymph node areas

Investigations Histology of tumor and IHC Haemogram
Creatinine, or full U/E if indicated ALT or full LFT if indicated
HIV serology Bone marrow
CXR Abdominal ultrasound
Echocardiogram at baseline and if cumulative Adriamycin dose >250 mg/m^2

CHEMOTHERAPY

PRE-OPERATIVE CHEMOTHERAPY

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl >150, except weekly Vincristine.

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

DRUG	**Dose**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 8**	**Wk 12**	
DATE								
Vincristine 2mg/m^2 (max 2.5mg) IV push								**RE – EVALUATE WITH appropriate imaging**
Adriamycin 50mg/m^2 (infusion over 4 hours)			XXXXX	XXXXX	XXXXX		XXXXX	
Cyclophosphamide 500mg/m^2day infusion over 1 hour, day 1 and 2			XXXXX	XXXXX				
Actinomycin-D 1.4 mg/m^2 IV push		XXXXX	XXXXX	XXXXX		XXXXX		
Signature / Name								
Planned next course								
Comment response / significant event pre – operative.								

NOTE: If weight <12 kg use 2/3 of dosages.

LOCAL TREATMENT

Surgery, radiotherapy or both.Plan for pediatric surgeon to review patient and clinically evaluate patient when they come for week 12 of treatment. If surgery is delayed for whatever reason for more than 1-2 weeks, consider to administer additional chemotherapy.

Note: Document Intraoperative and Pathology findings

_____

_____

_____

POST-OPERATIVE CHEMOTHERAPY

Name……IP No……..

Primary site…….. Stage……

Six cycles every 4 weeks. *CRITERIA to give chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl 150,*

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

DRUG	**Dose**	**Wk 16**	**Wk 20**	**Wk24**	**Evaluation with ultrasound**	**Wk 28**	**Wk 32**	**Wk 36**
DATE								
Vincristine 2mg/m² (max 2.5mg) IV push								
Adriamycin 30mg/m² (infusion over 4 hours)			XXXXX			XXXXX		XXXXX
Cyclophosphamide 500mg/m²day infusion over 1 hour, day 1 and 2								
Actinomycin D 1.4 mg/m² IV push		XXXXX		XXXXX			XXXXX	
Signature / Name								
Planning date of next course								
Comment response/ significant events post op.								

NOTE: If weight <12 kg use 2/3 of dosages.

FOLLOW UP. Start one month after last dose. Review monthly X 3 visits, three monthly X 3 visits, six monthly for 2 years then yearly. Focus on clinical exam, image if indicated and check for late effects of chemotherapy.

EWINGS SARCOMA MANAGEMENT

Name……IP No……

Primary site…… Stage……

History Duration

Physical exam Document size and site of masses, and adjacent lymph node areas

Investigations Histology of tumor and IHC Haemogram
Creatinine, or full U/E if indicated ALT or full LFT if indicated
HIV serology Bone marrow
CXR Abdominal ultrasound
Echocardiogram at baseline and if cumulative Adriamycin dose >250 mg/m^2

CHEMOTHERAPY

PRE-OPERATIVE CHEMOTHERAPY

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl >150, except weekly Vincristine.

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

DRUG	**Dose**	**Wk 1**	**Wk 2**	**Wk 3**	**Wk 4**	**Wk 8**	**Wk 12**	
DATE								
Vincristine 2mg/m^2 (max 2.5mg) IV push								**RE – EVALUATE WITH appropriate imaging**
Adriamycin 30mg/m^2 (infusion over 4 hours)			XXXXX	XXXXX	XXXXX		XXXXX	
Cyclophosphamide 500mg/m^2day infusion over 1 hour, day 1 and 2			XXXXX	XXXXX				
Actinomycin-D 1.4 mg/m^2 IV push		XXXXX	XXXXX	XXXXX		XXXXX		
Signature / Name								
Planned next course								
Comment response / significant event pre – operative.								

NOTE: If weight <12 kg use 2/3 of dosages.

LOCAL TREATMENT Surgery, radiotherapy or both.Plan for pediatric surgeon to review patient and clinically evaluate patient when they come for week 12 of treatment. If surgery is delayed for whatever reason for more than 1-2 weeks, consider to administer additional chemotherapy.

Note: Document Intraoperative and Pathology findings

_____

_____

_____

POST-OPERATIVE CHEMOTHERAPY

Name……IP No……..

Primary site…….. Stage……

Six cycles every 4 weeks. *CRITERIA to give chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl 150,*

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

DRUG	**Dose**	**Wk 16**	**Wk 20**	**Wk24**	**Evaluation with ultrasound**	**Wk 28**	**Wk 32**	**Wk 36**
DATE								
Vincristine 2mg/m² (max 2.5mg) IV push								
Adriamycin 30mg/m² (infusion over 4 hours)			XXXXX			XXXXX		XXXXX
Cyclophosphamide 500mg/m²day infusion over 1 hour, day 1 and 2								
Actinomycin D 1.4 mg/m² IV push		XXXXX		XXXXX			XXXXX	
Signature / Name								
Planning date of next course								
Comment response/ significant events post op.								

NOTE: If weight <12 kg use 2/3 of dosages.

FOLLOW UP. Start one month after last dose. Review monthly X 3 visits, three monthly X 3 visits, six monthly for 2 years then yearly. Focus on clinical exam, image if indicated and check for late effects of chemotherapy.

OSTEOGENIC SARCOMA

It's a malignant tumor characterized by the direct formation of bone or osteoid tissue by the tumor cells.

Epidemiology

Primary bone tumors have a peak incidence between 10-20 years of age. They account for less than 5% of childhood malignancies. Osteosarcoma and Ewings sarcoma account for over 90% of primary bone tumors occurring in children and adolescents with Ewings sarcoma being as half as common as osteosarcomas.

Aetiology/Risk factors

Genetic factors; There is an association with li-Fraumeni syndrome. Its also common in patients with inherited retinoblastoma .Other risk factors include prior radiation and alkylating agents therapy. There is a clear but unexplained association with rapid bone growth.

Clinical features

More than 50% of the tumors arise from the bones around the knee.
Pain is usually the most common compliant and is often ascribed to trauma. This is usually followed by a swelling.
Systemic symptoms are usually uncommon and may indicate unusually aggressive and extensive disease.

Investigations

Plain radiographs
MRI
Biopsy
Isotope bone scan and chest CT (for staging)
CBC, UECs, LFTs (for chemotherapy and planning for surgery)
Prognostic factors

Primary site

For patients with localized disease the site is a prognostic indicator. For those with extremity tumors distal site have a better prognosis than proximal sites .Axial skeleton tumor have the greatest risk of progression and death.
Tumor size: Large tumors are associated with worse prognosis
Presence of clinically detectable metastatic disease
Adequacy of tumor resection
Necrosis following neo-adjuvant chemotherapy: Those patients with >90% tumor necrosis have a better prognosis than those with less necrosis.
Treatment: all patients wil get three courses of combination chemotherapy every 3-4 weeks pre-operatively. Following surgery, another three courses are given.

OSTEOGENIC SARCOMA MANAGEMENT

Name……IP No……..

Primary site……Stage……Metastatic Y/N.....

PRE OPERATIVE CHEMOTHERAPY, courses to be given every 3-4 weeks

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl >150

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

DRUG	**DOSE**	**Cycle 1**			**Cycle 2**			**Cycle 3**			**Plan surgery with orthopedics**
		DATE									
Adriamycin day 1,2,3 25 mg/m² /day infusion four hours											
Cisplatinum day 1 and 2 60 mg/m² infusion four hours				XX XX			XX XX			XX XX	
Name , Signature											
New booking											

Note: Monitor renal function state with every cycle of chemotherapy.

Plan for Orthopaedic surgeon to review patient and clinically evaluate patient when they come for the 3rd course of treatment. If surgery is delayed for whatever reason for more than 1-2 weeks, administer additional chemotherapy pre-operatively.Cumulative dose of adriamycin should ideally not exceed 450 mg/m², however.

SURGERY

Document intra operative and histology findings:

_____
_____
_____
_____
_____
_____
_____

Histology findings:

_____
_____
_____
_____
_____
_____

POSTOPERATIVE CHEMOTHERAPY

Name……IP No…….

Primary site……. Stage……

Courses to be given every 3-4 weeks

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl >150

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**

DRUG	**DOSE**	**Cycle 4**			**Cycle 5**			**Cycle 6**		
		DATE								
Adriamycin day 1,2,3 25 mg/m² /day infusion four hours										
Cisplatinum day 1 and 2 60 mg/m² infusion four hours				XX XX			XX XX			XX XX
Name , Signature										
New booking										
Response/ significant events post OP										

FOLLOW UP: .Irrespective of size of tumor, initially monthly x 3 visits,three monthly x 3visits, then 6 monthly for 2 years, then yearly. Evaluate clinically, review chest X-rays 6 monthly for the first two years to look for any lung metastatic recurrence.

TOXICITY

Cis-platinum frequently causes severe electrolyte imbalance and requires special precautions on fluid and electrolyte replacement before, during and after its infusion which is briefly as follows:

- Start IV fluids with D/saline solution at 3000 ml/m² /day 4 hours before cis-platinum and continue for 24 hours after infusion.
- Add KCL at 40mEq/L infusion by adding 10 ml KCL 20% to every 500 ml bottle
- Use Mannitol (20%) 8gm/m² over 15 minutes before cis-platinum then 30gm/m² over 6 hours piggy-back during cis-platinum.
- Ensure urine output is >100mls/m²/hr during cis-platinum infusion.
- Give magnesium sulphate orally (or IV) at 0.25 mmol/kg/day for 7 days after cisplatin infusion (magnesium sulfate ampoule 50% has 2mmol magnesium/ml = 500 mg $MgSO_4$/ml)

Cisplatinum is very emetogenic, so start ondansetron ½ hour before cytotoxics, and continue every 6-8 hours for 3-7 days as required.

RETINOBLASTOMA

Retinoblastoma is the most common primary malignant intraocular tumor of childhood.
It occurs in 1:20,000 live births, and almost always before the age of 5 years.
It results from malignant transformation of premature retinal cells before final differentiation.
The predisposing gene (RB 1 gene) is located at region 14 in chromosome 13 (13q14)
60 % is non-hereditary, where there is no germline mutation. Only one eye is affected and the average age at presentation is 2 years.
It may be hereditary in 40% of cases, where all patients have a germline mutation, with mostly multifocal and bilateral disease. The age of presentation is around 1 year of age. All bilateral cases and about 15 % of unilateral cases fall into this category. There is a predisposition to develop secondary non-ocular malignancies, including pinealoblastoma and osteogenic sarcoma.

PRESENTATION is mostly with leukocoria, but also strabismus, glaucoma or inflammation of the eye, but in Kenya many patients come late and proptosis is a common presentation. Most patients are admitted and managed in the eye wards. Fundoscopy under anaesthesia of both eyes needs to be done in all suspected cases, supplemented by ultrasound, MRI preferably, or CT.

STAGING

I	Solitary or multiple tumors, size less than 4 disc diameters (dd) at or behind the equator
II	Solitary or multiple tumors 4 – 10 disc diameters in size, all behind the equator
III	Any lesion anterior to the equator or solitary tumors larger than 10 dd behind the equator
IV	Multiple tumors, some larger than 10dd, or any lesion extending anterior
V	Massive tumors involving over half the retina and vitreous seeding

MANAGEMENT objectives:
1. Survival of the patient
2. Preservation of the globe
3. Preservation of visual acuity

In unilateral retinoblastoma the treatment of choice should be enucleation. Small tumors can be treated locally with cryo- or laser therapy. Further treatment depends on pathology examination:
If the sclera of the enucleated eye is intact and no tumor invasion is present in the optic nerve or the chorioidea then there is no indication for post operative chemotherapy, only close follow up.
If primary enucleation is not possible due to the degree of proptosis, then chemotherapy should be given first to make enucleation possible. After surgery continue chemotherapy awaiting pathology report.

In bilateral retinoblastoma enucleation of the worst eye should be done. The other eye should be treated with laser, if necessary in combination with Carboplatin and / or the whole VEC treatment depending on the pathology result of the enucleated eye.

Teamwork is important between ophthalmologists, paediatric oncology team, pathologist, radio-oncologist, nursing team, counselors and child life specialists.

For chemotherapy the most effective drugs are vincristine, etoposide, cisplatinum / carboplatinum, cyclophosphamide and adriamycin. Chemotherapy alone is never curative. It should always be combined with laser or cryotherapy.

In meningeal or intracranial disease (including pinealoblastoma) give palliative treatment only.

FOLLOW UP: Needs to be done regular, irrespective of size of tumor, initially 3 monthly for 1 year, then 6 monthly for 2 years, then yearly.
Check for late effects of chemotherapy, include audiometry
Check for associated malignancies, including osteogenic sarcoma, of local tumors related to radiotherapy.and bilateral retinoblastoma. In case of bilateral disease younger siblings need to be checked also by ophthalmologist.

VEC REGIMEN For EXTENSIVE RETINOBLASTOMA

Name……IP No…….

Primary site…….. Stage……

If possible do audiogram and creatinine at baseline , and repeat if a decline is suspcted.Reduce dose of Carboplatin, or omit this drug when renal function is deteriorating.For each cycle: hydration over 4 hours, and anti emetics e.g. ondansetron ½ hour before chemotherapy

Continue hyperhydration until next morning. Ensure Hb > 10mg/dl, Platelets > 50, ANC >1000, U/E Creatinine within normal.If chemotherapy is used in combination with laser- or cryotherapy, then first give Carboplatin, followed bylaser / cryo 1 hour after completion of the infusion, and then continue with Vincristine and Etoposide.

If carboplatin is not available, replace by cisplatin at 100 mg/m^2 (if <12 kg, 3.3 mg/kg)

Unilateral/ Bilateral..... If Unilateral right or left.....

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

	CYCLES every 3 (-4) weeks	Dose	Cycle	1	2	Response
			Date			
Carboplatin	560 mg/m^2 or 18.7 mg/kg if < 12 kg		In 5% DW, 9 ml/kg ½ hour infusion			
Vincristine	2,0 mg/m^2 (or 0,05 mg/kg if <12 kg) max 2.5 mg		IV push			
Etoposide	230 mg/m^2 or 7.7 mg/kg if < 12 kg		In NS 30 ml/kg ½ hour infusion			
Next booking						
Name/sign						
EUA note						

SURGERY when tumor has regressed well, mostly after 2 (or 3) cycles. Plan for opthalmologist to review patient and clinically evaluate patient.If surgery is delayed consider additional chemotherapy

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

	CYCLES every 3 (-4) weeks	Dose	Cycle	3	4	5	6
			Date				
Carboplatin	560 mg/m^2 or 18.7 mg/kg if < 12 kg		½ hour infusion				
Vincristine	2,0 mg/m^2 (or 0,05 mg/kg if <12 kg) max 2.5 mg		IV push				
Etoposide	230 mg/m^2 or 7.7 mg/kg if < 12 kg		½ hour infusion				
Next booking							
Sign							
Name							
Response/							

RADIOTHERAPY if resistant disease only, can be given after 4th (or 6th) cycle.**Follow up** irrespective of size of tumor, initially 3 monthly for 1 year, then 6 monthly for 2 years, then yearly.

VAC-CIS REGIMEN

Name……IP No…….

Primary site…….. Stage……

This regimen is only used for retinoblastoma when other drugs are not available. The regimen is much more nephrotoxic, ototoxic and cardiotoxic. Especially because vision might be impaired, ototoxic drugs should be avoided as much as possible.
Consider Etoposide 100 mg/m^2 for 3 days instead of Cyclophosphamide or Adriamycin in alternate cycles

Do echocardiogram at baseline and after the last course
Do audiogram if hearing loss is suspected
Ensure Hb > 10mg/dl, Platelets > 50x10^9/L, ANC >1.2x10^9/L, U/E Creatinine within normal.
Check creatinine at baseline and every other cycle
Omit Cisplatinum when renal function is deteriorating.

Cis-platinum frequently causes severe electrolyte imbalance and requires special precautions on fluid and electrolyte replacement before, during and after its infusion which is briefly as follows:

- Start IV fluids with D/saline solution at 3000 ml/m^2 /day 4 hours before cis-platinum and continue for 24 hours after infusion.
- Add KCL at 40mEq/L infusion by adding 10 ml KCL 20% to every 500 ml bottle
- Use Mannitol (20%) 8gm/m^2 over 15 minutes before cis-platinum then 30gm/m^2 over 6 hours piggy-back during cis-platinum.
- Ensure urine output is >100mls/m^2/hr during cis-platinum infusion.
- Give magnesium sulphate orally (or IV) at 0.25 mmol/kg/day for 7 days after cisplatin infusion (magnesium sulfate ampoule 50% has 2mmol magnesium/ml = 500 mg $MgSO_4$/ml)

Cisplatinum is very emetogenic, so start ondansetron ½ hour before cytotoxics, and continue every 6-8 hours for 3-7 days as required.

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl 150

		Dose	Cycle	1	2	3		4	5	6
			Date							
Vincristine	2.0mg/m^2 max 2.5mg		IV push				SURGERY if needed			
Adriamycin	40mg/m^2		4hours infusion							
Cyclophosphamide	750 mg/m^2		1hour infusion							
Cisplatin	30mg/m^2 OD x 2 days		6hour infusion							
Next booking										
Sign										
Name										
Response										

Use 2/3 of dosages given in mg/m^2 if weight < 12 kg

FOLLOW UP:.Irrespective of size of tumor, initially 3 monthly for 1 year, then 6 monthly for 2 years, then yearly.Start one month after last dose. Focus on clinical exam (EUA three monthly)and check for late effects of chemotherapy.

GERM CELL TUMORS

Constitute a heterogenous group of tumors that vary significantly with respect to clinical presentation, histology and biology. In childhood they predominantly arise at extragonadal midline sites such as the sacrococcygeal region, the CNS and the anterior mediastinum. In adolescents they commonly arise in the gonads.

Epidemiology

Occur at a rate of about 2.4 cases per million and represents about 1% of all childhood cancers below the age of 15 year.

Teratomas are common in neonates and yolk sac tumors in infancy and early childhood

Histologic classification

There are three major categories

Mature teratoma:Most common histological variant in infants and young children.Contains well differentiated tissues from the ectodermal, mesodermal and andodermal germ cell layers.Majority are benign.

Immature teratoma:Contains innature tissue from the three layers and are usually divided inti three grads depending on the amount of immature tissue.

Malignant germ cell tumors:Young children; Yolk sac tumour and dysgermonima;
Adolescents;Seminoma,Dysgerminoma,Yolk sac tumors, Choriocarcinoma.

Diagnosis

These tumors tend to occur as indolent masses and clinical signs are related to the site of the tumour

Tumour markers

Teratoma(mature, immature)and yolk sac tumour:AFP

Choriocarcinoma and germonimas : beta-HCG

Staging

StageI	Localized disease, completely resected
StageII	Microscopic residual disease
StageIII	Gross residual disease
StageIV	Disseminated disease(lungs, liver, brain e.t.c)

Prognostic features

Age: younger age confers better prognosis

Stage of the disease

Histology

Therapy

Surgery

Chemotherapy

GERM CELL TUMORS MANAGEMENT

Name……IP No……..

Primary site…….. Stage……

TREATMENT OPTIONS:

First choice:	**JEB**	Carboplatin Etoposide Bleomycin	or **BEP**	Cis-platin Etoposide Bleomycin
Second choice:	**JVB**	Carboplatin Vinblastine Bleomycin	or **PVB**	Cisplatin Vinblastine Bleomycin
Third choice is: (If other drugs N/A)	**VAC**	Vincristine Adriamycin Cyclophosphamide		

JEB/BEP Regimens (Protect drugs from light during infusion)

Give two courses pre-operative every three weeks, then surgery, followedby at least two courses every 3weeks.

Plan for pediatric surgeon to review patient and clinically evaluate patient when they come for week 4 of treatment. If surgery is delayed for whatever reason for more than 1-2 weeks, consider to administer additional chemotherapy pre-operatively.

CRITERIA for chemotherapy: good clinical condition, Hb>9, ANC>1000, Ptl>150

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

PRE-OPERATIVE COURSES POST-OPERATIVE COURSES

DRUG	DOSE	Cycle 1			Cycle 2			Cycle 3			Cycle 4		
		DATE											
Carboplatin 200 mg/m^2 infusion one hour, day 1 (or Cis-platinum 100 mg/m^2)			XX	XX		XX	XX		XX	XX		XX	XX
Etoposide 120 mg/m^2/day infusion one hour, day 1,2,3													
Bleomycin 15,000 U (15mg) /m^2 infusion one hour, day 2		XX		XX	XX		XX	XX		XX	XX		XX
NAME and SIGN													
Alpha Fetoprotein / β-HCG levels.													
NEXT BOOKING													
Response/ Significant Events													

Monitor alpha-feto protein and / or β-HCG.

Repeat courses every three weeks until alpha-feto protein and β-HCG are within normal (αFP <15 units in children) then give two extra courses.

Precautions with use of cis-platin: good hydration, supplements of KCL and Mg sulphate

FOLLOW UP:Start one month after last dose.Initially 3 monthly for 1 year, then 6 monthly for 2 years, then yearly. Evaluate clinically, by abdomeno- pelvic ultrasound,alpha-feto protein and / or β-HCG.Focus on clinical exam, image if indicated and check for late effects of chemotherapy.

GERM CELL TUMORS MANAGEMENT

Name……IP No…….

Primary site…….. Stage……

JVB/PVB Regimens

Give two courses pre-operative every three weeks, then surgery, followed by at least two courses every 3weeks.

Plan for pediatric surgeon to review and clinically evaluate patient when they come for week 4 of treatment. If surgery is delayed for whatever reason for more than 1-2 weeks, consider to administer additional chemotherapy pre-operatively..

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl 150; interval between courses at least 3 weeks.

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

PRE-OPERATIVE COURSES POST-OPERATIVE COURSES

DRUG	DOSE	Cycle 1			Cycle 2			Cycle 3			Cycle 4		
		DATE											
Carboplatin 200 mg/m² infusion one hour, day 1 (or Cis-platinum 100 mg/m²)			XX	XX		XX	XX		XX	XX		XX	XX
Vinblastine 6 mg/m2, day 2 (if unavailable, vincristine 2.0 mg/m2, max 2.5 mg, on day 2		XX		XX	XX		XX	XX		XX	XX		XX
Bleomycin 15,000 U (15mg) /m² infusion one hour, day 2		XX		XX	XX		XX	XX		XX	XX		XX
NAME and SIGN													
Alpha Fetoprotein / β-HCG levels.													
NEXT BOOKING													
Response/ Significant Events													

Monitor alpha-feto protein and / or β-HCG.

Repeat courses every three weeks until alpha-feto protein and β-HCG are within normal (αFP <15 units in children) then give two extra courses.

Precautions with use of cis-platin: good hydration, supplements of KCL and Mg sulphate

FOLLOW UP:.Start one month after last dose. Initially 3 monthly for 1 year, then 6 monthly for 2 years, then yearly. Evaluate clinically, by abdomeno- pelvic ultrasound,alpha-feto protein and / or β-HCG.

VAC Regimen

INDUCTION

- IV Vincristine 2mg/M² (Max 2mg) weekly x 12 weeks
- IV Cyclophosphamide 750mg/M² 3 weekly x 4 courses
- IV Adriamycin 30mg/M² alternate with Actinomycin D 3 weekly x 4 courses (total)

MAINTENANCE (for 1 year)

- IV Vincristine 2mg/M2 (Max 2mg) 3 weekly
- IV Cyclophosphamide 750mg/M² 3 weekly
- IV Adriamycin 30mg/M² alternate with Actinomycin D 3 weekly (total of 8 doses of Adriamycin then give Actinomycin D alone)

GERM CELL TUMOR (YOLK SAC) MANAGEMENT

Name……IP No…….

Primary site…….. Stage……

Telephone No…….. Telephone No……

Give 4 courses every 3 weeks

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl 150

POST-OPERATIVE

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

DRUG	DOSE	1							2						
		DATE													
		DAY 1	2	3	4	5	8	15	DAY 1	2	3	4	5	8	15
Etoposide 100 mg/m²															
Cisplatin 20 mg/m²															
Bleomycin 30,000 IU (30 mg)/m² infusion one hour, day 1,8,15															
SIGN															
NAME															
NEXT BOOKING															

DRUG	DOSE	3							4						
		DATE													
		DAY 1	2	3	4	5	8	15	DAY 1	2	3	4	5	8	15
Etoposide 100 mg/m²															
Cisplatin 20 mg/m²															
Bleomycin 30,000 IU (30 mg)/m² infusion one hour, day 1,8,15															
SIGN															
NAME															
NEXT BOOKING															

Monitor alpha-feto protein and / or β-HCG.

Repeat courses every three weeks until alpha-feto protein and β-HCG are within normal (Afp <15 units in children) then give two extra courses.

Precautions with use of cis-platin: good hydration, supplements of KCL and Mg sulphate

PROTOCOL FOR MANAGEMENT OF INTRACRANIAL GERM CELL TUMOURS

Name……IP No…….

Primary site…….. Stage……

After confirmation of diagnosis do tumour markers(AFP and beta-HCG) and use them to monitor progress. Typically surgical resection is not required for intracranial germ cell tumours.

Beta-HCG level…….
AFP level……..

Chemotherapy consists of 4 courses of carboplatin, Etoposide and Cyclophosphamide.
Carboplatin is given as a 3 hour infusion while the Etoposide and Cyclophosphamide are given over 1 hour.

Course 1

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

	Date	Cisplatin (50 mg/m²)	Etoposide (100 mg/m²)	Cyclophosphamide (1000 mg/m²/day)	Name/sign
Day 1					
Day 2					
Day 3					
Day 4					

Course 2

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

	Date	Cisplatin (50 mg/m²)	Etoposide (100 mg/m²)	Cyclophosphamide (1000 mg/m²/day)	Name/sign
Day 1					
Day 2					
Day 3					
Day 4					

Course 3

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

	Date	Cisplatin (50 mg/m²)	Etoposide (100 mg/m²)	Cyclophosphamide (1000 mg/m²/day)	Name/sign
Day 1					
Day 2					
Day 3					
Day 4					

Course 4

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

	Date	Cisplatin (50 mg/m²)	Etoposide (100 mg/m²)	Cyclophosphamide (1000 mg/m²/day)	Name/sign
Day 1					
Day 2					
Day 3					
Day 4					

After the chemotherapy evaluate with an MRI and the tumour markers as well.
MRI Findings (Date…….. _)
……
……
……

Beta-HCG level……. (Date……)
AFP level……. (Date……..)

Proceed with craniospinal irradiation of 30 Gy with boost to the tumour bed of 54 Gy.

HEPATOBLASTOMA

Epidemiology:
Liver Tumors account for about 1% of all paediatric malignancies with hepatoblastoma accounting for 2/3 of the cases.
Mean age at diagnosis is one and half years with males being affected more than females (1.4:1 to 1:2)

Etiology
Genetics: Many genetic disorders are associated with increased risk of hepatoblastma. These include Familial adenomatous polyposis, Beckwith Wiedeman syndrome, Li-Fraumenis syndrome among others.
Environmental: Prematurity

Clinical presentation
An asymptomatic abdominal mass is the commonest mode of presentation.
Pain, weight loss, anorexia, nausea and jaundice may occur but they are relatively rare.

Evaluation
Radiological
Abdomonal Ultrasound: Usually the first investigation done in the work-up
Abdominal CT scan
Chest CT scan: for metastasis
Laboratory
Alpha-feto protein: elevated in 90% of the cases. Important marker for evaluating response
CBC
LFTs
Creatinine

Staging (Paediatric oncology group system)

Stage I :Completety resected tumor
Stage II: Grossly resected tumor with evidence of microscopic residual disease
Stage III: partially resected tumor, Lymph node involvement
Stage IV: Distant metastasis.

Treatment
Surgery: It's the main mode of therapy
Chemotherapy: Useful drugs include Cisplatin, Vincristine, Doxorubicin and 5-FU
Liver transplantation
Consider palliative treatment if after (extended) preoperative chemotherapy the primary tumor is irresectable and/or the lung metastases have not disappeared

Prognosis
Low or normal alpha-feto protein confers poor prognosis
Resectability of tumor during surgery
Pure fetal histology is associated with a good prognosis
Presence of metastasis has a worse prognosis

HEPATOBLASTOMA MANAGEMENT

Name……IP No…….

Primary site…….. Stage……

History Duration of symptoms

Physical exam Document presence of jaundice, size of tumor

Investigations
- Histology of tumor
- Haemogram
- Creatinine, or full U/E if indicated
- LFT's
- HIV serology
- Hepatitis B surface antigen
- α-Feto-protein
- CXR
- Abdominal ultrasound
- Echocardiogram as baseline, and after 250 mg/m2 adriamycin (before 5th course)

Audiometry baseline and repeat if hearing loss is suspected

Normally, three courses are given pre-operatively. Plan for pediatric surgeon to review patient and clinically evaluate patient when they come for the 3rd course of treatment. If surgery is delayed for whatever reason for more than 1-2 weeks, administer additional chemotherapy pre-operatively. Cumulative dose of adriamycin should ideally not exceed 450 mg/m2, however.

CRITERIA for chemotherapy: good clinical condition, Hb > 9, ANC > 1000, Ptl 150

PRE-OPERATIVE COURSES *POST-OPERATIVE COURSES*

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**)

DRUG	DOSE	Cycle1		Cycle 2		Cycle 3		SURGERY	Cycle 4		Cycle 5	
		DATE										
Adriamycin 30 mg/m²/day infusion four hours, day 1, 2												
Cisplatinum 100 mg/m² infusion one hour, day 2		XX		XX		XX			XX		XX	
SIGN												
NAME												
Next booking												
Response												

In standard risk disease, when 3 or fewer sections of the liver are diseased, treatment with monotherapy cisplatinum showed good results.

TOXICITY

Cis-platinum frequently causes severe electrolyte imbalance and requires special precautions on fluid and electrolyte replacement before, during and after its infusion which is briefly as follows:

- Start IV fluids with D/saline solution at 3000 ml/m² /day 4 hours before cis-platinum and continue for 24 hours after infusion.
- Add KCL at 40mEq/L infusion by adding 10 ml KCL 20% to every 500 ml bottle
- Use Mannitol (20%) 8gm/m² over 15 minutes before cis-platinum then 30gm/m² over 6 hours piggy-back during cis-platinum.
- Ensure urine output is >100mls/m²/hr during cis-platinum infusion.
- Give magnesium sulphate orally (or IV) at 0.25 mmol/kg/day for 7 days after cisplatin infusion (magnesium sulfate ampoule 50% has 2mmol magnesium/ml = 500 mg $MgSO_4$/ml)

Cisplatinum is very emetogenic, so start ondansetron ½ hour before cytotoxics, and continue every 6-8 hours for 3-7 days as required.

NASOPHARYNGEAL CARCINOMA

It's a malignant tumour that arises in the epithelial lining of the nasal cavity and the pharynx.

Epidemiology
It is uncommon in children under 10 years of age but has an incidence of about 0.8and 1.3 per million in children aged 11 to 14 years and 15-19 years respectively.
There is a high frequency in south East Asia and North Africa.

Aetiology

Genetic factors
Environmental factors: EBV virus

Clinical features
Painless cervical adenopathy
Nasal obstruction
Epistaxis
Recurrent otitis media
Cranial nerve palsies
Headache
Sore throat

Diagnostic work-up

Biopsy of the mass for histological confirmation and EBV DNA screening
CT and/or MRI of the nasopharyngeal area
Chest CT or x-ray
Abdominal Ultrasound
Bone scan
Haemogram
Blood chemistry

Histologic sub-types

Type 1: squamous cell carcinoma
Type 2: non-keratinizing carcinoma
Type 3: undifferentiated carcinoma

Treatment

Radiotherapy is the mainstay of therapy
Chemotherapy is used as an adjunct to radiotherapy.

NASOPHARYNGEAL CARCINOMA MANAGEMENT

Name……IP No…….

Primary site…….. Stage……

Lab: CBC, LFT, U/E, Creatinine
If Intracranial extension: endocrine screen like thyroid function, LH, FSH
EBV diagnostics eg EBV PCR, EBV IgG, IgM, IgA, anti-VCA etc
Imaging: MRI, CT thorax, abdomen, skeleton scintigraphy, PETscan
Audiogram, Echo/ECG at baseline

Treatment

All patients should receive chemotherapy and radiotherapy as local treatment. Plan radiotherapy at the earliest opportunity available. Re-evaluate the tumor size with imaging in consultation with the radio-oncologist to decide on the appropriate time for radiotherapy.

Hydration starts 6 hours before chemotherapy at dose of 1500 ml/m^2/12h,
Add: 2 ml KCL 7.45% / 100 ml
1.2 ml magnesium 20% / 100 ml.
2.6 ml Ca Gluconate 19% / 100 ml
10 ml mannitol 20% / 100 ml

15 min before cisplatin give 40 ml/m^2 mannitol 20% as bolus
Give cisplatinum 100 mg/m2 dissolved in 100 ml NS piggyback over 6 hours while continuing IVF
After cisplatin infusion continue hydration 2400 ml/m^2/day (5DW, 0.9 NaCl) with all additions, but without the mannitol addition.
Start folinic acid half hour before starting 5-FU infusion; continue for a total of 6 doses every 6 hours
Dissolve 5FU 1000 mg/m^2 in NS 500 mg/10 ml, protect from light

Give over 24 hours as piggyback
Continue 5FU infusion same dose as continuous infusion over 5 days
Only if severe mucositis exists, then only give 4 days 5-FU

Substitute Mg 180 mg/m^2/day PO for the total duration of treatment
Keep input/output chart. If output <2/3 x input, then give mannitol 20% 40 ml/m^2 as bolus.

Criteria good general condition, ANC > 0.75, ptl > 100, normal creatinine

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

	DOSE	Cycle 1 DATE:	Cycle 2 DATE:	Response evaluation, UECs,Plan radiotherapy if indicated.	Cycle 3 DATE:	Cycle 4 DATE:	Cycle 5 DATE:
Cisplatinum 100 mg/m^2 6 hour infusion							
Folinic Acid 15 mg/m^2 PO every 6 hourly x 6 doses							
5-FU 1000 mg/m^2/day continuous infusion x 5 days (protect from light)							
Name							
Sign							
Next booking							
Response / Significant events							

FOLLOW UP.Irrespective of size of tumor, initially monthly X 3 months, three monthly for 3 months, then 6 monthly for 2 years, then yearly. Evaluate clinically, imaging if indicated.

KAPOSI'S SARCOMA

Kaposi's sarcoma (KS) was first described in 1872 by the Hungarian dermatologist, Moritz Kaposi. The skin lesions are typically painless, non pruritic, and often occur in a linear pattern. The skin lesions may progress from small, fleshy lesions to purplish nodules. KS was a rare tumor until the current HIV/AIDS epidemic.
The disseminated, fulminant form of KS associated with HIV disease is referred to as epidemic KS to distinguish it from the classic, African, and transplant-related varieties of the neoplasm.
HHV-8 was identified in KS tissue biopsies from virtually all patients KS but was absent from noninvolved tissue.
Paediatric Kaposi Sarcoma is relatively rare in the western world, only 2 % of all children with AIDS. In Eldoret several children are seen, all associated with presence of HIV.

Epidemic KS was first reported in 1981 in young homosexual or bisexual men. It is usually characterized by multifocal, widespread lesions at the onset of illness. These lesions may involve the skin, oral mucosa, lymph nodes, and visceral organs such as the gastrointestinal tract, lung, liver and spleen. Progression often proceeds in an orderly fashion from a few localized or widespread mucocutaneous lesions to more numerous lesions and generalized skin disease with lymph node, gastrointestinal tract disease, and other organ involvement. Pleuro-pulmonary KS is an ominous sign usually occurring late in the course of the disease.

STAGING.
The AIDS Clinical Trials Group (ACTG) Oncology Committee has published a staging system that incorporates measures of extent of disease, severity of immunodeficiency, and presence of systemic symptoms.
As shown below, the ACTG criteria categorizes the extent of the tumor as localized or disseminated, the CD4 cell number as high or low, and a systemic illness as absent or present.
Multivariate analysis showed that immune system impairment was the most important single predictor of survival. In patients with relatively high CD4 counts, tumor stage was predictive.

ACTG Staging	Good Risk (0)	Poor Risk (1)
Tumor (T)	Confined to skin and/or lymph nodes and/or minimal oral disease [*Note: Minimal oral disease is non-nodular KS confined to the palate.*]	Tumor-associated edema or ulceration
		Extensive oral KS
		Gastrointestinal KS
		KS in other non-nodal viscera
Immune system (I)	CD4 cells $\geq$ 200/microL - for paediatrics CD4 % $\geq$ 15 %	CD4 cells <200 per microlitre - for paediatrics CD4 % $\leq$ 15 %
Systemic illness (S)	No "B" symptoms (*unexplained fever, night sweats, >10% involuntary weight loss, or persistent diarrhea.)*	"B" symptoms present
	Performance status ≥70 (Karnofsky)	Performance status <70
		Other HIV-related illness (e.g., neurological disease or lymphoma)

TREATMENT
Good risk patients: HAART alone, consider chemotherapy after 2-6 month if progression of disease
Solitary lesions: local treatment as surgical excision, cryotherapy or intralesional Vincristine 0.25 - 0.5mg

Widespread skin disease or GI/Chest involvement needs HAART in combination with chemotherapy, preferably after at least 2 months of HAART. Only in life threatening disease chemotherapy can be started earlier.

DRUGS. Studies in epidemic KS have used the following drugs as single agents or in combinations: doxorubicin, bleomycin, vinblastine, vincristine, etoposide, paclitaxel, and docetaxel.
Good response and less toxicity is seen with pegylated liposomal doxorubicin or liposomal daunorubicin.
Also interferon alfas have been studied and show a 40% objective response rate.
There are very few studies published on treatment of children with Kaposi Sarcoma.
Other essential components of KS treatment include prophylaxis for opportunistic infections, improvement of nutritional status and rapid recognition and treatment of intercurrent infections.

KAPOSI'S SARCOMA MANAGEMENT

Patient Name……IP. No…….

HIV status……..Primary site……Stage…….

History Duration of symptoms, presence of fever, weight loss,

Physical exam Document size and site of skin problems, adjacent lymphnode areas and intra oral lesions

Investigations

Histology of tumor	Haemogram
Creatinine, or full U/E if indicated	ALT or full LFT if indicated
HIV serology confirmation	CD 4 counts and percentage
CXR	

Echocardiogram at baseline and after cumulative adriamycin dose of 250 mg/m^2

Treatment

The presence of KS qualifies the patient for anti-retroviral therapy.
If KS is life threatening, start chemotherapy immediately or preferably 2 weeks after start of ARV's.
If KS is not life threatening, but extensive or progressive, then start chemotherapy after 2 – 6 months.

Give courses with bleomycin and vincristine every **two** weeks for a total of 6 cycles. In case of inadequate response after three courses, add adriamycin every other course.
Criteria good general condition, ANC > 0.75, ptl > 100, normal creatinine

CHEMOTHERAPY **Ht** (**cm**) **Wt** (**kg**) **SA** (**m^2**)

	Cycle 1	Cycle 2	Cycle 3
Bleomycin15mg/m2			
Vincristine 2mg/m2			
Date			

If adequate respose continue with three more courses, if inadequate response add adriamycin to the regimen

	Cycle 4	Cycle 5	Cycle 6
Bleomycin 15mg/m2			
Vincristine 2mg/m2			
Adriamycin 50mg/m2 (only if response is inadequate after 3 cycles)		++++++++++++++++++	
date			

- Follow up monthly X 3 visits, three monthly x 3visits then 6monthly. Monitor the clinical, CD4 and viral load response to HAART treatment.

PROTOCOL FOR MANAGEMENT OF MEDULLOBLASTOMA

Name……IP No…….

Primary site…….. Stage……

After surgery, Patients should receive craniospinal irradiation of 36 Gy with a boost to the posterior fossa of 55.8 Gy . The radiotherapy should start preferably within 4 weeks of surgery and not later than than 7 weeks. The radiotherapy should last 6 weeks. The patient then proceeds for chemotherapy.

CHEMOTHERAPY

Chemotherapy consists of 8 cycles of 2 alternating regimes: A-B-A-B-A-B-A-B. every 21 days.

Course A:

Carboplatin (500mg/m2) IV over 1 hour in 5% dextrose

Etoposide (200mg/m2) IV over 2 hours

Vincristine (2.0 mg/m2, maximum dose 2.5 mg) IV push or 1-hour infusion

Course B:

Cyclophosphamide (1000 mg/m2) IV over 1 hour

Vincristine (2.0 mg/m2, maximum dose 2.5 mg) IV push or infusion

Cycle 1 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Carboplatin (500mg/m2 over 1 hour in 5% dextrose	Etoposide (200mg/m2) IV over 2 hours	Vincristine (2.0 mg/m2, max. 2.5mg)	Name/sign
Dose				
[redacted]				

Cycle 2 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Cyclophosphamide (1000 mg/m2)	Vincristine(2.0 mg/m2, max. 2.5mg)	Name/sign
Dose			
[redacted]			

Cycle 3 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Carboplatin (500mg/m2 over 1 hour in 5% Dextrose	Etoposide (200mg/m2) IV over 2 hours	Vincristine (2.0 mg/m2, max. 2.5mg)	Name/sign
Dose				
[redacted]				

Cycle 4 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Cyclophosphamide (1000 mg/m2)	Vincristine(2.0 mg/m2, max. 2.5mg)	Name/sign
Dose			
[redacted]			

Cycle 5 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Carboplatin (500mg/m2 over 1 hour in 5% dextrose	Etoposide (200mg/m2) IV over 2 hours	Vincristine (2.0 mg/m2, max. 2.5mg)	Name/sign
Dose				
[redacted]				

Cycle 6 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Cyclophosphamide (1000 mg/m2)	Vincristine(2.0 mg/m2, max. 2.5mg)	Name/sign
Dose			
[redacted]			

Cycle 7 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Carboplatin (500mg/m2 over 1 hour in 5% dextrose	Etoposide (200mg/m2) IV over 2 hours	Vincristine (2.0 mg/m2, max. 2.5mg)	Name/sign
Dose				
[redacted]				

Cycle 8 (duration 3 weeks)

Ht (cm) Wt (kg) SA (m^2)

Date:	Cyclophosphamide (1000 mg/m2)	Vincristine(2.0 mg/m2, max. 2.5mg)	Name/sign
Dose			
[redacted]			

PROTOCOL FOR MANAGEMENT OF LOW GRADE GLIOMA

Name……IP No……

Primary site……. Stage……

Surgery should be done upfront for all cases (may be total or not), but only if feasible.
Patients should then proceed to chemotherapy which consists of induction and consolidation phases. The entire treatment duration should be a maximum of 18 months. In case some courses are not given by this time due to treatment delays they should be omitted.
If there is relapse or disease progression repeat surgery should be done. Radiotherapy should only be used in case of inoperable disease.

INDUCTION PHASE

CHEMOTHERAPY **Ht (cm) Wt (kg) SA (m^2)**

Week	Date	Vincristine (2.0mg/m^2 max. 2.5mg) (0.07mg/kg if <10kg)	Carboplatin(550mg/m^2) (18.3 mg/kg if < 10kg)	Name/sign
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
13				
17				
21				

Do an MRI on week 24 to assess the response
MRI Findings
……
……
……

CONSOLIDATION PHASE

The consolidation phase consists of 10 cycles of 6 weeks each. This should be started as soon as the MRI has been done and at least 3 weeks after the last doses of the induction phase. If the MRI shows no improvement, consult with the Paediatric oncologist.
Some children develop allergy against carboplatin. In that case, alternating cycles of cisplatin with vincristine and cyclophosphamide with vincristine can be used.

Course 1(week 25. Ht (cm) Wt (kg) SA (m^2)

Date	Vincristine (2 mg/m^2 max. 2.5mg) (0.07mg/kg if <10kg)		Carboplatin 550mg/m^2 18.3 mg/kg if < 10kg)	Name/sign
	Day 1			
	Day 8			
	Day 15			

Course 2 (week 31). **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**

Date	Vincristine (2 mg/m² max. 2.5mg) (0.07mg/kg if <10kg)		Carboplatin 550mg/m² (18.3 mg/kg if < 10kg)	Name/sign
	Day 1			
	Day 8		[redacted]	
	Day 15			

Course 3 (week 37) **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**

Date	Vincristine (2 mg/m² max. 2.5mg) (0.07mg/kg if <10kg)		Carboplatin 550mg/m² (18.3 mg/kg if < 10kg)	Name/sign
	Day 1			
	Day 8		[redacted]	
	Day 15			

Course 4 (week 43) **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**

Date	Vincristine (2 mg/m² max. 2.5mg) (0.07mg/kg if <10kg)		Carboplatin 550mg/m² (18.3 mg/kg if < 10kg)	Name/sign
	Day 1			
	Day 8		[redacted]	
	Day 15			

Course 5 (week 49) **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**

Date	Vincristine (2 mg/m² max. 2.5mg) (0.07mg/kg if <10kg)		Carboplatin 550mg/m² (18.3 mg/kg if < 10kg)	Name/sign
	Day 1			
	Day 8		[redacted]	
	Day 15			

Course 6 (week 55) **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**

Date	Vincristine (2 mg/m² max. 2.5mg) (0.07mg/kg if <10kg)		Carboplatin 550mg/m² (18.3 mg/kg if < 10kg)	Name/sign
	Day 1			
	Day 8		[redacted]	
	Day 15			

Course 7 (week 61) **Ht** (**cm**) **Wt** (**kg**) **SA** (**m²**

Date	Vincristine (2 mg/m² max. 2.5mg) (0.07mg/kg if <10kg)		Carboplatin 550mg/m² (18.3 mg/kg if < 10kg)	Name/sign
	Day 1			
	Day 8		[redacted]	
	Day 15			