Ministry of National Health
Services Regulations & Coordination
GOVERNMENT OF PAKISTAN

World Health Organization

FACILITATOR'S MANUAL

EARLY DETECTION OF CHILDHOOD CANCER

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Facilitator's Manual

Early Detection of Childhood Cancer

World Health Organization

Special Acknowledgment

to the

Technical Partners

Message from Ministry of National Health Services, Regulation and Coordination (M/ONHSR&C)

It brings me great pleasure to share this training manual with our stakeholders from various government and private sectors and healthcare professionals involved in dealing with childhood cancers.

Children are the building blocks of a nation. Prioritizing their health will have overall positive impact in shaping the future of the nation. Over 7000 to 8000 children are diagnosed each year with cancers causing significant emotional and financial burden to the family.

Health care providers at primary health care level are the children´s first opportunity for correctly recognizing and responding to early signs and symptoms of childhood cancers by appropriately referring them to tertiary care hospitals. Insufficient knowledge about the warning signs and symptoms of pediatric cancer usually leads to improper diagnosis or delay to diagnose and hence loss of many precious lives of these children. Childhood cancers are curable when detected and treated early, there is a need to build strong partnerships with private and public sectors to address the challenge of late presentation of such cases at the hospital.

This manual is one of the essential steps towards improving capacity building in line with the vision of Government of Pakistan and WHO Global Initiative for childhood cancers. I have witnessed the thorough efforts in developing this manual and I am confident that it gives an excellent insight to pick up the red flags for childhood cancers at primary health care level leading to early detection and prompt referral hence improve survival.

Our mission is to equip healthcare professionals with the expertise and training necessary to identify childhood cancer at its earliest stages, when treatment is most effective. Through collaborative efforts, we aim to decrease cancer-related illnesses and deaths, and enhance the quality of life for children and families impacted by cancer.

I would thank World Health Organization for always being there to support member states at global, regional and country level.

At the federal level, we commit to supporting provinces and regions in their efforts, to train healthcare professionals and enhance the detection and care of childhood cancer.

Mr. Nadeem Mahbub
Federal Secretory Health,
Ministry of NHSR&C,
Government of Pakistan.

Message from World Health Organization

Each year, an estimated 400,000 children are diagnosed with cancer around the world. The vast majority of these children live in low- and middle-income countries. There is a huge survival gap as compared to high income countries due to lack of access, financial constraints or poor quality of treatment.

A child's survival should not depend on where he or she lives and to address this profound inequity, World Health Organization (WHO) and St. Jude Children's Research Hospital launched the WHO Global Initiative for Childhood Cancer in 2018. The Initiative brings together partners and stakeholders across sectors towards a shared goal of improving health and wellbeing for children with cancer using the CureAll framework as a shared operational approach.

By 2030, the Initiative aims to achieve at least 60% survival for childhood cancer globally and reduce suffering for all. It requires a specialized workforce, complex multidisciplinary care and advocacy. Capacity building is one of the crucial steps and this manual on early detection of childhood cancers will provide a guide to equip healthcare professionals with basic knowledge of childhood cancers enabling early detection and prompt referral to get definitive treatment.

The goal to achieve universal health coverage based on primary health care means that governments, health systems, communities, and all other stakeholders must work together to address the underlying inequalities. The Ministry of National Health Services, Regulations, and Coordination (M/NHSR&C) has collaborated with the WHO Pakistan to undertake a comprehensive effort to improve childhood cancer care, and the development of this manual is a significant milestone in this endeavor.

I appreciate the efforts of Pakistan Society of Pediatric Oncology and Pakistan Pediatric Association in their endless support in achieving our objectives and development of this manual.

Every step helps us getting closer to our goal of increasing equitable access to health, advancing quality of care and saving lives of children suffering from cancers and I believe together we can make this dream come true.

Dr. Dapeng Lou
WHO Representative and Head of Mission in Pakistan,
WHO Islamabad.

Acknowledgements

Ministry of National Health Services Regulation and Coordination (M/ONHSR&C) acknowledges the candid contributions of different stakeholders from health and other related sectors who sincerely participated in development of this manual, whether in individual meeting, focused group discussions, consultation workshops or feedback on different steps.

We extend our sincere appreciation to Dr. Maryam Sarfaraz, Director Program, and Mr. Naeem Akhtar, Deputy Director Program, from M/NHSR&C for their invaluable guidance and unwavering support throughout this endeavor.

In particular we acknowledge the contributions of Brig. Tariq Ghafoor, Dr. Asim Belgaumi, Dr. Alia Ahmed and Dr. Rabia Wali from Pakistan Society of Pediatric Oncology (PSPO) who served as facilitators in National Training of Trainers Workshop to pilot the training manual.

We appreciate very much the technical and financial support of WHO team at Country, Regional and HQ Offices. In particular we acknowledge the persuasion and guidance provided by Dr. Lamia Mahmood, Regional advisor, cancer prevention and control, WHO Eastern Mediterranean Regional Office (EMRO), Dr. Giuseppe Troisi, Technical officer cancer control, WHO EMRO, Ms Ellen Thom, Team lead Healthy Population Through Life Course Cluster and Dr. Qudsia Uzma, Technical Officer RMNCAH at WHO country office Pakistan.

We greatly appreciate efforts and technical support provided by Dr. Sumbal Saeed, Consultant childhood cancer prevention, WHO, Pakistan in the process of development of the manual. We also acknowledge Dr. Shumaila Ihtesham, consultant WHO, for her support in drafting and editing the training manual.

Meaningful contributions and support by Dr.Khalid Shafi, General secretory Pakistan Pediatric Association and all healthcare professionals are acknowledged in finalization of this manual.

This manual represents a pivotal moment in our efforts to improve the lives of children with cancer, and we assure our stakeholders that it will serve as a catalyst for positive change, shaping the future of childhood cancer care.

Table of Contents

AGENDA

Training of Trainers (TOT)

EARLY DETECTION OF CHILDHOOD CANCER

Timing	Activity	Facilitator
08:00-08:30	Registration of the participants	
08:30-09:00	Recitation from Holy Quran & introduction Introduction of participants Pre-test	TBD
09:00-09:40	Welcome & Objectives	
09:40-09:50	Remarks by PPA	
09:50-10:00	Keynote address	
10:00-10:30	Introduction to childhood cancer Childhood cancer in Pakistan	
10:30-10:45	Most frequent cancers in children	
10:45-11:15	How to assess the possibility of cancer	
11.15-11:30	TEA BREAK	
11:30-12:00	How to classify the possibility of cancer	
12:00-12:30	How to manage the child with possible cancer	
12:30-13:00	The child with a cancer diagnosis seen at the first level of care	
13:00-14:00	LUNCH	
14:00-14:30	Childhood Leukaemia	
14:30-15:00	Childhood Brain Tumors	
15:00-15:30	Lymphoma	
15:30-15:45	TEA BREAK	
15:45-16:15	Solid Tumors	
16:15-16:30	Post Test	
16:30-17:00	Concluding Remarks Vote of Thanks Certificates Distribution	

The Pre and Post Test Questionnaire for TOT Workshop Paediatric Oncology

1. Each year, how many children are diagnosed with cancer world over?
    a) 200,000
    b) 400,000
    c) 600,000
    d) 800,000
    e) 1000,000
2. Each year, how many children are diagnosed with cancer in Pakistan?
    a) 5,000
    b) 7,500
    c) 20,000
    d) 30,000
    e) 40,000
3. Survival of childhood cancer in the developed countries is.
    a) Less than 40%
    b) Less than 50%
    c) Less than 60%
    d) More than 60%
    e) More than 80%
4. The most common leukaemia of childhood is.
    a) Acute lymphoblastic leukaemia
    b) Acute myeloid leukaemia
    c) Chronic lymphoblastic leukaemia
    d) Chronic myeloid leukaemia
    e) Juvenile Myelomonocytic Leukaemia
5. WHO Global Initiative for Childhood Cancer (GICC) aims to improve outcomes for children with cancer around the world and achieve at least a survival of.
    a) 60 % by 2030.
    b) 70 % by 2030.
    c) 80 % by 2030.
    d) 90 % by 2030.
    e) 100 % by 2030.
6. Features concerning for malignancy in Lymphadenopathy.
    a) Localized adenopathy
    b) Generalised adenopathy
    c) Cervical and inguinal lymphadenopathy
    d) Size < 1 m
    e) Tenderness
7. The appropriate management of fever in a child with cancer is.
    a) Intravenous Antibiotic
    b) Oral Antibiotic
    c) Oral Paracetamol

d) Cold Sponging
e) Reassurance of the family

8. The classic triad of tumour lysis syndrome in
    a) hyperuricemia, hypophosphatemia, and hypercalcaemia.
    b) hyperuricemia, hyperphosphatemia, and hypercalcaemia.
    c) hyperuricemia, hypercalcaemia, and hyperkalaemia.
    d) hyperuricemia, hyperphosphatemia, and hyperkalaemia.
    e) hyperuricemia, hypocalcaemia, and hyperkalaemia.
9. The following is the good risk feature of acute lymphoblastic leukaemia.
    a) Male gender
    b) High white cell counts at presentation.
    c) Age below one year and above 10 years
    d) Pre-B ALL
    e) Overt CNS leukaemia
10. T-ALL is most frequently associated with.
    a) A superior outcome compared with those with B-precursor cell ALL.
    b) Low leukocyte counts at presentation.
    c) Overt CNS leukaemia
    d) Usually seen in girls
    e) Younger age at diagnosis
11. Following is true regarding CNS directed therapy in ALL.
    a) CNS therapy is required for CNS leukaemia only.
    b) Cranial radiation is the method of choice in children.
    c) Intrathecal medication can result in long term neurological complications.
    d) Methotrexate is the most used intrathecal medication.
    e) Vincristine can be used as intrathecal medicine.
12. Allopurinol is used most to manage what in acute leukaemia of childhood?
    a) To induce remission
    b) To maintain remission
    c) To help alkalinize the urine.
    d) To prevent vomiting from chemotherapy
    e) To prevent hyperuricemia associated with tumor lysis syndrome.
13. Which is the most common brain tumour?
    a) Astrocytoma
    b) Brain stem glioma
    c) Ependymoma
    d) Craniopharyngioma
    e) Medulloblastoma
14. What is the preferred treatment of low-grade glioma (LGG)?
    a) Grass total resection
    b) Radiotherapy
    c) Chemotherapy
    d) Observation, as LGG can resolve with time.
    e) High dose dexamethasone

15. What are the bad prognostic factors of Hodgkin lymphoma.
    a) Delay in starting treatment for more than one year,
    b) Use of anti-tuberculosis treatment,
    c) Malnutrition,
    d) Presence of B symptoms
    e) All of the above
16. Common symptoms of Non-Hodgkin lymphoma include
    a) Lymphadenopathy
    b) Abdominal swelling /pain, constipation, or urinary retention
    c) B Symptoms (Fever, Weight loss, Night sweats)
    d) All of the above
17. The main stay of treatment of non-Hodgkin lymphoma is.
    a) Surgery
    b) Radiation therapy
    c) Combination chemotherapy
    d) Autologous bone marrow transplant
    e) Surgery followed by chemotherapy.
18. Following is true about Wilms tumour (WT).
    a) WT is the most common paediatric renal tumour.
    b) Can be cured with surgery alone.
    c) Can be cured with chemotherapy alone.
    d) Typically found in children older than 10 years
    e) Has a bad prognosis
19. The Most common Malignant Abdominal Mass in infants is
    a) Burkitt's lymphoma
    b) Neuroblastoma
    c) Wilms Tumor
    d) Hepatoblastoma
    e) All of the above
20. The Horner syndrome is associated with which tumour.
    a) Burkitt's lymphoma
    b) Hepatoblastoma
    c) Neuroblastoma
    d) Rhabdomyosarcoma
    e) Wilms Tumor

Introduction Of the Training

GOAL AND OBJECTIVES

GOAL

To improve early detection and referral of patients suffering from childhood cancers at Primary & Secondary Healthcare Facilities in Pakistan.

OBJECTIVES

- To build capacity among primary healthcare service providers to recognise early signs and symptoms of childhood cancers and appropriately refer relevant cases; and
- To establish a referral network between PHC and paediatric oncologists at tertiary care facilities to streamline learning opportunities and referral pathways.

LEVEL AND DURATION OF TRAINING

- Training of Trainers (TOT) at Primary & Secondary Healthcare Facilities in Pakistan.
- Step-down training. Duration of training is one day.

FACILITATORS & PARTICIPANTS

- Facilitators are paediatric oncologists and/ or FCPS qualified Paediatricians.
- Participants are Paediatricians of Primary and Secondary Healthcare Facilities in Pakistan

MATERIALS

- Agenda
- Flip Chart
- File
- Markers (Blue, Black and Red)
- Multimedia
- Laptop
- Attendance sheet
- Notebook / blank papers
- Ball point
- Printed Manual
- Pre- and Post-Course Knowledge Check Questionnaire
- Prints of Course evaluation Form

KEY SOURCES

Following sources have been followed in preparation of this module:

- WHO Guidelines
- Presentations
- Early Diagnosis of Childhood Cancer. Washington, DC: PAHO, 2014
- Other literature – provided in footnotes at relevant places.

Instructions for facilitators

Familiarity with Course Material

As a facilitator, you need to be very familiar with the material being taught. It is important that facilitators and Master Trainers go through and develop and understanding of the course material, its contents including the materials thereof referred in the main content.

Facilitation Techniques

As a facilitator and master trainer, it is your job to give explanations, do demonstrations, answer questions, talk with participants about, their answers to exercises, conduct role plays, lead group discussions, organize and supervise practice sessions. The use of mix of techniques are helpful in keeping the participants engaged.

Supporting Participants

As a facilitator and/or lead trainer you are required to give participants any help they need to successfully complete the course. This help may be required for understanding the group work, compiling information, clarity of questions etc.

Avoid Formal Lectures

You are not expected to teach the content of the course through formal lectures. (Nor is this a good idea, even if this is the teaching method to which you are most accustomed). Plan the use of different facilitation techniques beforehand and practice those during different sessions.

Keep All Participants Involved in Discussions

Be always available to the participants. Frequently ask questions of participants to check their understanding and to keep them actively thinking and participating. Questions that begin with "what," "why, " or "how" require more than just a few words to answer. Avoid questions that can be answered with a simple "yes" or "no" as these tend to limit discussion and may not encourage active participation.

To ensure active participation and encourage contributions from all participants, follow these guidelines:

- Give Participants Time to Respond:
  After posing a question, allow a brief pause to give participants time to formulate their thoughts and volunteer a response.
- Avoid Answering Your Own Questions:
  Refrain from immediately answering your own question if no one responds. Instead, consider rephrasing the question to prompt engagement. However, avoid repetitive rephrasing as some silence can be productive.
- Acknowledge and Value Responses:
  Acknowledge all participants' responses with a comment, a "thank you," or a nod. This recognition fosters a sense of value and encourages continued participation.
- Address Misunderstandings Diplomatically:
  If you believe a participant has misunderstood the question or missed the point, diplomatically ask for clarification, or invite other participants to share their perspectives. Avoid ridiculing or ignoring contributions to maintain a supportive atmosphere.

Answer participants' questions willingly and encourage participants to ask questions when they have them rather than to hold the questions until a later time.

Do not feel compelled to answer every question yourself. Depending on the situation, you may turn the question back to the participant or invite other participants to respond. You may need to discuss the question with the Course Director or another facilitator before answering. Be prepared to say, "I don't know but I'll try to find out ".

Use names when you call on participants to speak, and when you give them credit or thanks. Use the speaker's name when you refer to a previous comment.

Always maintain eye contact with the participants so everyone feels included. Be careful not to always look at the same participants. Looking at a participant for a few seconds will often prompt a reply, even from a shy participant.

KEEP THE SESSION FOCUSED AND LIVELY

Keep your presentations lively:

- Present information conversationally rather than read it,
- Speak clearly. Vary the pitch and speed of your voice.
- Use examples from your own experience and ask participants for examples from their experience.

Write key ideas on a flipchart as they are offered. (This is a good way to acknowledge responses. The speaker will know that the suggestion has been heard and will appreciate having it recorded for the entire group to see.)

When recording ideas on a flipchart, use the participant's own words if possible. If you must be briefer, paraphrase the idea and check it with the participant before writing it. You want to be sure the participant feels you understood and recorded the idea accurately.

DO NOT TURN YOUR BACK TO THE GROUP FOR LONG PERIODS AS YOU WRITE

At the beginning of a discussion, write the main question on the flipchart. This will help participants stay on the subject. When needed, walk to the flipchart, and point to the question.

Paraphrase and summarize frequently to keep participants focused. Ask participants for clarification of statements as needed. Also, encourage other participants to ask a speaker to repeat or clarify the statement.

Restate the original question to the group to get them focused on the main issue again. If you feel someone will resist getting back on track, first pause to get the group's attention, tell them they have gone astray, and then restate the original question.

Do not let several participants talk at once. When this occurs, stop the talkers, and assign an order for speaking. (For example, say "Let's hear Dr. Samina's comment first, then Dr. Farhan's, then Dr. Ayesha's ") People usually will not interrupt if they know they will have a turn to talk.

Thank participants whose comments are brief and to the point.

Try to encourage quieter participants to talk. Ask to hear from a participant in the group who has not spoken before or walk toward someone to focus attention on him/her and make him/her feel he/she is being asked to talk.

MANAGE ANY PROBLEMS

- Some participants may talk too much.
- Here are some suggestions on how to handle an overly talkative participant:
- Do not call on this person first after asking a question.
- After a participant has gone on for some time say, "You have had an opportunity to express your views. Let's hear what some of the other participants have to say on this point. " Then rephrase the question and invite other participants to respond, or call on someone else immediately by saying, "Dr. Samina, you had your hand up a few minutes ago".
- When the participant pauses, break in quickly and ask to hear from another member of the group or ask a question of the group, such as, "What do the rest of you think about this point? "
- Record the participant's main idea on the flipchart. As he/she continues to talk about the idea, point to it on the flipchart and say, "Thank you, we have already covered your suggestion. Then ask the group for another idea.
- Do not ask the talkative participant any more questions. If he/she answers all the questions directed to the group, ask for an answer from another individual specifically or from a specific subgroup. (For example, ask, "Does anyone on this side of the table have an idea?")

HOW TO REINFORCE & REASSESS A WEAK PARTICIPANT

Try to identify participants who have difficulty understanding or speaking the course language. Speak slowly and distinctly so you can be more easily understood and encourage and support the participants' communication efforts.

Discuss with the Course Director/Organizer any language problems which seriously impair the ability of a participant to understand the written material or the discussions. It may be possible to arrange help for the participant.

Discuss disruptive participants with your co-facilitator or with the Course Director. (The Course Director may be able to discuss matters privately with the disruptive individual.)

REINFORCE PARTICIPANTS EFFORTS

- Appearing interested, say "That's a good question/suggestion."
- Reinforce participants who:
    - Try hard.
    - Ask for an explanation of a confusing point.
    - Do a good job on an exercise.
    - Participate in group discussions.
    - Help other participants (without distracting them by talking at length about irrelevant matters).

INTERACTION WITH PARTICIPANTS/BEHAVIOUR

Compliment the participants on their correct answers, improvements, or progress.

Make sure that there are no major obstacles to learning (such as too much noise or not enough light).

Plan and ensure that all necessary supplies are obtained prior to each day, so that they are readily available in the classroom or training site when needed.

Monitor the progress of each participant throughout the course.

Show enthusiasm for the topics covered in the course and for the work that the participants are doing.

Be attentive to each participant's questions and needs. Encourage the participants to come to you at any time with questions or comments. Be available during scheduled times.

Watch the participants as they work and offer individual help if you see a participant looking troubled, staring into space, not engaging or busy with their mobile phones. These are clues that the participant may need help.

Promote a friendly, cooperative relationship. Respond positively to questions (by saying, for example, "Yes, I see what you mean," or "That is a good question"). Listen to the questions and try to address the participant's concerns, rather than rapidly giving the "correct" answer.

During time scheduled for course activities, do not work on other projects, or discuss matters not related to the course.

In discussions with participants, avoid using facial expressions or making comments that could cause participants to feel embarrassed.

Avoid being too much of a showman. Enthusiasm (and keeping the participants awake) is great, but learning is most important. Keep watching to ensure that participants understand the materials. Difficult points may require you to slow down and work carefully with individuals.

Do not be condescending. In other words, do not treat participants as if they are children. They are adults.

Do not talk too much. Encourage the participants to talk.

Do not be shy, nervous, or worried about what to say. Following facilitator guidance will help you remember what to say.

Session 1: Introduction and pretest

DURATION OF SESSION

- 08:30 – 9:45am

LEARNING TARGETS/OBJECTIVES

- After completing this session participants will learn about the incidence of childhood cancer globally and in Pakistan, the WHO GICC (Global Initiative for Childhood Cancer) and **CureAll** technical framework.

PRE TEST

- 08:50 – 9:00 am

KEY POINTS

WHAT IS CHILDHOOD CANCER

- Children are diagnosed with many different forms of cancer. There are ***12 major types of cancer*** that can affect various parts of the body including the blood, bones, brain, muscles, liver, kidney, and eyes. The ***six index cancers of the WHO Global Initiative for Childhood Cancer*** are ***Acute Lymphoblastic Leukaemia*** (ALL), ***Hodgkin's Lymphoma*** (HL), ***Burkitt's Lymphoma*** (BL), ***Retinoblastoma*** (RB), ***Low-Grade Glioma*** (LGG), and ***Wilms Tumour*** (WT).
- Common adult cancers (Lung, breast, colon etc) are rarely seen in children.
- Of the estimated 400,000 children diagnosed with cancer each year, most live in low- and middle-income countries, where access to treatment is frequently limited or unaffordable.
- Only about 20–30% of those children survive, compared to more than 80% in high-income countries.

Globally, **acute lymphoblastic leukaemia** is the most common childhood cancer and is estimated to account for 19% of total childhood cancer incidence, followed by **non-Hodgkin lymphoma** (5%), **nephroblastoma** (5%), **Burkitt lymphoma** (5%) and **retinoblastoma** (5%).

In many countries, cancer is the second leading cause of death in children over 1 year of age, exceeded only by accidents. Annual incidence of all malignant tumours is 12.45 per 100,000 children under 15 years.

In this regard, given the complexity of current therapies, children with cancer should be referred as early as possible to facilities that have specialized human and technical resources, and where they can be treated by people trained in paediatric haematology/ oncology. The purpose of this manual is to help primary care personnel identify children with cancer, to enable timely referral and to "GIVE CHILDREN WITH CANCER A CHANCE FOR A CURE.

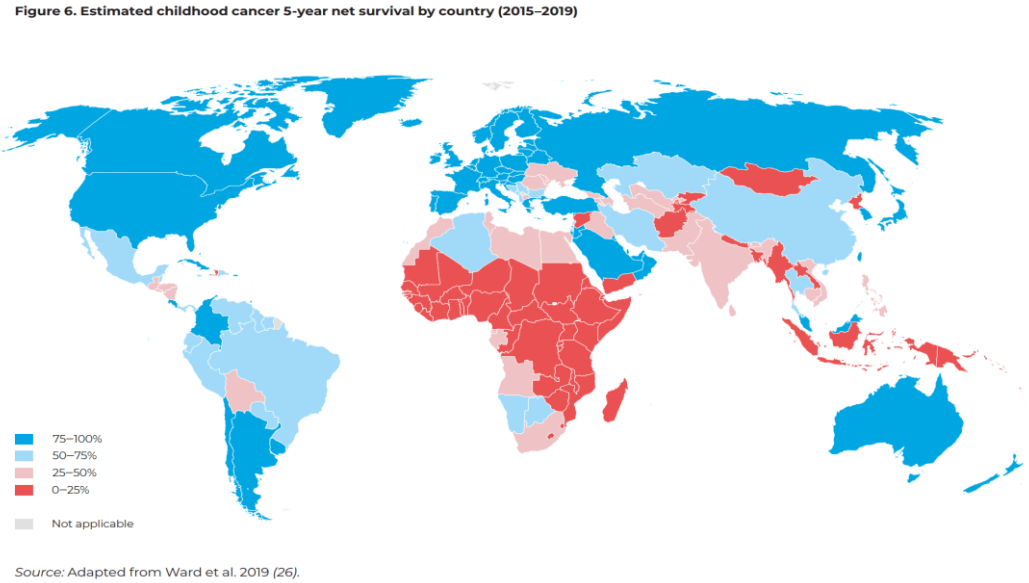
There is scarcity of data about the incidence and prevalence of childhood cancers in Pakistan. Previously there were only two cancer registries located in Karachi and Lahore cities and recently (in 2015) a National Cancer Registry has been established in Pakistan Health Research Council (PHRC) Islamabad[1],[2]. About 7000 to 7500 children get cancer every year in Pakistan[3] and childhood cancer

[1] Pakistan Health Research Council. Cancer Registry (2018). Available at http://phrc.org.pk/cancer-registry.html (accessed on 22-09-2018).
[2] Yusuf A. (2013). Cancer Care in Pakistan. Jpn J Clin Oncol, 43(8)771–775. [PubMed] [Google Scholar]
[3] DAWN News, Pakistan (2020). https://www.dawn.com/news/1464231 (accessed on 09-07-2020).

accounted for 10% of all reported cancers in 2017. Leukaemia (31%) and lymphomas (20%) are the major childhood cancers as per Karachi cancer registry Pakistan. Punjab cancer registry data showed that lymphomas (31%) are relatively higher in prevalence than leukaemia (23%)[4]. With respect to treatment, in Pakistan, almost half of children with cancer have no access to treatment whereas a large number were unable to complete their treatment. While the survival rate in childhood cancers is relatively high and approximately 80% of the patients in western countries receive curative treatment Pakistan has low cancer survival rate[5]. In Pakistan, while no data is available, the trend shows that only 20%-30% are cured, owing mainly to treatment delays and misdiagnosis[6].

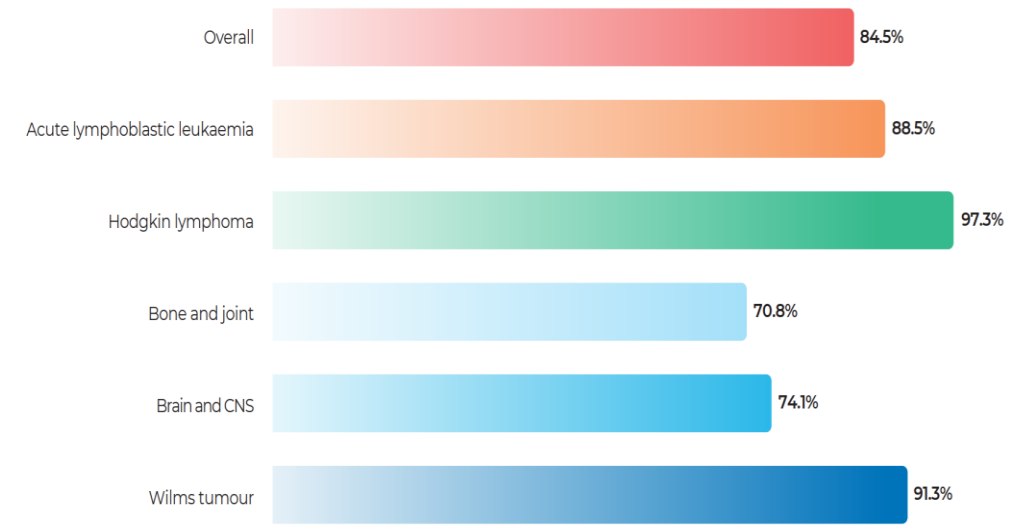
INEQUITIES IN OUTCOMES

CHILDHOOD CANCER 5-YEAR SURVIVAL



[4] Cancer Registry Report. Shaukat Khanum Memorial Cancer Hospital and Research Center, Pakistan (2017). http://shaukatkhanum.org.pk/wp-content/uploads/2018/08/acrr-2017.pdf (accessed on 22-09-2018).
[5] https://www.dawn.com/news/1464231
[6] https://hospitals.aku.edu/pakistan/AboutUs/News/Pages/Childhood-Cancer-Day-2022.aspx

5-YEAR SURVIVAL RATE FOR CHILDHOOD CANCERS IN THE UNITED STATES



CNS: central nervous system
Source: Noone et al. 2018 *(27)*.

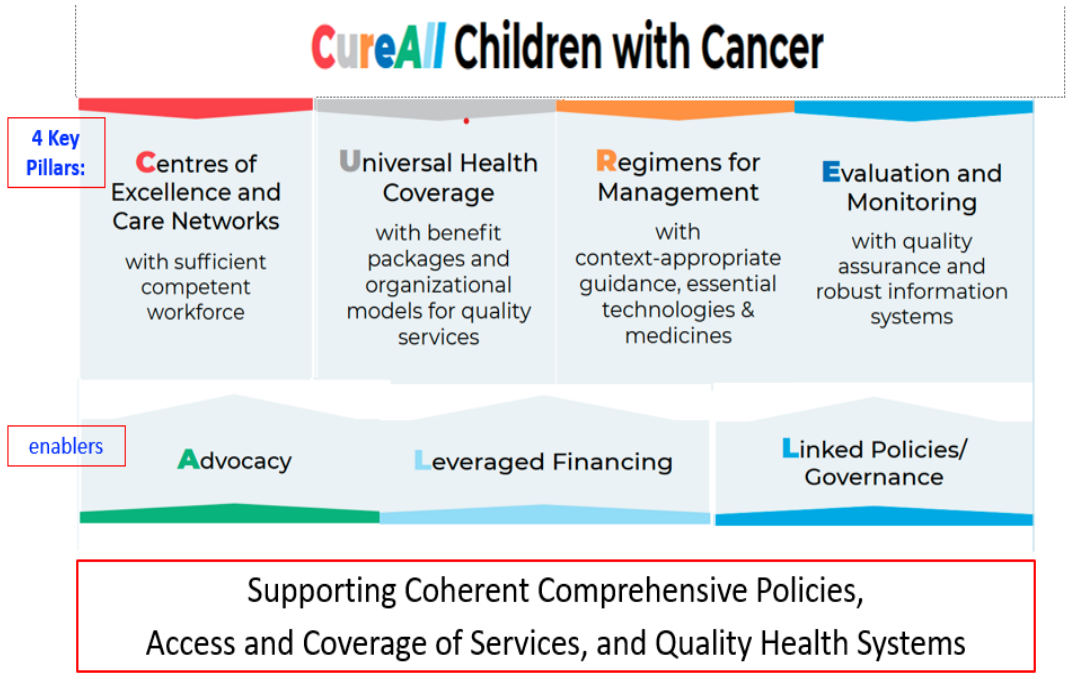
WHO GICC

The World Health Organization (**WHO**) Global Initiative for Childhood Cancer (**GICC**) aims to improve outcomes for children with cancer around the world.

The goal is to give all children with cancer **the best chance to survive,** to live full and abundant lives and to live and die without suffering.

CURE ALL CHILDREN WITH CANCER

- ***CUREALL*** *IS AN ACRONYM USED TO IDENTIFY THE* ***FOUR KEY PILLARS*** *AND* ***THREE ENABLERS*** *OF THE GLOBAL INITIATIVE*



Pillars

- ***Centres of excellence & care networks*** with enough trained workers to deliver services.
- **Universal health coverage** for comprehensive and essential quality services.
- **Regimens and roadmaps for diagnosis and treatment**. These tailored plans will aid delivery of quality services through evidence-based technologies and medicines.
- **Evaluation and monitoring**. Robust information systems and research will ensure effective implementation, quality assurance and constant improvement.

Cross-cutting enablers:

- **Advocacy**; Generates political will and advances implementation.
- **Leveraged financing**; Ensures families do not suffer financial hardship, in line with universal health coverage.
- **Linked governance**; Optimize coordination and accountability for collective impact.

If the time between appearance of the first signs or symptoms and referral to an oncology centre for confirmation of a cancer diagnosis is to be shortened, greater emphasis must be placed on enhancing human resources, including **undergraduate and graduate medical and nursing education, as well as primary care staff training.** This will enable them to effectively identify the early signs of cancer. The purpose of this specific module is to contribute towards this goal for **the Integrated Management of Childhood Illness (IMCI).**

SIX COMMON, CANCERS FOR THE GLOBAL INITIATIVE

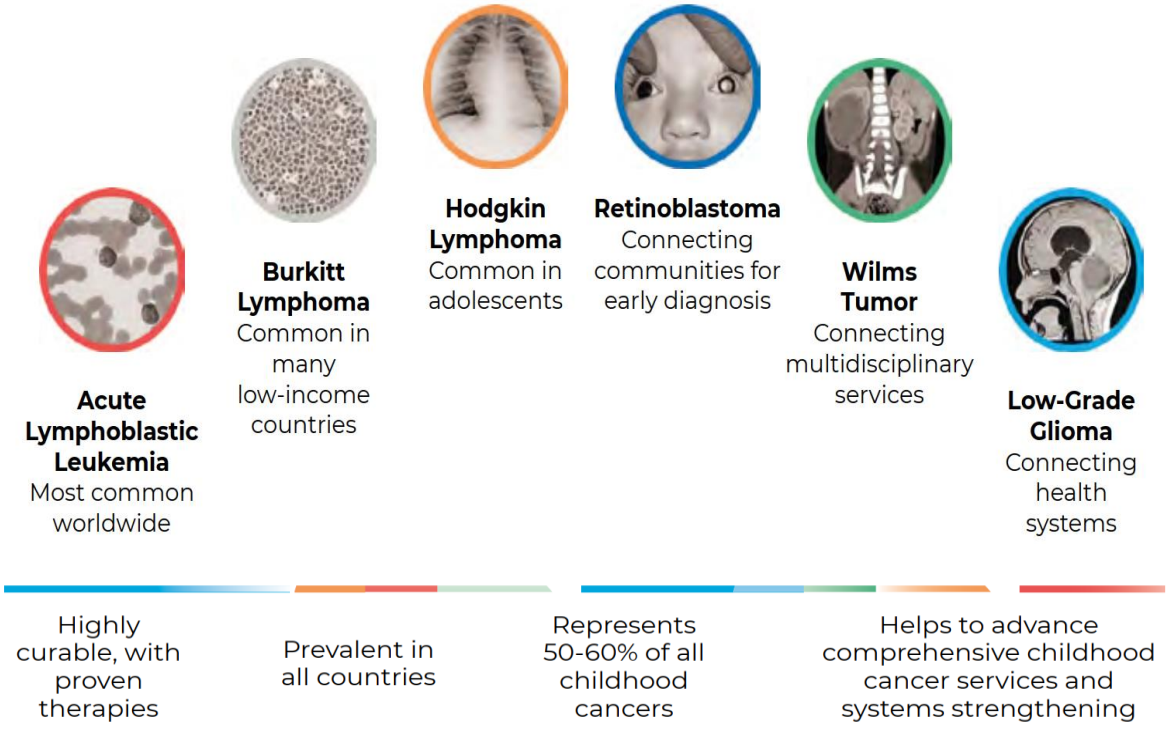


TABLE 1:DIFFERENCE BETWEEN PAEDIATRIC AND ADULT CANCERS

Parameter	Children	Adult
Site	Tissue	Organ
Status at Diagnosis	80% Disseminated	Local or Regional
Early Detection	Usually, accidental	Improves with education and screening
Screening	Difficult	Adequate
Response	Most respond to chemotherapy	Lower response to chemotherapy
Prevention	Unlikely	80 % Preventable

Session 2: Most Frequent Cancers in Children

SESSION DURATION

- 09:45 am-10:45 am (60 mins)

LEARNING TARGETS/OBJECTIVES

- After completing this session, participants will have learned about most frequent childhood cancers and their common presenting signs and symptoms.

KEY POINTS

Most frequent cancers in childhood by age groups are:

- < 5 years
  - Leukaemia
  - Neuroblastoma
  - Wilms's tumour
  - Testicular tumours (yolk sac)
  - Retinoblastoma
- 5 – 10 Years age
  - Leukaemia
  - Non – Hodgkin's Lymphoma
  - Hodgkin's Lymphoma
  - Tumours of the CNS
  - Soft tissue sarcoma
- > 10 Years age
  - Leukaemia
  - Non – Hodgkin's Lymphoma
  - Hodgkin's Lymphoma
  - Tumours of the CNS
  - Germ cell tumours (ovarian, extragonadal GCT)

TABLE 2: MOST FREQUENT CANCERS IN CHILDREN, BY AGE GROUP

Most Frequent Cancers		
< 5 years	**5 – 10 years**	**> 10 years**
Leukaemia	Leukaemia	Leukaemia
Neuroblastoma	Non-Hodgkin's Lymphoma	Non-Hodgkin's Lymphoma
Wilms tumour	Hodgkin's Lymphoma	Hodgkin's Lymphoma
Testicular tumours (yolk sac)	Tumours of CNS	Tumours of CNS
Retinoblastoma	Soft Tissue Sarcoma	Germ Cell Tumours (ovarian, extragonadal)

Most Frequent Cancers in children

1. *LEUKAEMIA*

This is a group of malignant diseases that cause an uncontrolled increase of white blood cells in bone marrow. It is **the most common cancer in children** and the cure rate is around 90%. Symptoms are nonspecific, such as fatigue, loss of appetite, bone pain (often the only symptom), and night sweats. The most frequent signs are low-grade fever lasting for days or weeks (average of two or three weeks), pallor, petechiae, ecchymoses, signs of bleeding, hepatosplenomegaly, lymphadenopathy, and infiltration of other organs (testis, central nervous system, or kidneys). Weight loss is rare. Leukaemia has a characteristic **triad of fever, anaemia, and bleeding**. Definitive diagnosis is made by bone marrow aspiration and immunophenotyping.

2. *TUMOURS OF THE CENTRAL NERVOUS SYSTEM*

These are solid tumours of the cranial cavity; they are more frequent in early childhood, appearing primarily from 5 to 10 years of age and declining after puberty.

Symptoms range from nonspecific to focal neurological symptoms, depending on the tumour's location in the cranial cavity. The most frequent symptom is ***headache***, which at first is generalized and intermittent, increasing in intensity and frequency over time. Headache is usually accompanied by nausea, vomiting, and visual or auditory disturbances, etc. The classic **triad** of symptoms is ***headache, nausea, and vomiting*** secondary to intracranial hypertension. The headache wakens the child at night and is more intense in the morning, improving during the day with vertical position. Projectile vomiting sometimes occurs, not preceded by nausea.

Other symptoms may occur, such as ***altered mental status***, personality changes, or sudden changes in mood or behaviour (periods of irritability alternating with lethargy), which also tend to lead to a notable decline in school performance. Convulsions may occur.

Another frequent symptom is ***visual disturbances***, such as double vision, abnormal eye movements, or decreased visual acuity. Optic nerve glioma may present with progressive blindness of one eye.

Infants may display ***irritability*** from increased intracranial pressure, anorexia, vomiting, weight loss or poor weight gain, regression in development, increase in head circumference, or separation of sutures. The anterior fontanelle may bulge or feel tense.

3. *LYMPHOMAS*

This group of diseases of the lymphatic system are fast growing and are called solid haematological tumours to differentiate them from leukaemia. They are **the third most common of child cancers**, following leukaemia and brain tumours. Symptoms are nonspecific, such as fatigue and loss of appetite, and, depending on location, other varying symptoms due to the mass effect. ***Thoracic lymphomas*** present as mediastinal masses with or without pleural effusion and may be accompanied by difficult breathing and superior vena cava compression. ***Abdominal lymphomas*** present with abdominal distention, pain, and masses, usually in the lower right quadrant.

Lymphoma can also present in the skin, central nervous system, the face, bones, and other organs as a lump in the affected area. Other signs include low-grade fever, anaemia, weight loss, and drenching night sweats. ***Hodgkin's lymphoma's*** clinical presentation is often asymptomatic cervical or supraclavicular lymphadenopathy.

4. WILMS TUMOUR

This is a malignant neoplasm of the kidney cells, which can affect one or both kidneys. It is the most common kidney cancer in young children, with greatest frequency among 2- and 3-year-olds. It may be associated with congenital malformations.

The typical clinical manifestation is a **palpable asymptomatic abdominal mass**, which may be detected by the parents or physician during routine examination. It may be accompanied by **pain, haematuria, & hypertension**. Other less frequent signs include **anaemia, fever, and constipation**.

5. NEUROBLASTOMA

This is an extracranial malignant solid tumour of nerve tissue. It is most frequently located in the adrenal glands, but may occur in any part of the body, such as the neck, thorax, or spinal cord. It occurs most frequently before 5 years of age; on average at 2 years of age. Neuroblastoma is **highly malignant**. It has usually already spread by the time it is diagnosed.

Tumour can grow in any part of the nervous system. Symptoms depend on the mass effect of the tumour in the affected region, which can be the head, neck, thorax, or paraspinal or lumbosacral. Neuroblastoma most frequently **metastasizes** to bones, lymph nodes, bone marrow and liver.

6. *OSTEOSARCOMA AND EWING SARCOMA*

Osteosarcoma and Ewing sarcoma are the most common primary bone tumours. These malignant neoplasms are more frequent in male adolescents, or young adults, with incidence the greatest at 10 years of age. The main clinical manifestations of these sarcomas are pain and enlargement of the affected area and, as the disease progresses, functional limitation and even pathologic fracture.

Osteosarcomas are most often found at the **sites of rapid growth— metaphysis** (e.g. femur, tibia, and humerus). They can sometimes be found in the shoulder, upper arm, pelvis, and skull, while **Ewing sarcoma** affects the diaphysis of long and flat bones and is most often found in the pelvis, thighs, ribs, and upper arms.

The main clinical manifestations of these sarcomas are **pain** and **enlargement of the affected area** and, as the disease progresses, functional limitation, and even pathologic fracture. A painful limp and enlargement of the affected area without a history of trauma is very significant, since almost half of osteosarcomas are located around the knee. Ewing sarcoma is more likely to also cause symptoms such as fatigue, fever, and weight loss.

Late diagnosis worsens the prognosis, which is directly related to the number and size of the metastases. Survival is close to 70% if the cancer has not spread to other areas of the body. Survival decreases to less than 30% if the cancer has spread. Normally, there are no clinical metastases at the time of diagnosis.

7. RETINOBLASTOMA

This malignant neoplasm originates in the primitive cells of the retina. It ranks 5th to 9th among child cancers, with its greatest incidence in children under 3 years of age. It is more frequent in developing countries; some studies have shown an association with viral infections such as adenovirus and human papillomavirus.

The most common sign is **leukokoria** (white eye or cat's eye) in one or both eyes. Leukokoria is the absence of the normal red reflex of the retina when illuminated with a light.
The second most common sign is **strabismus**.
Heterochromia (different coloured irises) sometimes occurs as the first sign of retinoblastoma.
Usually there is **no pain** unless there is an associated cause.
The most important prognostic factor for both vision and for survival or cure is the stage at which treatment begins. Thus, early detection is crucial to reducing morbidity and mortality.

8. RHABDOMYOSARCOMA

This is a malignant soft-tissue neoplasm of skeletal muscle origin. It occurs in the first 10 years of life. Its location varies greatly and is age-related: bladder and vagina, primarily in the first year of life; trunk and limbs after the first year of life; and head and neck at any age, more frequently in the first 8 years of life.

The most frequent presentation is a painful or painless **mass**. Clinical manifestations may vary widely, depending on the tumour's location. A mechanical mass effect can occur.

It is aggressive, with rapid local growth, and directly invades neighbouring structures. Its clinical presentation will depend on the structures it affects.

9. GERM CELL TUMOUR

This is a **benign or malignant** germ cell neoplasm, which can grow in the **ovaries or testes**, or in **other sites**, such as the sacrococcygeal region, retroperitoneum, mediastinum, neck, and brain.

It ranks 7th or 8th as a cause of child cancer.

Occurrence peaks in two age groups: before the age of 4 years and after 15 years. Of all tumours of the ovary, over half are benign.

It presents with general clinical symptoms, such as fever, vomiting, weight loss, anorexia, and weakness.

The most common symptom of **ovarian GCT is chronic pain**. A mass may be felt that, if it is very large, produces constipation, genitourinary disorders, and absence of menstruation.

The testicular GCT presents as a hard, slightly painful mass that does not transilluminate.

Session 3: How to Assess the possibility of Cancer

SESSION DURATION

10.45-11.15 am (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session, Participants will be able to identify suspected cancer signs through observation, questions related to the clinical history, and a complete physical examination.

KEY POINTS

Assessing the possibility of cancer typically involves a combination of medical history review, physical examination, diagnostic tests, and imaging studies.

Here's a general overview:

- **Medical History Review**:

Gathering information about symptoms, risk factors, family history of cancer, and any previous medical conditions or treatments.

- **Physical Examination**:

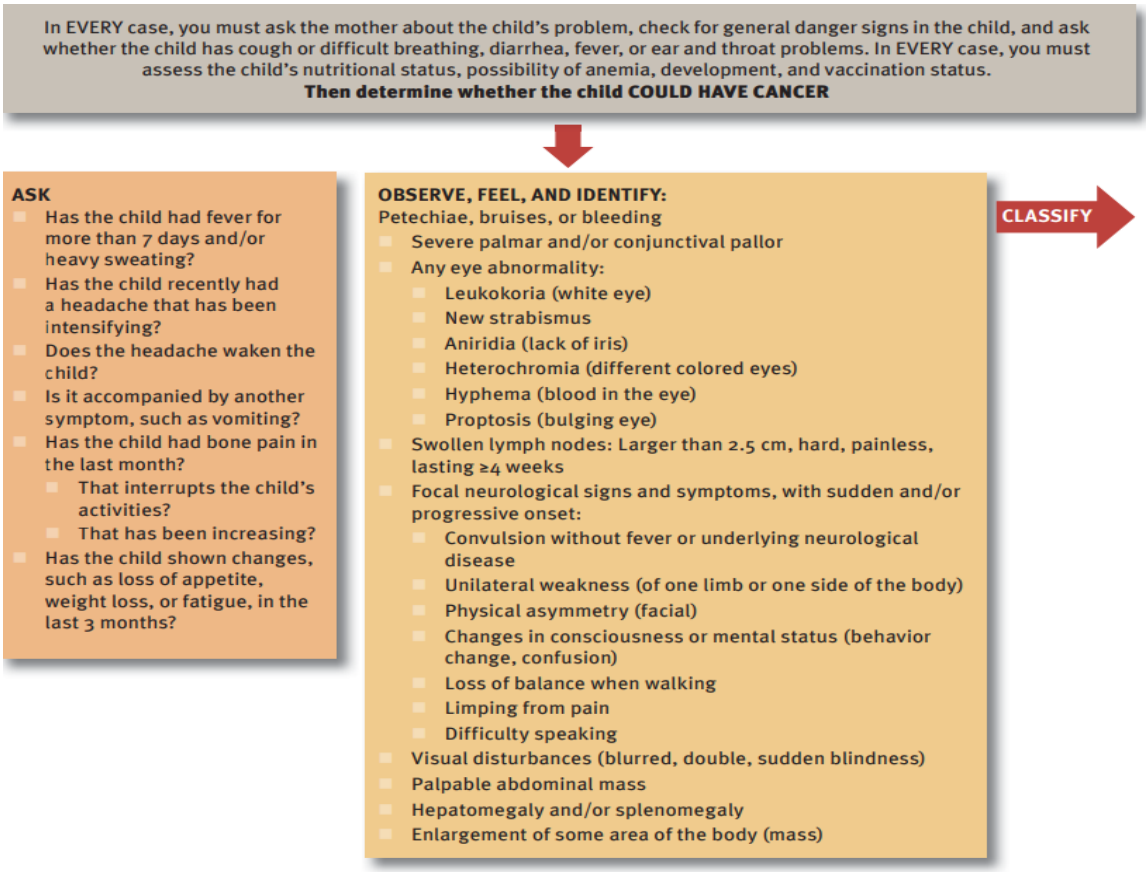
Conducting a thorough examination to look for any signs or symptoms that may indicate cancer, such as lumps or masses, changes in skin color or texture, enlarged lymph nodes, or other abnormalities.

- **Diagnostic Tests**
- **Screening**:

Retinoblastoma and neuroblastoma may be detected early through specific screening methods for high-risk populations or through routine well-child check-ups.

- Genetic Testing
- Consultation with Specialists:

Depending on the suspected type of cancer and the results of initial assessments, further evaluation by specialists such as oncologists, haematologists, surgeons, or radiologists may be necessary.



Remember that you should think and look in order to find cancer.

Diagnosing cancer early makes the difference between life & death.

No clinical test replaces a good clinical history and careful physical examination.

EVERY TIME THE CHILD VISITS A HEALTH SERVICE, whether for a well child visit, growth monitoring, or an outpatient or emergency visit for any cause, in first, second, or third level facilities, ***you should assess the possibility that the child may have some type of cancer.*** This directive is carried out simply by means of questions that are recorded in the clinical record and by classifying the nonspecific signs or symptoms that may be found during a complete physical examination.

ASK: HAS THE CHILD HAD FEVER AND/OR HEAVY SWEATING FOR MORE THAN 7 DAYS?

Fever is usually caused by an infection, but ***some cancers can manifest with fever***, such as leukaemia, lymphoma, histiocytosis, medulloblastoma, and Ewing sarcoma. Fever lasting several days or weeks, without characteristics of viral illness and with no obvious source, should be studied. Cancer is one of the differential diagnoses in the study of "fever of unknown origin." Every child with prolonged fever should be referred to a hospital for supplementary studies and to clarify the cause of the fever. In general, fever in the child with cancer is usually associated with other symptoms such as bone pain, weight loss, and pallor. The ***triad of anaemia + purpura + fever*** appears in two-thirds of leukaemia cases and, if these are accompanied by hepatomegaly, splenomegaly, lymphadenopathy, and

hyperleukocytosis, the diagnosis is highly probable. The neoplastic disease that most frequently causes prolonged fever without significant findings on physical examination is lymphoma (especially Hodgkin's lymphoma). Usually, peripheral lymphadenopathy or splenomegaly is also found during a thorough physical examination. Another sign is heavy sweating—lymphoma patients often leave the sheets wet at night.

Usually, the first step in studying fever of unknown origin, after ruling out infection, is a complete blood count and peripheral blood smear. If these tests are not available and there are significant signs of cancer, referral of the child should not be delayed, it should be done immediately.

ASK: HAS THE CHILD HAD A HEADACHE RECENTLY? DOES THE HEADACHE AWAKEN THE CHILD? DOES THE HEADACHE OCCUR AT A PARTICULAR TIME OF DAY? ARE THERE OTHER SYMPTOMS, SUCH AS VOMITING?

Headache is a frequent cancer symptom in children and adolescents. When pain awakens the child at night or he has a headache when he wakes up, and he also has vomiting and papilledema, the first diagnosis that must be investigated to rule out is intracranial hypertension secondary to brain tumour. Brain tumours are manifested by continuous, persistent, and disabling headaches. These headaches worsen with coughing or abdominal straining, such as with defecation. Over time, the headaches increase in frequency and intensity, affecting the child's well-being and requiring the use of analgesics. When a headache is accompanied by other signs of intracranial hypertension, such as vomiting, double vision, strabismus, ataxia (uncoordinated gait), or some other neurological disturbance, there is a very high probability of a brain tumour and referral of the child to a specialized centre should not be delayed. Keep in mind that brain tumours are most likely to occur in children aged 5 to 10 years, when headaches of other etiologies are infrequent. Brain tumours are rarely accompanied by fever, which is a symptom that accompanies headaches from infectious causes.

ASK: DOES THE CHILD HAVE BONE PAIN?

Bone pain is a frequent symptom in diagnosing bone cancer in the child. It is the initial symptom and precedes a soft tissue mass, with very intense pain that awakens the child at night. It is important to distinguish between pain that is located in one bone and pain in several bones. ***Pain in several bones*** occurs from metastasis and has similar characteristics. Both "leg pain" after an afternoon of strenuous exercise and "back pain" from carrying a school bag for weeks are frequent reasons for visits to the paediatrician or general practitioner. When a ***child's back hurts***, since this is the first symptom of spinal cord compression, a complete physical exploration should be done, as well as laboratory and imaging studies if available, to rule out this diagnosis. Since school-age children and adolescents engage in sports and roughhousing that produce tendon and muscle injuries, little attention is given to claudication. Pain from bone tumours is unrelated to the intensity of a possible injury and does not disappear over time, but, on the contrary, increases progressively. If the child is ***limping from pain*** and it is disabling and progressive, he should be studied to look for a mass or deformity in the large joints, characteristic of osteosarcoma. Furthermore, since the enlargement that accompanies bone tumours occurs after a variable length of time, and tends to occur later, every child or adolescent with painful claudication should be referred for study and to rule out a tumour disease. ***Bone (and joint) pain*** is also one of the initial symptoms of leukaemia, especially acute lymphocytic leukaemia, occurring in up to 40% of cases. This is an erratic, intermittent, and, at the beginning, poorly defined pain, that can be confused with rheumatologic disease. For this reason, any bone pain of disproportionate intensity to the history of injury or without injury that lasts several days merits examination to rule out neoplasm.

ASK: HAVE THERE BEEN CHANGES IN THE CHILD, SUCH AS LOSS OF APPETITE, WEIGHT LOSS, OR FATIGUE, IN THE LAST THREE MONTHS?

Some nonspecific acute or subacute symptoms are associated with tumours in children. These include recent loss of appetite with no apparent cause, weight loss, and fatigue that lead the child to refrain from usual activities. These symptoms are associated with some neoplasms, especially leukaemia and lymphomas, and should be always investigated.

OBSERVE IF THE CHILD HAS ECCHYMOSES OR PETECHIAE, OR MANIFESTATIONS OF BLEEDING.

You should examine the child completely, without clothes. Pay attention to the skin. Usually, in diseases that cause thrombocytopenia (low blood platelet count), characteristic lesions appear, such as bruises or petechiae that are usually not related to trauma or are too large for minor trauma, as well as manifestations of bleeding, such as epistaxis, gingival bleeding (bleeding of the gums), gastrointestinal bleeding, or urogenital bleeding. If you observe any sign of bleeding, ask the mother how long it has lasted. As mentioned earlier, purpura is one of the characteristic signs of leukaemia, together with ecchymoses, evidence of mucous membrane bleeding, and petechiae that multiply and become easily visible. Every case of purpura should be studied through laboratory tests. This means that the first level of care will need to refer the child for study.

OBSERVE WHETHER THE CHILD HAS SEVERE PALMAR OR CONJUNCTIVAL PALLOR.

Anaemia, as well as fever, is a sign of disease that merits investigation.

In children, the most frequent causes of anemia are:

- **Iron deficiency**: this type of anemia is more prevalent in poor populations and where health care is substandard.
- **Infections**.
    - Parasites, such as hookworm or whipworm, which can cause blood loss.
    - Malaria, which rapidly destroys red blood cells.
- **Oncological** diseases, mainly leukaemia

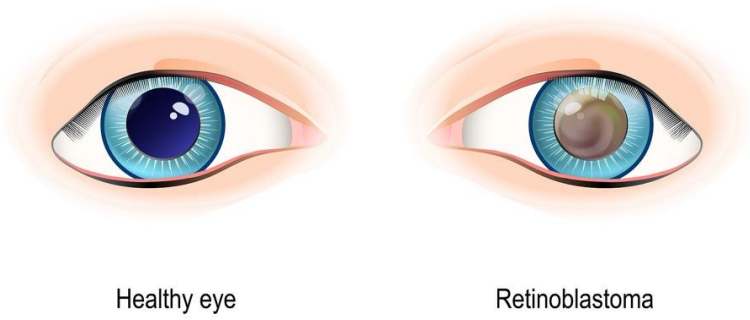
According to World Health Organization criteria, children aged 6 months to 6 years should be diagnosed as anaemic when their haemoglobin levels are lower than 11 g/dl. One sign of anaemia is excessive skin pallor. To see if the child has **palmar pallor**, look at the skin of the child's palm. Hold the child's palm open by grasping it gently from the side. Do not stretch the fingers backwards. This may cause pallor by blocking the blood supply. Compare the colour of the child's palm with your own palm and, to the extent possible, with the palms of other children. If the skin of the palm is very pale, the child has severe palmar pallor. Another clinical test that can be used to detect anaemia is **conjunctival pallor**, but in places where conjunctivitis is common, pallor is replaced by conjunctival hyperaemia. Furthermore, palm examination is not traumatic for children, while examination of the conjunctiva often makes them cry.

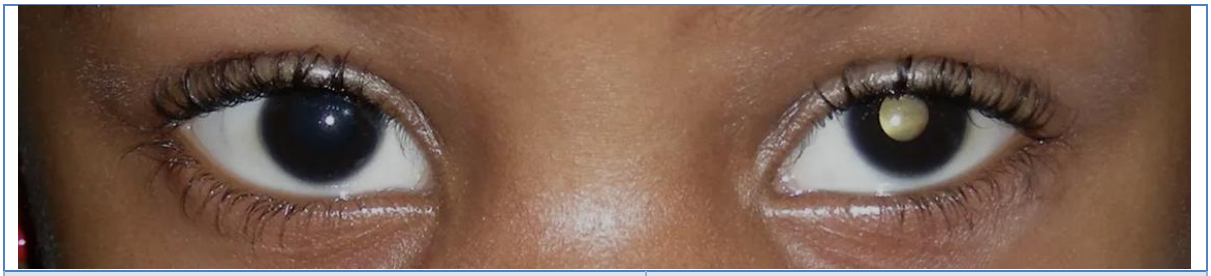
EXAMINE THE CHILD'S EYES TO SEE THERE ARE ANY ABNORMALITIES

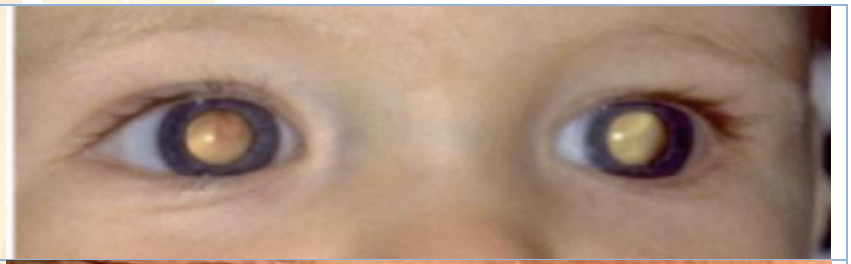
It is essential to examine the child's eyes to look for the normal red fundus reflex. If instead you see a whitish reflex, a sign that parents tend to mention as a "shining eye" or "cat's eye" or "white reflection at night," the child has ***leukokoria***, which is the principal external manifestation of retinoblastoma. Sometimes, it is not easy to detect this sign during the visit, even by moving or tilting the child's head. In this case, if the parents have mentioned this colour change in the pupil, the best option is to refer the child for ophthalmological assessment. Until it is ruled out with certainty, leukokoria should be

considered synonymous with retinoblastoma. Another eye disorder related to child cancer is aniridia, a rare malformation in which there is only a vestigial iris. Children with this dysfunction have photophobia and reduced vision. Since **aniridia is associated with Wilms tumour**, renal sonography is recommended every three months, up to five years of age. Acquired strabismus, in turn, can be the first sign of a brain tumour. Retinoblastoma can cause strabismus when vision is lost in the eye where the tumour is located and is usually accompanied by leukokoria.

Other late changes that should be looked for are **heterochromia** (different coloured irises), and proptosis (bulging eye).

Unilateral retinoblastoma, leukokoria (white eye on left), and normal red reflex on right	 Healthy eye Retinoblastoma

	
Normal eye	Retinoblastoma

Bilateral retinoblastoma	
LEUKOKORIA (WHITE EYE)	

FEEL THE NECK, AXILLAE, AND GROIN TO LOOK FOR LYMPHADENOPATHY

The human body has about 600 lymph nodes, which are from 2 to 10 mm in diameter and are in lymph node stations. Generalized lymphadenopathy is a sign of systemic disease, usually a viral infection. Enlargement of cervical nodes usually corresponds to inflammatory lymphadenopathy, of which 80% have an infectious cause and 20% have other origins, including tumours and neoplasms. The malignant causes of lymphadenopathy are:

- Lymphoma
- Leukaemia
- Langerhans cell histiocytosis
- Metastatic: Rhabdomyosarcoma, Neuroblastoma, Nasopharyngeal Carcinoma

Suspected signs of malignancy that suggest the need for thorough evaluation of lymphadenopathy:

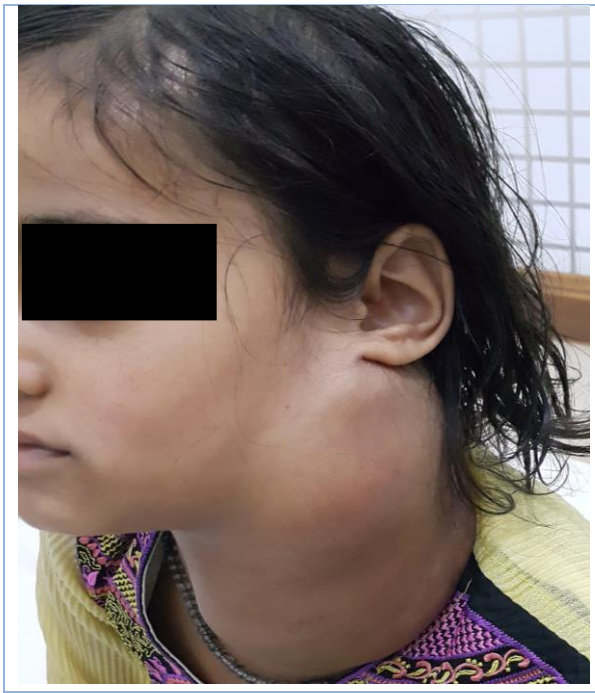
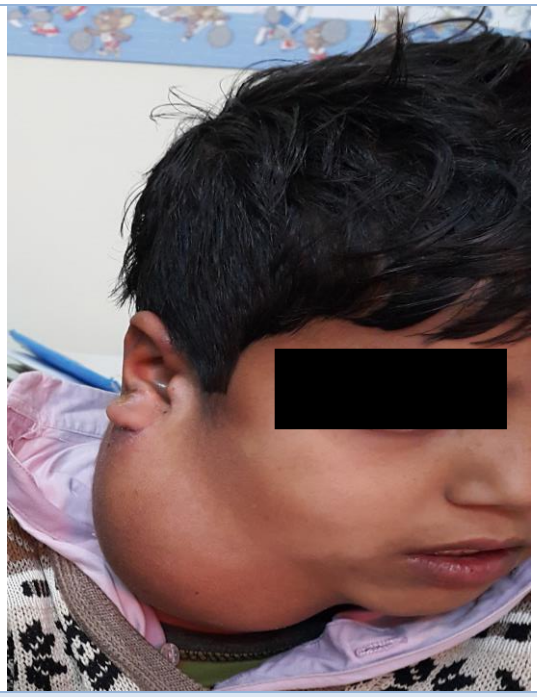
- Unilaterality (not required)
- Size greater than 2.5 cm.
- Absence of inflammatory characteristics (painless)
- Hard and firm in consistency
- Location posterior to or over the sternocleidomastoid or supraclavicular region
- Progression or absence of regression over a four-week period
- Absence of oropharyngeal or cutaneous site of infection
- Adhesion in deeper layers.

TABLE 3: FEATURES CONCERNING FOR MALIGNANCY IN LYMPHADENOPATHY

Less concerning findings	Increased risk of malignancy
• Localized adenopathy • Cervical, inguinal, and axillary regions • < 1-2 cm (depending on location) • Erythema • Tender • Warm • Fluctuant	• Generalized adenopathy. • Occipital, auricular, supraclavicular, mediastinal, epitrochlear or posterior cervical nodes • 2 cm • Firm and Matted • Nontender • Systemic symptoms

Over half of all malignant neck masses are lymphomas. Ninety percent of **Hodgkin's lymphoma** patients have cervical lymphadenopathy (usually unilateral), with packet formation by several closely interrelated nodes. In non-Hodgkin's lymphoma, there are usually multiple lymphadenopathies, and they can appear on both sides of the neck, while in acute leukaemia they are numerous and often widespread.

- *As a rule, every nodal mass suspected of malignancy should be **examined by skilled personnel**, who will decide if biopsy needs to be done and will select the node.*
- *An **excisional biopsy** should be done because fine needle aspiration cytology (FNAC) often is inconclusive and delays the diagnosis.*

Hodgkin Lymphoma presenting as Cervical lymphadenopathy

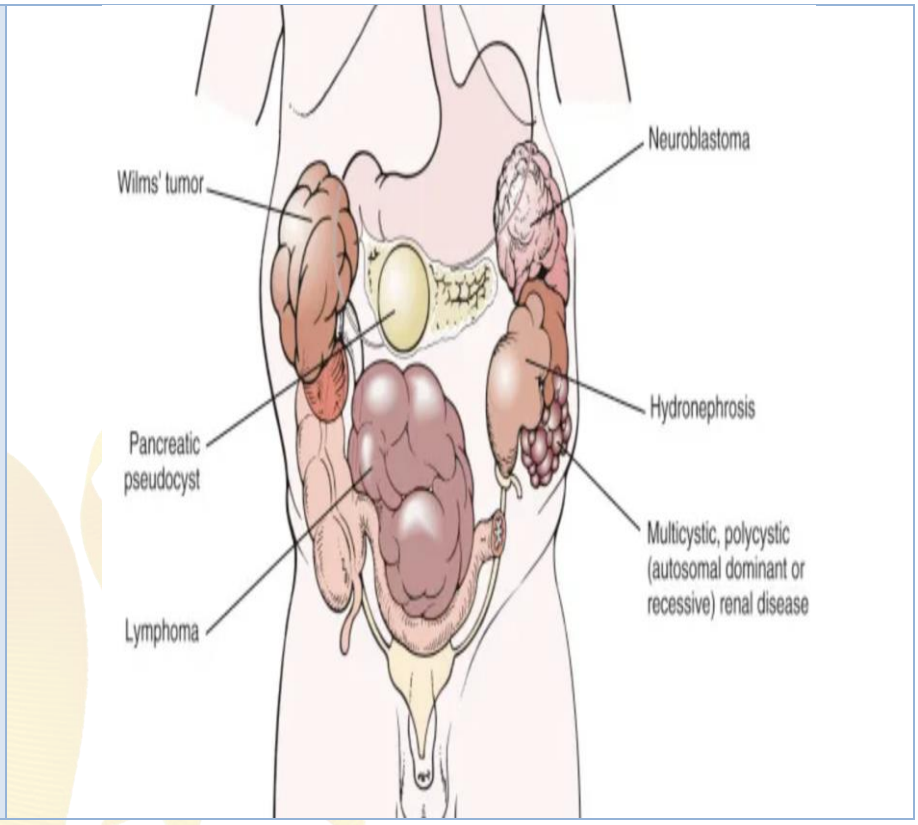
LOOK FOR ACUTE AND/OR PROGRESSIVE FOCAL NEUROLOGICAL SIGNS

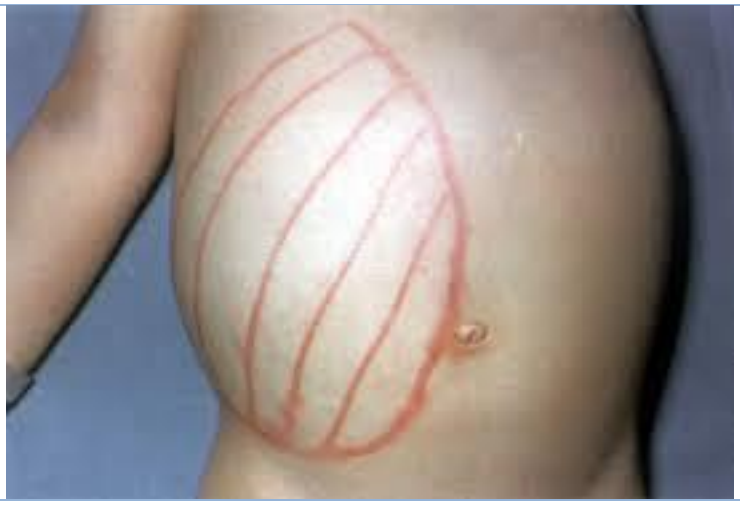
Acute neurological problems are those that have been diagnosed recently or during the visit. The neurological examination can detect weakness in one limb or in the limbs on one side of the body. Asymmetries can be seen in the face, such as paralysis and deviation of the mouth and eyes, which is a manifestation of cranial nerve dysfunction due to the mass effect of different tumours. Changes can also be seen in consciousness, mental status, or behaviour; there may also be confusion, as well as disorders of coordination, balance, and gait (ataxia). Ataxia is an abnormal swaying "drunken" gait. When it presents acutely or subacutely, the possibility of a brain tumour should be considered, especially if accompanied by symptoms of intracranial hypertension, such as headache, vomiting, diplopia, or strabismus. Specific focal findings, such as difficulty speaking (e.g., aphasia, dysphasia, or dysarthria) or visual field defects (e.g., progressive or sudden onset of blurred vision, incomplete vision, double vision, strabismus, or progressive blindness), can be related to more complex neurological problems and the first differential diagnosis is tumours of the nervous system.

FEEL THE ABDOMEN AND PELVIS TO LOOK FOR MASSES

The physical examination of a child, regardless of the reason for the visit, should always include a careful examination of the abdomen. Numerous tumours are asymptomatic in their first stages and are only detected if a good physical assessment is done.

Malignant tumour masses are hard, with a firm consistency and, depending on the affected organ, are in the **flank (renal tumours),** in the **right hypochondrium (liver tumours**), and in the **hypogastrium** (**bladder** or ovarian tumours). **Neuroblastomas** are found in the retroperitoneum, as is Wilms' tumor, but usually cross the midline. **Burkitt's lymphoma** (a very fast-growing lymphoma) is in the ileocecal region and can be accompanied by peritoneal lymphadenopathy. Since any mass felt in the abdomen should be considered malignant until proven otherwise, the physician who detects one should refer the patient without delay to a specialized centre. Masses felt in the newborn are usually of benign origin.

Location of selected retroperitoneal tumours and masses.	

Right sided Wilms tumour	

LOOK, FEEL, AND IDENTIFY IF THERE IS A MASS OR ENLARGEMENT IN ANY REGION OF THE BODY

Any enlargement of any organ or in any region of the body without inflammatory characteristics is suspicious for cancer and therefore should be investigated. In children, **malignant testicular neoplasms** appear before the age of 5 years, while yolk sac tumours, the most frequent testicular mass in early childhood, occur before the age of 2 years. In general, they all manifest as progressive, slow, and painless enlargement, and have no inflammatory signs, increased consistency, and negative transillumination. In masses in limbs, the two principal symptoms are pain (which can secondarily produce functional disability) and enlargement. Pain can precede enlargement and is usually progressive and persistent, without the inflammatory manifestations of infectious diseases. Children with neuroblastoma

Session 4: How to classify the possibility of Cancer

SESSION DURATION

11.30 am-12.00 pm (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session, participants will be able to identify suspected cancer and classify childhood cancer.
- Diagnosis and treatment are not delayed for any child with cancer because of bureaucracy, red tape, or the health team's lack of knowledge.

KEY POINTS

CLASSIFY:

Classify through colour coding, the child's health status, and note the required actions:

  - Urgent treatment and referral (red)
  - Outpatient treatment and advice (yellow)
  - Advice on treatment and home care (green).

- ***When a child has any suspected sign or symptom of cancer, the only procedure is to refer the patient immediately to a specialized centre.***
- Without testing and even without certainty in the diagnosis. The reason is that any study to confirm or rule out a diagnosis can take weeks or even months.
- The classification of a child according to the probability that he or she has cancer is done using traffic-light colours to identify the severity of clinical symptoms.
- According to the child's signs and symptoms, he will be placed in a row for greater or lesser severity. Whenever **IMCI classification tables** are used, you should begin to look for signs or symptoms from the top down; that is, first ruling out classifications of greater severity, which are red. When you find a sign or symptom in the child, follow that row to the right, where you will find the procedure to follow. Once confirmed by the IMCI table, the child should be classified in one of the following blocs: **possible cancer or very severe disease (red section), some risk of cancer (yellow section**), or **does not have cancer (green section)** (Table 4).

NOTES ON THE THREE IMCI CLASSIFICATIONS

Red area: "***Possible cancer or very severe disease***" Any child coming to you because of some illness or for growth and development monitoring or immunization and having some of the signs or symptoms included in the red area of the IMCI classification (see Table 4), should be studied immediately because the cause might be a neoplasm or another very severe disease. The safest and the most appropriate thing to do is to immediately refer the child to a specialized center, which will prevent wasting days or weeks on laboratory testing and imaging that will probably need to be repeated later.

Yellow area: **"Some risk of cancer**" Any child having some of the signs or symptoms included in the yellow area of the IMCI classification (see Table 4). Some of these clinical signs, such as loss of appetite or weight, tiredness or fatigue, or significant night sweats, can be manifestations of many disorders

including malignancy and infectious diseases, such as tuberculosis and HIV/AIDS. These children should be referred for studies to identify the causes of those signs and to begin appropriate treatment.

Anemia in children is usually secondary to iron deficiency, infections, or parasites, but it can also be a manifestation of a neoplasm, such as leukaemia. If you prescribe iron to any child, it has to be for a limited time. Schedule the child for an appointment every 14 days to give him more iron and re-examine him: if the anaemia has worsened clinically, refer immediately, and if the anaemia still persists clinically following one month of treatment with iron, studies need to be done, including a complete hemogram and peripheral blood smear.

Lymphadenopathy with inflammatory characteristics can have many causes, the main one being infection, which means that the child with these signs should be treated and then followed up, expecting improvement. Nevertheless, if lymphadenopathy persists or worsens or the signs of inflammation disappear but not the enlargement of the part of the body, the child should be referred, because among the diagnoses that should be ruled out are neoplasms. Teach parents danger signs requiring child to return immediately and ensure a 14-day follow-up appointment is made.

Green area: "Does not have cancer" The child has been placed in the green area of the classification; this means that for the time being, the child does not have any sign or symptom suggestive of cancer. Make sure growth and development monitoring and immunization are done, and teach the mother preventive health measures, such as:

- Maintaining a smoke-free environment.
- A healthy diet that includes fruits and vegetables, five times a day.
- Decrease high-fat foods, such as fried food, primarily if the child is overweight or obese.
- Get regular physical activity.

This module aims to ensure that diagnosis and treatment is not delayed for any child with cancer because of bureaucracy, red tape, or the health team's lack of knowledge.

When a primary health care team committed to early diagnosis, we will reduce cancer deaths in our children to a minimum.

TABLE 4 : CLASSIFICATION TABLE FOR CANCER PROBABILITY IN CHILDREN

Assess	Classify	Treat

One of the following signs:
• ***Fever for over 7 days*** with no apparent cause
• Headache: persistent and progressive, and primarily nocturnal, that awakens the child or appears when rising in the morning and may be accompanied by vomiting
• Bone pain that has increased progressively in the last month and disrupts the child's activities.
• ***Petechiae, bruises, and/or bleeding***
• Severe palmar or conjunctival ***pallor***
• ***Leukokoria*** (white eye)
• ***Strabismus*** that has newly appeared
• ***Aniridia*** (lack of iris)
• ***Heterochromia*** (different colored eyes)
• ***Hyphema*** (blood in the eye)
• ***Proptosis*** (bulging eye)
• ***Nodes*** >2.5 cm in diameter, hard, painless, lasting ≥4 weeks
• Acute and/or progressive focal neurological signs and ***symptoms***:
  ○ Convulsion without fever or underlying neurological disease
  ○ Unilateral weakness (of one limb or one side of the body)
  ○ Physical asymmetry (facial)
  ○ Changes in consciousness or mental status (behavior change, confusion)
  ○ Loss of balance when walking
  ○ Limping from pain
  ○ Difficulty speaking
• ***Visual disturbances*** (blurred, double, sudden blindness)
• Palpable abdominal ***mass***
• ***Hepatomegaly*** and/or ***splenomegaly***
• Mass in some region of the body with no signs of inflammation
	POSSIBLE CANCER OR VERY SEVERE DISEASE	• Refer urgently to a high complexity hospital with a pediatric hematology/oncology service; if not possible, refer to a pediatric hospital
		• Stabilize the patient, and if necessary, begin intravenous liquids, oxygen, and pain management.
		• If a brain tumor is suspected and there is neurological deterioration, begin management of intracranial hypertension.
		• Speak with the parents: explain the need for and importance of the referral and its urgency
		• Resolve all administrative problems that occur.
		• Communicate with the referral facility

One of the following: • Loss of ***appetite*** in the last 3 months • ***Weight loss*** in the last 3 months • ***Tiredness*** or fatigue in the last 3 months • Significant night ***sweats***, with no apparent cause • Mild palmar or conjunctival ***pallor*** • Painful ***lymphadenopathy*** or lasting <4 weeks, or ≤2.5 cm in diameter, or not hard in consistency • Enlargement in any region of the body with signs of inflammation	**SOME RISK OF CANCER**	• Do a complete physical examination to look for a cause for the signs found • Review the child's diet and correct any problems found • If there is weight loss, loss of appetite, or fatigue or tiredness, refer for pediatric consultation to begin studies and to investigate possible TB, HIV • If there is mild palmar pallor, begin iron and followup every 14 days. If it worsens, refer urgently. If there is no improvement at one-month follow-up visit, request hemogram and blood smear to look for cause of anemia and to treat or refer as appropriate. • Treat the cause of lymphadenopathy with antibiotics, if necessary and follow-up in 14 days; if there is no improvement, refer. • Treat with antibiotics any inflammatory process that produces enlargement in a region of the body and follow-up in 14 days; if there is no improvement, refer. • Teach danger signs requiring child to return immediately. • Ensure immunization and growth and development monitoring
Does not meet criteria for be classified in either of the above classifications	**DOES NOT HAVE CANCER**	• Ensure immunization and growth and development monitoring. • Ensure a tobacco-free environment. • Recommend a healthy diet and regular physical activity.

Session 5: How to manage the child with possible Cancer

SESSION DURATION

12.00-12.30 (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session, participants can refer a child with suspected cancer immediately after providing basic emergency treatment.
-

KEY POINTS

HOW TO TREAT THE CHILD WITH POSSIBLE CANCER

- ***This module is not meant to teach proper treatment for each of the types of cancer*** that can affect children, but instead it focuses on the early diagnosis and proper referral of the child to the appropriate health facility. Its purpose is to have the entire health care team, starting at the first level of care, work to offer the child with cancer the best chances possible for survival.
- Hence, the importance of understanding that, when there is a suspected possibility of cancer, the child should be referred to a centre that specializes in its diagnosis. Although it is necessary to refer the child immediately, it is important to do so under appropriate conditions. ***Some children will need to be stabilized before being sent to a specialized centre***, as described below.

OXYGEN

- Every child classified with severe or very severe disease, with danger signs, with respiratory problems, or symptoms of shock, and all those who required any resuscitation procedure, should be referred with supplementary oxygen.
- How oxygen is administered depends on the availability of equipment, the adaptation of the child to the method (mask or nasal cannula), and the required concentration of oxygen.

HEMODYNAMIC STABILITY

- A child with signs of severe dehydration, or with hypovolemia of another aetiology, or shock should be stabilized before referral.
- Lack of a paediatric blood pressure monitor is no excuse for not doing a good assessment of volume status. In this regard, it is necessary to know that some clinical signs are good predictors of hypovolemia and low perfusion and of the need to improve volume.
- These are the signs that indicate hypoperfusion:
    - Capillary refill time >2 seconds
    - Pale or mottled skin
    - Heart rate: tachycardia >180 beats per minute
    - Altered state of consciousness.
- **Initial treatment** in these cases consists of rapid fluid loading, usually with lactated Ringer's or 0.9% normal saline solution at a volume of 20 mL/kg in 30 minutes or less if necessary.
- It is important to remember, however, that some children with cancer can have severe anaemia, which means that a rapid load of fluids can produce pulmonary oedema in them. In

these cases, as a result, fluids should be administered more slowly until the patient is transfused if required.

PAIN MANAGEMENT

If the child is in pain, treat before referring:

MILD PAIN:

- Paracetamol 10-20 mg/kg/dose every 4-6 hours orally or IV

MILD OR MODERATE PAIN:

- Ibuprofen: 5-10 mg/kg/dose; Single dose only
- Tramadol 1-2 mg/Kg/dose every 6 hours orally
- ***Note: NSAIDS are avoided as they can cause platelets dysfunction.***

MANAGEMENT OF INTRACRANIAL HYPERTENSION

If a patient with a suspected brain tumour is exhibiting neurological deterioration, you must begin management of intracranial hypertension before referring, according to these steps:

- Bed rest with head of bed elevated 45°.
- Administration of high doses of steroids: Oral or intramuscular or intravenous dexamethasone 0.25 mg/kg/dose twice daily.
- In case of convulsions, diazepam should be administered at a dose of 0.3 mg/kg/IV with a maximum dose of 10 mg and a maximum of three doses; infusion should not exceed 1 mg/ min. Following administration of diazepam, phenytoin should be administered at a dose of 10-15 mg/kg/IV.

Urgent implementation of these measures makes it possible to transfer the patient to the third level of care.

RECOMMENDATIONS IN CASE OF BLEEDING AND SEVERE ANAEMIA

- ***Transfuse only if the child's life is in danger.*** If the child has a very low haematocrit and hemodynamic disturbances, packed red blood cells should be transfused at 10 mL/kg; avoid blood transfusion in case of WBC count more than 100 x 10^9/L. This is because of the risk of hyperviscosity syndrome.
- Transfuse platelets in case of active bleeding or platelet counts less than 10 x 10^9/L.
- ***Discuss any transfusion needs with a physician at the referral center prior to transfusing any blood products.***

RECORDING AND MONITORING

- All children with serious classifications must be monitored to ensure detection of new problems, signs, or symptoms and to keep them stable.
- Monitoring does not necessarily require expensive equipment.
- The best monitoring is that done by health workers, when they make sure to observe the signs of children with serious classifications, such as heart rate, respiration rate, capillary refill time, difficult breathing, dehydration, and presence and quantity of diuresis, every 15 minutes or as appropriate based on clinical status until the child arrives at the destination hospital.

- This means that the health worker must accompany the child in the ambulance on the way to the hospital to monitor him throughout the trip.

INFORMING PARENTS

It is crucial to keep the parents informed: remember that they are very worried because their child has a serious problem. Listen to all their fears and try to clear up their doubts:

- ***Explain to the parents*** the need for referring the child to the hospital and obtain their consent.
- ***Calm the parents and reassure them*** that the hospital where you are referring the child has the specialized medical team & everything necessary to properly diagnose and treat the child.
- ***Explain to them*** what will happen in the hospital and how that will help their child.
- Ask questions and make suggestions about who could help at home while they are with their other child at the hospital.
- You may not be able to help the parents solve all their problems but is important to do everything you can to help so ***they feel supported***.
- Remember that if you do not refer the child immediately, his chances of survival can decrease, and his prognosis could change completely.

STEPS FOR REFERRING THE CHILD

Write a referral note for the parents to give to the facility where the child will be transferred. Tell them to give it to the health workers in the hospital. Write:

- The name and age of the child.
- The date and time of referral.
- Description of the child's problems.
- The reason for referral (symptoms and signs leading to severe classification).
- Treatment that you have given, including time and dosage of drugs.
- Any other information that the hospital needs to know in order to care for the child, such as earlier treatment of the illness.
- Your name and the name of your clinic.

Remember that you should ***communicate with the referral facility*** and provide information on the child you are referring. Most likely, they will tell you some things that you can do in the meantime, they will be expecting the child, they will facilitate admittance to the hospital, and they will help with any needed paperwork.

HOW TO TREAT THE CHILD CLASSIFIED WITH "SOME RISK OF CANCER"

- Children with this classification have clinical signs shared by many diseases including cancer.
- Since cancer perhaps produces these signs at a much lower percentage than other diseases, children should be treated based on the most frequent aetiology.
- The most important thing is to ***follow up on the child***. Following up will make it possible to observe the course of the illness and response to treatment and will also help to know precisely when other possible pathologies should be investigated.
- ***Weight loss, loss of appetite, and fatigue and tiredness of recent onset*** can be caused by many diseases, among them infections such as tuberculosis and HIV, nutritional or gastrointestinal system problems, and rheumatologic diseases.
- Tumours can also be associated with these symptoms, but usually the acute presentation of many of them means that they are not classical symptoms, as in many of the tumours of

adults. However, every child with these symptoms should be assessed and if no improvement is seen at the follow-up appointment and they persist, or if they are associated with any of the symptoms described in the "possible cancer" classification, the child should be referred immediately.

- **Anaemia** is often produced by many diseases, although the most frequent is iron deficiency due to inadequate diet. Even though it is one of the cardinal symptoms of the **leukaemia triad**, anaemia alone, without other symptoms such as purpura, should be considered to have another aetiology and should primarily be treated with iron.
- Nevertheless, if at the one-month follow-up, there is no clinical improvement, a blood complete picture and peripheral blood smear should be done to study the cause of anaemia and the absence of response to treatment with iron.
- Cancer will be the cause in a minority of children, and this will be evident from the blood complete picture, and the patient will be referred to complete the study and begin management.
- **Lymphadenopathy** with enlargement that has infectious inflammatory characteristics and does not meet the criteria to be considered malignant should be treated with an antibiotic.
- If no improvement is seen at the follow-up visit, or if lymphadenopathy persists after treatment for infection, the child should be referred for the diagnostic workup that may include lymph node biopsy.
- These children should be scheduled for follow-up visits every 14 days until there is improvement in the sign or until a cause is found that better explains the symptoms and the corresponding management is begun.
- ***Parents should be taught danger signs*** requiring the child to return immediately and should continue with growth and development monitoring, immunization, and home care.
- The child with enlargement from an inflammatory or infectious aetiology in any part of the body should be treated as appropriate and followed-up.
- If the enlargement persists after a month —or immediately, if it worsens—the child should be referred to a specialized centre.
- In this group, ***proper counselling of the parents is of the utmost importance***, so they can detect danger signs and know when to return immediately.

HOW TO TREAT THE CHILD CLASSIFIED AS "DOES NOT HAVE CANCER"

Fortunately, at the time of the visit, these children do not have any sign or symptom that justifies classifying them with "possible cancer" or "risk of cancer." Even so, with these patients, the usual assessment, management, and recommendations procedure in the IMCI handbook should be continued, along with providing preventive recommendations and promoting healthy lifestyles. Therefore, it is important to ensure that the child's immunizations are complete, and if not, bring them up to date, along with growth and development monitoring.

COUNSELLING THE CHILD'S PARENTS OR CARETAKER

The child with cancer requires treatment and follow up at a specialized centre that provides integrated patient management and has a multidisciplinary team that includes psychological support for the child and his family. Often, you know the child and his family because the child is a regular patient of the clinic, and the parents trust you. This relationship makes you a person who can support the family and can collaborate with the specialized centre in counselling the parents. In this regard, you can give the parents or caretaker the following key advice, among other things:

- ***Cancer is a curable*** disease if the child is given proper treatment.

- They should ***strictly comply with the treatment recommended*** by the oncology team.
- ***Alternative treatments and special diets have not been demonstrated to cure cancer***. If these things are not harmful and the family relies on them and uses them without stopping or changing the underlying management protocol, they can continue them. It is crucial to not stop treatment with false expectations of a cure.
- ***Abandonment is one of the major causes of treatment failure***. You should help the family complete the treatment regimen and follow-up prescribed by the specialized centre.
- Reinforce danger signs and remind parents that they should seek immediate attention if the child shows any change or associated symptom.
- The specialist will give recommendations on when the child can return to school based on the treatment protocol and degree of immunosuppression.

> "Insist on the importance of following these recommendations."

TEACH DANGER SIGNS THAT REQUIRE IMMEDIATE ATTENTION

You should teach parents danger signs that mean they must bring the child to the clinic to receive additional care. If parents know the danger signs and return in time, the child will receive the required care. ***Use words that the parents understand and remember that you should teach a limited number of signs so the mother can easily remember them***, instead of trying to teach every sign a disease may have. Explain to the mother that she should seek immediate care if the child with cancer:

- Has a fever.
- Vomits everything.
- Cannot drink liquids.
- Has manifestations of bleeding.
- Has breathing difficulty.
- Is very pale.
- Does not look well or is worsening.

FOLLOW-UP VISIT

The child classified with "some risk of cancer" should return for a follow-up visit in 14 days to be reassessed. When he does, assess as follows:

Ask whether the child has any new problems:

- If the mother says yes, you should assess the child as though it were an initial visit.
- If the mother says no, ask: Has the child improved or gotten worse?
- If the child had loss of appetite, weight loss, or fatigue, you referred him to a paediatric consultation for study of a disease such as tuberculosis or HIV/AIDS. Ask whether he went to the hospital for the studies, what laboratory tests were done, and what they were told. Ask what you can do to help.
- If you prescribed iron, ask the mother whether she is administering it. Observe the pallor; does it look better?
- If the child had lymphadenopathy in a region of the body, with signs of inflammation, see how it is: Is it better? Has the inflammation disappeared? Has the mass or adenopathy grown?

In this follow-up visit with the child:

- The child may be better, in which case continue with usual visits or an additional follow-up visit in 14 days, if necessary, because of the underlying disease.
- The child may be the same, in which case it is best to refer to the outpatient clinic for testing.
- The child may be worse, or some sign of “possible cancer or severe disease” may have appeared, in which case he should be immediately referred a specialized centre.

Session 6: The child with a Cancer diagnosis seen in the first level of care

SESSION DURATION

12.30 pm -13.00 pm (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session, participant will learn how to manage the oncology patient if patient arrive at first level of care instead specialized haematology/oncology service.

KEY POINTS

As mentioned earlier, the child with cancer will receive integrated management in a specialized haematology/oncology service. However, at times the child will be taken to an emergency or urgent care service because the mother thinks the child has a different disease or because it is difficult to reach the specialized centre—and the first level of care is closer—or for several other reasons.

Complications in children with cancer are always emergencies because they have the potential to be fatal and require immediate assessment and treatment. They can also affect different organs or systems, thus worsening the initial prognosis.

FEVER IN PATIENTS ON CHEMOTHERAPY

- Oncology patients are particularly susceptible to potentially severe infections. This depends on different risk factors, which include:
    - Impairment of the barrier function of the skin and mucous membranes (e.g., mucositis or venipuncture)
    - Malnutrition
    - Impaired immunity.
    - The principal risk factor is neutropenia (reduction in the number of neutrophils).
- Although infections are a frequent complication in these children, there are other causes of fever to keep in mind, such as:
    - The administration of certain chemotherapy agents
    - Transfusions
    - Allergic reactions, or from the tumour process itself.
- Some 60% of neutropenic patients who develop febrile syndrome have an infection and up to 20% of those whose neutrophil count is under 500 have bacteraemia.
- Fever in a cancer patient requires a very meticulous, complete physical examination to look for a focus of infection, which can be difficult to find especially in the neutropenic patient.
- A complete hemogram and microbiological cultures should be requested.
- Furthermore, always remember that a febrile neutropenic child without evident cause requires treatment with a ***wide-spectrum antibiotic*** until culture results are available or the cause of the fever is found.
- Most infections are caused by bacteria in the patient's own flora, in particular **gram-positive cocci** in relation—mainly—to catheters, and **gram-negative bacilli** that are responsible for potentially more serious infections.
- **Invasive fungal infections** should also be considered, especially in patients with neutropenia on prolonged treatment with wide spectrum antibiotics or prolonged treatment with corticosteroids or other immunosuppressive drugs.

- Every child with leukaemia or cancer who is on treatment and who goes to the emergency service with a high fever (≥101F or ≥100.4F lasting for an hour) and has a neutrophil count less than 500, should be hospitalized immediately on a haematology/oncology service.
- Patients with **febrile neutropenia** who do not urgently receive antibiotics are at risk of **sepsis**, which can rapidly become complicated with **septic shock,** which has very high **mortality**.

The antibiotics for **febrile neutropenia** should cover gram-negative bacterial infections, because of the fulminant nature of the infection and its high mortality. The initial empirical therapy is as follows:

- **Monotherapy**: cefepime, imipenem, meropenem.
- **Combination therapy**: aminoglycoside (amikacin, gentamicin) + antipseudomonal penicillin (ticarcillin, piperacillin, piperacillin + tazobactam) or + cefepime or + ceftazidime or carbapenem (imipenem or meropenem).

TUMOUR LYSIS SYNDROME

Tumour lysis refers to significant destruction of tumour cells, which can occur spontaneously when tumours are very large, or, in leukaemia with hyperleukocytosis, when administering chemotherapy to destroy malignant cells. Tumour lysis can lead to life threatening metabolic changes (e.g., **hyperkalaemia, hypocalcaemia, hyperphosphatemia, hyperuricemia**), from renal failure, arrhythmia, or cardiac arrest.

The classical **triad** is **hyperuricemia, hyperphosphatemia, and hyperkalaemia**.

- ***Hyperuricemia***: This is produced by increased nucleic acid degradation secondary to tumour cell destruction. Uric acid precipitates in the renal medulla, distal and collecting tubule, where urinary concentration and acidity is greater.
- ***Hyperkalaemia***: Potassium accumulates from tumour cell destruction.
- **Hyperphosphatemia**: Lymphoblasts contain four times more phosphates than normal lymphocytes. With tumour cell destruction, phosphorus is elevated. When the calcium: phosphorus ratio is greater than 60, the calcium phosphate precipitates in the microvasculature, producing hypocalcaemia, metabolic acidosis, and acute renal failure.
- ***Acute renal failure***: Oliguria before the beginning of treatment accompanied by calcium phosphate precipitation favours development of acute renal failure. It is manifested by cardiac disturbances; neuromuscular symptoms, such as paraesthesia, weakness, and hyporeflexia; and respiratory failure from hyperkalaemia. ***Hypocalcaemia*** is manifested by abdominal pain, fine tremor, muscular fibrillation, tetany, convulsions, and impaired consciousness.

Prevention of tumour lysis syndrome should focus on three basic aspects:

- ***Hyperhydration***: 3,000 to 4,000 ml/m^2/day with Dextrose 4.3% and Sodium Chloride 0.18% to ensure urinary volume >3 mL/kg/h and urinary specific gravity ≤1010.
- Reduction of uric acid with ***allopurinol*** at 10 mg/ kg/day or 300 mg/m^2/day divided into 3 doses.

SUPERIOR VENA CAVA SYNDROME

- This syndrome results from obstruction of blood flow in the superior vena cava, obstructing venous return from the head and neck. When compression of the windpipe also occurs, it is called ***upper mediastinal syndrome.***
- Its most frequent ***aetiology*** is malignant neoplasm, such as non-Hodgkin's lymphoma, Hodgkin's lymphoma, and T-cell type acute lymphoblastic leukaemia. There can also be obstruction from thrombi in any patient with a central venous catheter.
- ***Clinical symptoms*** can be acute or subacute, with profuse perspiration, facial plethora with cyanosis and upper limb oedema, jugular distension, and superficial collateral thoracic circulation. If there is compression of the windpipe, there will be symptoms of airway obstruction: cough, dyspnoea, orthopnoea, and stridor.
- ***Management*** includes airway maintenance, elevation of the head of the bed, oxygen, & diuretics with caution, and immediate referral to the specialized centre where this is being treated.

Session. 7: Childhood Leukamia

SESSION DURATION

- 14:00 - 14:30 pm (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session, Participants will be able to identify childhood leukaemia, its signs and symptoms through observation, the clinical history, and a complete physical examination.

KEY POINTS

To understand leukaemia, participants should first have knowledge of hematopoietic cells and their phases.

WHAT IS LEUKAEMIA?

A malignant disease is characterized by:

1. ***Unregulated proliferation of one cell type***.
    a. It may involve any of the cell lines or a stem cell common to several cell lines.
2. ***Differentiation blocked at an early stage***.
    a. Clonal expansion and arrest at a specific stage of normal myeloid or lymphoid haematopoiesis.
    b. 97% of all childhood leukaemia and consist of the following types:
        i. Acute lymphoblastic leukaemia (ALL)—75%:
        ii. Acute myeloblastic leukaemia (AML) —20%.
        iii. Acute undifferentiated leukaemia— 0.5%.
        iv. Acute mixed-lineage leukaemia.
    c. Chronic Myeloid Leukaemia constitute 3% of all childhood leukaemia and consists of
        i. CML: Philadelphia chromosome-positive myeloid leukaemia.
        ii. JMML: Juvenile myelomonocytic leukaemia.

EPIDEMIOLOGY AND RISK FACTORS

≈ 6000 cases of ALL are diagnosed in US annually.

- Half the cases occur in children and teenagers.
- ALL is the most common cancer among children.
- The most frequent cause of death from cancer before 20 years of age.
- 30 cases/million in < 20 years of age, with the peak incidence occurring at 3 to 5 years of age.
- **Incidence in Pakistan**[7]
    - Papulation; 247,653,551
    - 0-14 years: 34.81%: 86.2 million; ALL cases= 2586
    - 15-24 years: 21.31%: 43.0 million; ALL cases=1290
    - **3876 new cases/Year**

ETIOLOGY AND PATHOPHYSIOLOGY

- No single causative agent
- the exact cause is frequently not known, but predisposing factors are known:

[7] https://www.cia.gov/library/publications/the-world-factbook/geos/pk.html

- Increased inherited predisposition to develop leukaemia.
    - Identical twins – If one twin develops leukaemia during the first 5 years of life the risk of the second twin developing leukaemia is 20%.
    - Incidence of leukaemia in siblings of leukaemia patient is 4 times > that of the general population.

CHROMOSOMAL ABNORMALITIES:

- Down syndrome
    - 1 in 95, <10 Yrs of age
- Bloom syndrome.
    - 1 in 8, <30 Yrs of age
- Fanconi anaemia
    - 1 in 12, <16 Yrs of age

GENETICALLY DETERMINED CONDITIONS (↑INCIDENCE)

- Congenital agammaglobulinemia
- Shwachman–Diamond syndrome
- Ataxia telangiectasia
- Li–Fraumeni syndrome (germ line p53 mutation) – the familial syndrome of multiple cancers
- Neurofibromatosis
- Diamond–Blackfan anemia
- Kostmann disease

CHRONIC MARROW DYSFUNCTION (↑ INCIDENCE)

- Myeloproliferative diseases
- Myelodysplastic syndromes
- Aplastic anemia, or
- Paroxsymal nocturnal hemoglobinuria (PNH).

ENVIRONMENTAL FACTORS

- Exposure to ionizing radiation
- Exposure to mutagenic chemicals and drugs
- Viral infections

CLASSIFICATION

The childhood leukaemias can be classified:

- Myeloid/ Lymphoid/ Mixed or Biphenotypic
- Acute or chronic.
    - Acute leukemia: characterized by clonal expansion of immature hematopoietic or lymphoid precursors (ALL/AML),
    - Chronic leukemia:Characterized by the expansion of **mature** marrow elements (CML/CLL)
- Congenital leukemia
    - Leukaemias diagnosed within the **first 4 weeks** of life.

TABLE 4:COMPARISON OF ACUTE & CHRONIC LEUKEMIA

Feature	Acute	Chronic
Age	All ages	Usually adults
Clinical Onset	Sudden	Insidious
Course (untreated)	6 months or less	2 to 8 years
Leukemic Cells	Immature >30 % blasts	More mature cells
Anemia	Prominent	Mild
Thrombocytopenia	Prominent	Mild
WBC Count	Variable	Increased
Lymphadenopathy	Mild	Present, often prominent
Splenomegaly	Mild	Present, often prominent

CLINICAL MANIFESTATIONS

- Leukaemic **proliferation, accumulation, and invasion** of normal tissues, including the liver, spleen, lymph nodes, CNS, and skin
- Short course of symptoms (4-8 weeks)

Symptoms due to:

MARROW FAILURE

- Anaemia is manifested as Pallor, fatigue, lethargy and palpitation.
- Thrombocytopenia leads to easy bruising, bleeding.
- Leukopenia results in fever, infection.

LEUKOSTASIS causes hyperviscosity syndrome manifesting as headache**,** confusion and respiratory distress

TISSUE INFILTRATION

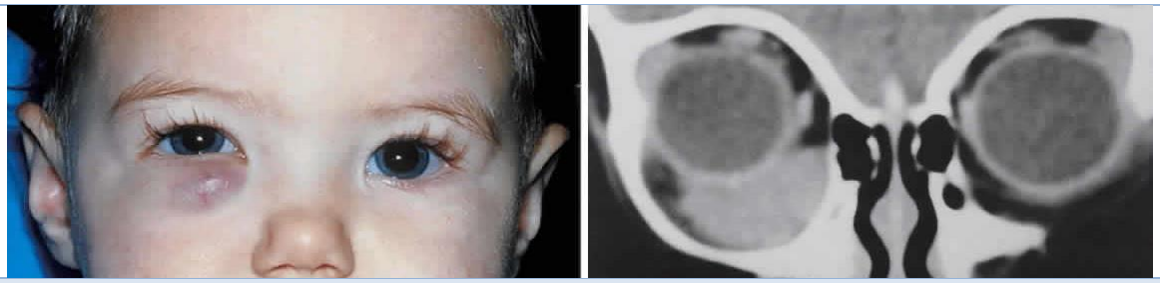
- Hepatomegaly/Splenomegaly
- Lymphadenopathy
- CNS involvement
- Gum hypertrophy
- Other organs: Skin, testis, any organ
- **Bone/joint pain**

CONSTITUTIONAL SYMPTOMS:

- Fever
- Weight loss
- Night sweats
- Anorexia

GRANULOCYTIC SARCOMA/ CHLOROMA

- Localized mass of primitive myeloid cells that infiltrate extramedullary sites
- Involvement of every organ system has been reported



Retrobulbar Mass: Granulocytic Sarcoma
**Picture with permission of the family*

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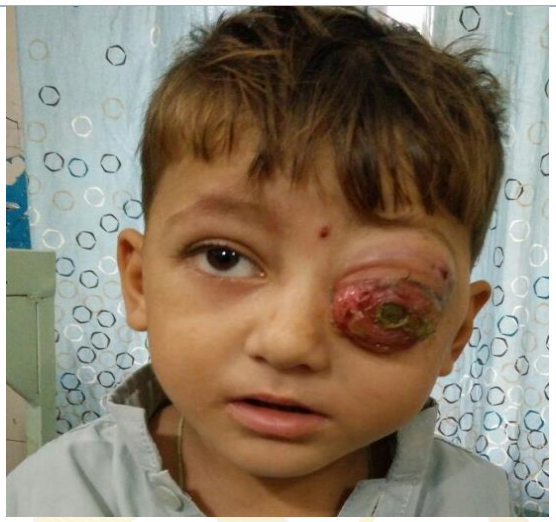
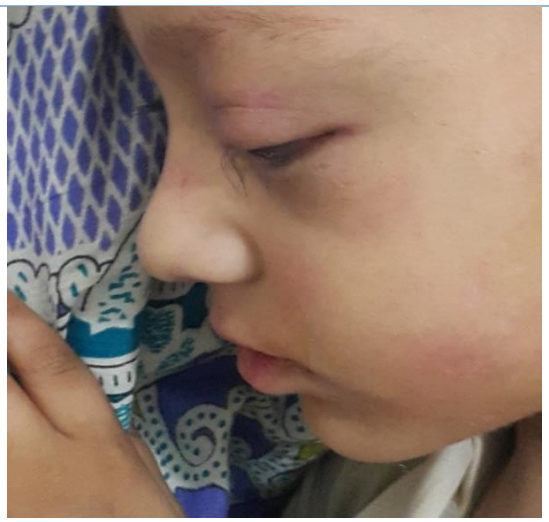




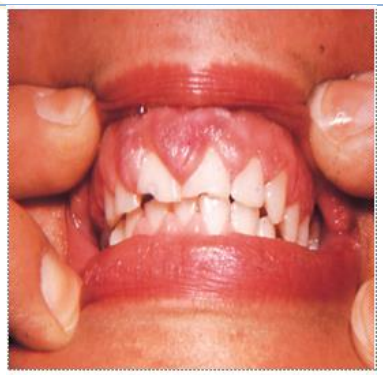
Prescription IPB 9.4.
CLINICAL HAEMATOLOGIST
CONSULTATION regarding
Fitness for eye surgery (Excision)
↓ GA + Special Instruction during & Post Surgery

Granulocytic Sarcoma of the left Orbit

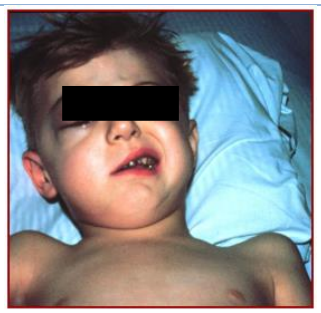
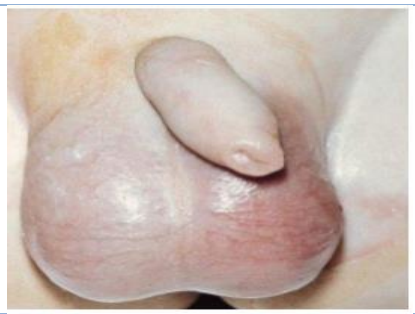
Same patient after first course of chemotherapy
**Picture with permission of the family*

Clinical Manifestations

OCCULAR INVOLVEMENT (HYPOPION)



GUM HYPERTROPHY

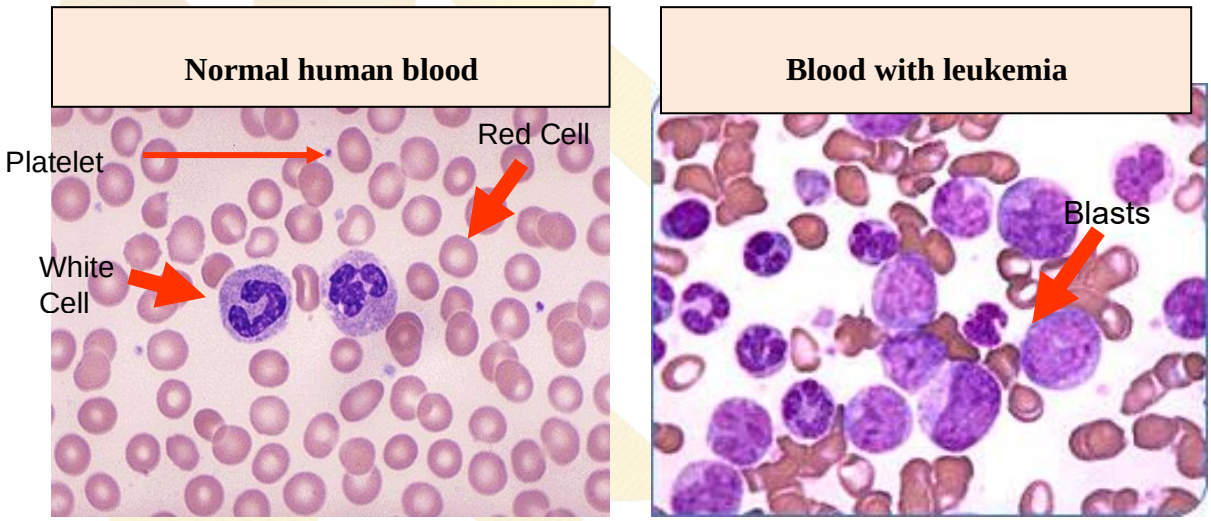
	
CNS LEUKAEMIA: FACIAL NERVE PALSY	***TESTICULAR INVOLVEMENT***

- Renal Involvement
- Gastrointestinal Involvement
- Bone and Joint Involvement
- Skin Involvement
- Cardiac Involvement
- Lung Involvement

INVESTIGATIONS

BLOOD COUNT:

- Anaemia (normochromic, normocytic)
- Thrombocytopenia
- Variable WBC count
    - The degree of peripheral blood involvement determines classification:
    - **Leukemic** – increased WBCs due to blasts
    - **Sub leukemic** – blasts without increased WBCs
    - **Aleukemic** – decreased WBCs with no blasts
- Blood morphology:
    - Presence of blast cells



- Blood Chemistry; (U&Es, LFTs, Uric acid, Phosphate, Calcium)
- Coagulation profile
- CXR- Mediastinal lymphadenopathy- T cell ALL
- Cardiac function- Echo, ECG
- Infectious disease profile

CSF EXAMINATION

- Identification of blast cells on cytocentrifuge examination.
- TdT stain for suspicious cells.
- CNS3 status is also given to patients with **clinical or radiological evidence of CNS-leukaemia,** irrespective of CSF findings e.g. cranial nerve palsies, or other neurological symptoms.
- Identification of blast cells on cytocentrifuge examination-
    - CNS 1: <5 WBCs/mm^3 , no blasts on cytocentrifuge slide.
    - CNS 2: <5 WBCs/mm^3 , blasts on cytocentrifuge slide.
    - CNS 3: >5 WBCs/mm^3 , blasts on cytocentrifuge slide.
    - TdT stain for suspicious cells.
    - Traumatic puncture

IMMUNOPHENOTYPING

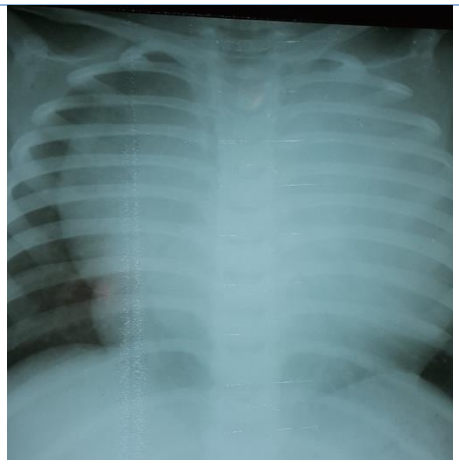
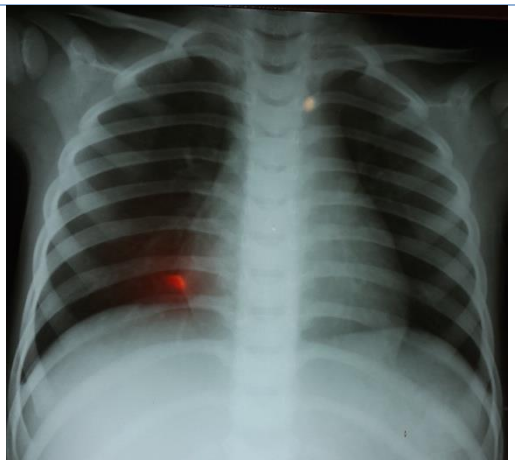
- An important **diagnostic tool** for leukaemia & lymphoma.
- **Define cell lineage** as myeloid or lymphoid.
- Identify **stage of differentiation** such as early precursor cells versus mature cell types
- Determine **subtypes of AML**
- **Classify lymphoid disorders** as B cell, T cell or NK cell lineage.

TABLE 5:ALL (ACUTE LYPHOBLASTIC LEUKEMIA) CLASSIFICATION

Immunophenotype	Frequency
B- Precursor ALL **Pro- B ALL** **Early Pre- B ALL** **Pre- B ALL**	80 % 3-4% 60-70% 20-30%
T Cell ALL	15 – 20 %
Mature B cell ALL **Clinically indistinguishable from disseminated Burkitt lyphoma** **Treated as NHL**	

T-CELL ALL comprises of ***15% to 20%*** of childhood ALL and more frequently associated with

- Older age at diagnosis
- Higher presenting leukocyte counts
- Bulky extramedullary disease manifesting as lymphadenopathy, anterior mediastinal mass, hepatosplenomegaly
- Overt CNS leukaemia
- An inferior outcome compared with those with B-precursor cell ALL,

	
Mediastinal Lymphadenopathy with T-ALL	After one week of treatment

CYTOGENETICS

- Used for diagnosis & prognosis of hematologic malignancies.
- Much leukaemia are characterized by specific chromosomal abnormalities, including specific translocations.

Better prognosis

- Normal karyotype
- Hyper diploidy

Poor prognosis

- t (8; 14)
- t (4; 11)

Very poor prognosis

- t (9; 22); BCR/ABL (+)

GENETICS OF CHILDHOOD ACUTE LYMPHOBLASTIC LYMPHOMA

Translocation	Fusion	Incidence	Cure rates
t(12;21)	*TEL-AML1*	25%	90%
t(1;19)	*E2A-PBX1*	5-6%	75%
t(4;11)	*MLL-AF4*	2-5%	35%
t(9;22)	*BCR-ABL*	3-5%	<30% (70 %) with TKI's

AML-ASSOCIATED CHROMOSOMAL ABNORMALITIES

Abnormality	Fusion	FAB	Incidence
t(8;21)	*AML1-ETO*	M2	15%
inv (16)	*CBFβ-MYH11*	M4Eo	8-12%
t(15;17)	*PML-RARα*	M3	8- 10%
t(9;11)	*MLL-AF9*	M4,M5	7%
t(11;19)	*MLL-ELL*	M4, M5	1%
t(1;22)	Unknown	M7	1%

DIFFERENTIAL DIAGNOSIS

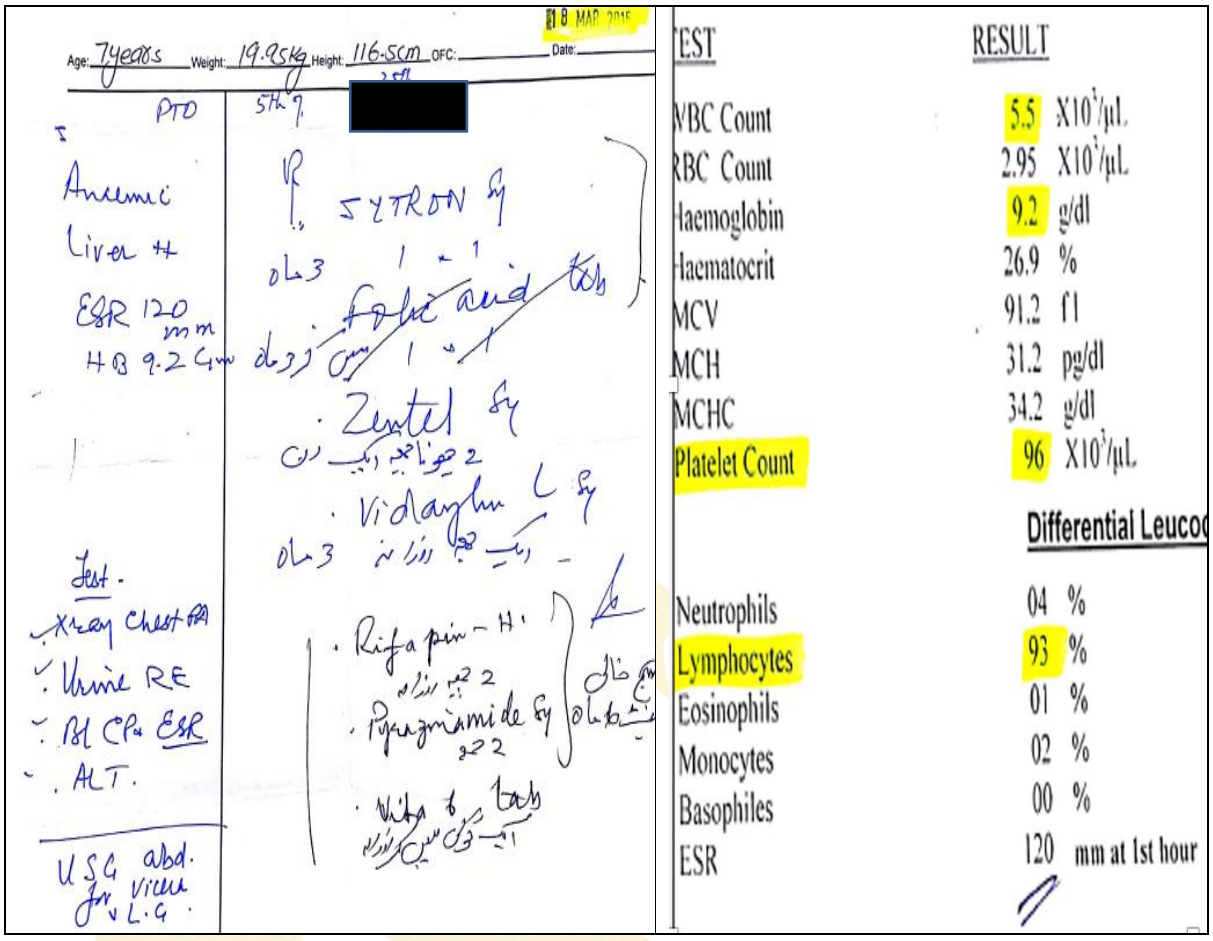
- Juvenile Rheumatoid Arthritis-
  - caution to use steroids / oral methotrexate before completely ruling out leukaemia
- Mycobacterial infections (TB & non-TB)
- Infectious mononucleosis
- Aplastic anemia
- Idiopathic thrombocytopenic purpura
- Neuroblastoma

DIFFERENTIAL DIAGNOSIS OF ACUTE LEUKAEMIA: CASE HISTORIES

CASE- 1

- **7 years girl**
- **H/O**
  - **Fever off and on**
  - **Leg pains.**

4 months



Age: 7years Weight: 19.95kg Height: 116.5cm OFC: Date: 18 MAR 2015

PTO 5th d.

Anemic
Liver +
ESR 120 mm
HB 9.2 Gm

Rx
SYTRON Sy
od 3 1 - 1
. folic acid Tab
od 3 1 - 1
. Zentel Sy
. Vidaylin L Sy
od 3

Test.
. X-ray Chest PA
. Urine RE
. Bl CP, ESR
. ALT.

USG abd.
for viral L.G.

. Rifapin - H
. Pyrazinamide Sy
. Vitamin B Tab

TEST	RESULT	
WBC Count	5.5	$X10^3/\mu L$
RBC Count	2.95	$X10^3/\mu L$
Haemoglobin	9.2	g/dl
Haematocrit	26.9	%
MCV	91.2	fl
MCH	31.2	pg/dl
MCHC	34.2	g/dl
Platelet Count	96	$X10^3/\mu L$
		Differential Leuco
Neutrophils	04	%
Lymphocytes	93	%
Eosinophils	01	%
Monocytes	02	%
Basophiles	00	%
ESR	120	mm at 1st hour

CASE NO. 2

Idiopathic Thrombocytopenic Purpura

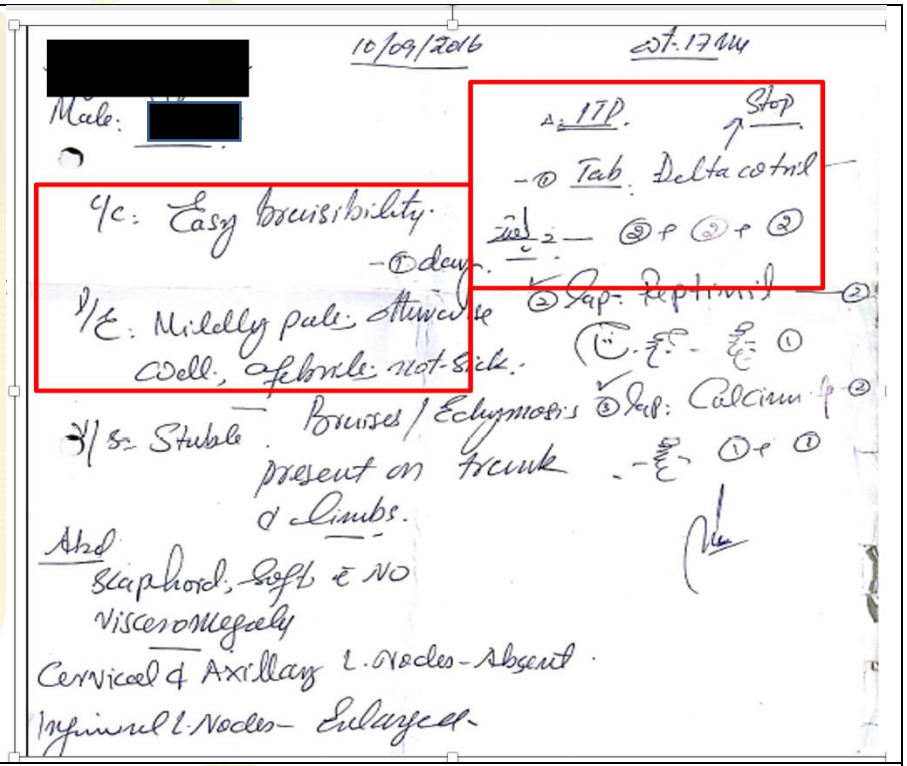
caution to use steroids before completely ruling out leukemia

- 13 yrs old girl
- 3 months H/O
  - Body aches
  - Fever off and on
  - WBC-10.2, Hb-8.7, PLTs-30
- **ITP**
  - Platelets transfusion
  - Prednisone
- Neck Swellings – 1 month
- FNAC- NHL

19/12/13

- WBC-14.86, Hb-7.7, PLTs-8
- BMA- ALL
- Immunophenotyping: T ALL
- CSF- Clear
- Cytogenetics: 46 XX
- Echo-EF 65%
- UKALL2011 Regimen B

CASE-3

5 years old boy Presented with Easy bruisibility for few days On Examination Mildly pale Otherwise Well Afebrile Not sick No visceromegaly **Blood CP** Hb: 9.9 TLC: 36.2 Plts: 65,000 **Treatment** Deltacortil 2 tabs TDS	
AFTER 10 DAYS OF PREDNISONE	**BONE MARROW ASPIRATION PERFORMED**

19/09/16

After 10 days of prednisone

Bone marrow Aspiration

Iron Deficiency Anaemia

Megaloblastic Anaemia

Name [redacted] Age :5 Years Sex : Male
Ref. By Date : 19-09-2016 Time : 19:34:54
Request : Peripheral Smear - Reticulocyte Count - Bone Marrow With Aspiration - Trephine Biopsy -

BONE MARROW

SITE	: Rt. PIS.
CELLULARITY	: Normocellular.
ERYTHROPOIESIS	: Active and mainly normoblastic with prominent megaloblasts.
MYELOPOIESIS	: Active with all stages of maturation.
MEGAKARYOCYTES	: Increased.
PLATLETS	: Reduced.
LYMPHOPOIESIS	: Normal.
PLASMA CELLS	: Normal.
ABNORMAL CELLS	: Nil. No storage cells seen.
HAEMOPARASITES	: Nil.
HAEMOPHAGOCYTOSIS	: Nil.
M/E RATIO	: 1 : 1
IRON	: Absent.

OPINION : (1) Iron Deficiency and Megaloblastic Anemia.
(2) Thrombocytopenia is also suggestive of peripheral destruction.

The child presented after one month with high WBC counts.

22 October 2016

WBC	188.47 *	[10^3/uL]		
RBC	1.22 -	[10^6/uL]		
HGB	2.7 -	[g/dL]		
HCT	8.9 -	[%]		
MCV	73.0 -	[fL]		
MCH	22.1 -	[pg]		
MCHC	30.3 -	[g/dL]		
PLT	8 *	[10^3/uL]		
RDW-SD	49.3	[fL]		
RDW-CV	20.2 +	[%]		
PDW	----	[fL]		
MPV	----	[fL]		
P-LCR	----	[%]		
PCT	----	[%]		
NEUT	----	[10^3/uL]	----	[%]
LYMPH	----	[10^3/uL]	----	[%]
MONO	----	[10^3/uL]	----	[%]
EO	0.34 *	[10^3/uL]	0.2 *	[%]
BASO	0.09 *	[10^3/uL]	0.0 *	[%]

TLC 1,88,470/cmm

Hb 2.7g/dl

platelet count 8000/ml

DLC

N: 05%

L: 25%.

Blast cell 70%.

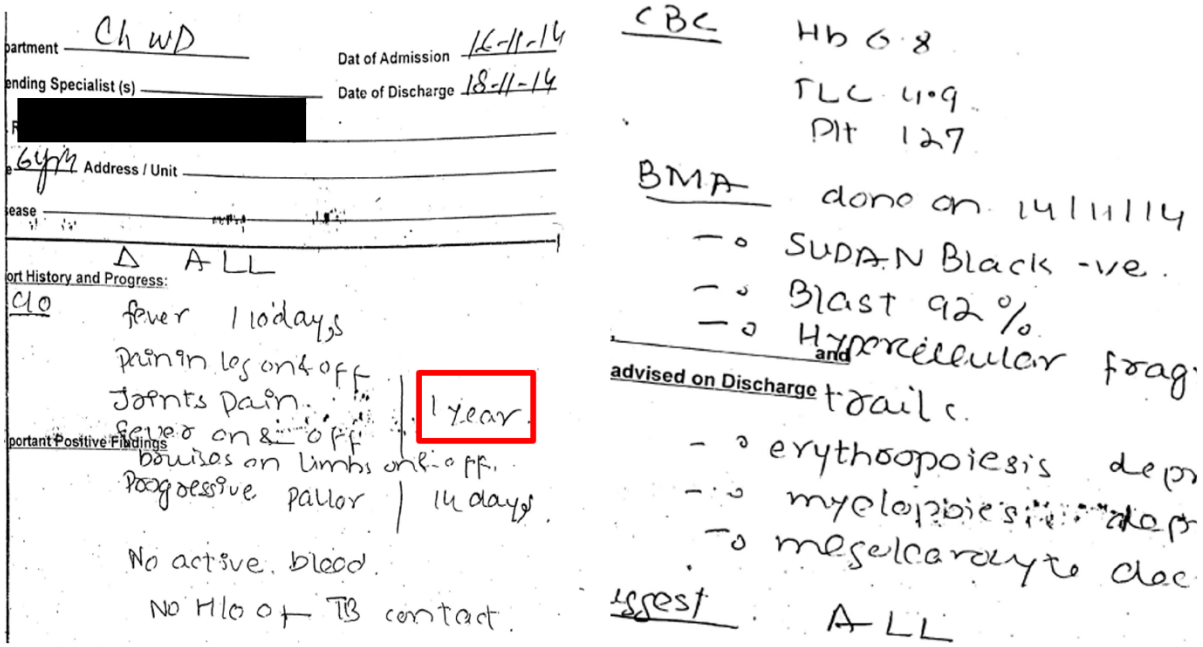
Bone Marrow Cytology

PARAMETERS	RESULT
Bone Marrow Cytology	
SITE:	Rt.PSIS.
CELLULARITY:	Hypercellular.
GRANULOPOIES	Depressed.
ERYTHROPOIESI	Depressed.
LYMPHOPOIESIS	Depressed.
Advice:	Immunohistochemistry.
PLASMA CELLS:	Depressed.
ABNORMAL CEL	About 85% of the bone marrow cells are blasts which are small to m
HEMOPARASITE	Nil.
SPECIAL STAIN:	POX negative in blasts.
Opinion:	Acute leukemia morphologically suggestive of acute lympoblastic le
MEGAKARYOCY	Depressed.

JUVENILE RHEUMATOID ARTHRITIS-

Juvenile Rheumatoid Arthritis-

caution to use steroids / oral methotrexate before completely ruling out leukemia



partment Ch WD
Dat of Admission 16-11-14
ending Specialist (s)
Date of Discharge 18-11-14
[redacted]
64yM Address / Unit
ease
Δ ALL
ort History and Progress:
C/O fever 1 10 days
Pain in leg on & off
Joints pain
fever on & off
bruises on limbs on & off.
Progressive Pallor 14 days
1 year
portant Positive Findings
No active bleed.
No H/O of TB contact.

CBC Hb 6.8
TLC 4.9
Plt 127
BMA done on 14/11/14
- SUDAN Black -ve.
- Blast 92%
- Hypercellular frag
and
advised on Discharge trail c.
- erythropoiesis dep
- myelopoiesis dep
- megakaryocyte dec
Assess ALL

AUTOIMMUNE HEPATITIS

Autoimmune Hepatitis

- June 2015
- 5 years old girl from Gilgit
- Jaundice→ resolved

Patient: [redacted] (F) (5 Y)

Function Test

Serum ALT	*92* *	Upto 36 U/l
Serum Albumin	35	35 - 50 g/l
Serum Total Bilirubin	7	0 - 17 umol/l
Serum Alkaline Phosphatase	*289* *	< 258 U/L

Thyroid Profile

Serum Free T4	15.6	8.0-21.0 (pmol/l)
Serum TSH	4.1	0.4 - 4.5 m IU/L

Comment Results suggest biochemically euthyroid status

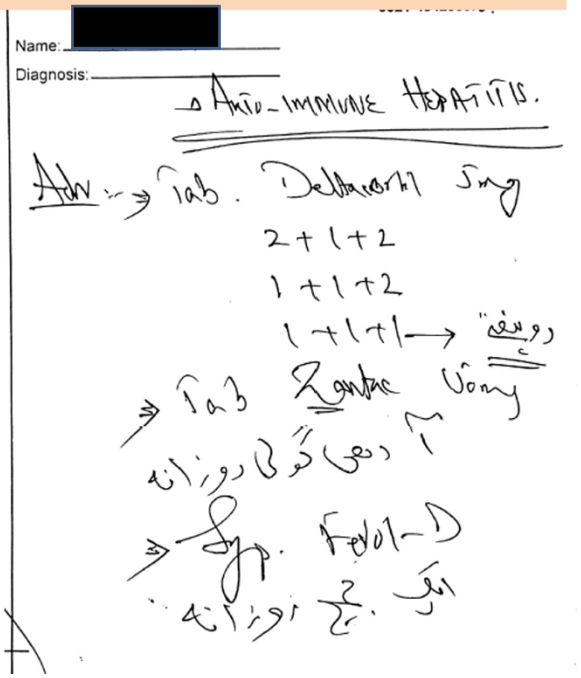
Report Authorized By: Capt.Saima Bashir

Hepatitis C Markers

Anti HCV — Negative — By 3rd Generation ELISA

Hepatitis B Markers

HBsAg — Negative — BY ELISA Method



Presented with pallor and bruses and BMA confirmed the diagnosis of ALL

22 June 2015

Entered By [redacted]
Entered At 4/6/2015 4:24:28 PM
Print Date 4/6/2

[redacted]

Blood Complete Picture

Blood Counts

TLC	2.7	4.0 - 10.0 X 10^9 /l
RBC	2.49	3.80 - 5.80 X 10^12 /L
Haemoglobin	7.6	12.0 - 15.0 g /dL
PCV	0.24	0.37 - 0.47 l/L
MCV	96.4	76.0 - 96.0 fL
MCH	30.5	27.0 - 32.0 pg
MCHC	31.7	31.5 - 34.5 g/dL
Platelet Count	161	150 - 400 x10^9/L

Differential Leucocyte Count

Neutrophils	16	40 - 80 %
Lymphocytes	83	20 - 40 %
Monocytes	01	2 - 10 %

Entered By [redacted]
Entered At 26-10-2015 12:39:19
Print Date 29-10-

[redacted]

Bone Marrow Aspiration

Blood Counts

TLC	19.35	4.0 - 10.0 X 10^9 /L
RBC	2.17	3.80 - 5.80 X 10^12 /L
Haemoglobin	5.4	12.0 - 15.0 g /dL
PCV	0.16	0.37 - 0.47 l/L
MCV	77.0	76.0 - 96.0 fL
MCH	24.9	27.0 - 32.0 pg
MCHC	32.3	31.5 - 34.5 g/dL
Platelet Count	08	150 - 400 x10^9/L

Differential Leucocyte Count

Lymphocytes	26	20 - 40 %
Monocytes	04	2 - 10 %
Blast Cells	70	
Nucleated RBCs	01	/ 100 WBC

Red cell morphology

Hypochromia	+
Microcytosis	+

Sampling

Bone marrow aspirate no.	1407/2015
Site	Posterior iliac spine
Aspiration	Easy
Consistancy of bone	Normal

Microscopy

Cellularity	Aparticulate marrow with Cellular trails
Erythropoiesis	Depressed
Myelopoiesis	Depressed
Megakaryocytes	Depressed
Blasts	85 %

Cytochemistry

Sudan Black	Negative

Opinion Acute lymphoblastic leukemia
Suggest MLL, E2A-PBX, BCR-ABL, TEL-AML1 rearrangements from Hematology Department, AFIP.

TREATMENT PRINCIPLES

- Supportive medical care
- Chemotherapy

SUPPORTIVE CARE

- Psychosocial support of patient and family
- Tumour Lysis Syndrome Prevention
    - Hyper-hydration
    - Allopurinol (Rasbruicase for high-risk cases)
    - Management of electrolyte abnormalities
- Transfusion of blood products (RCC, Platelets, FFP)
- Treatment of infection with broad spectrum antibiotics

TREATMENT- ALL

The aim of therapy in acute leukaemia is to cure the patient.

A complete remission usually achieved after 1 month of treatment.

RISK STRATIFICATION

- Age of the patient
    - < 1 yr, 1-10 yrs and ≥10 yrs
- WBC count at diagnosis WBC-≥ 50 x10 ^{9}
- Immunophenotype of leukemic cells
    - T lineage
    - Early b lineage (pre-b)
    - Mature b lineage,
- Cytogenetics

RISK CLASSIFICATION AND REMISSION INDUCTION THERAPY IN ALL

- Standard risk (around 60-65%)
    - All children >1 <10 yrs with WBC <50 x 10^{9}/l without any high-risk cytogenetics-regimen A (three drug; Dexamethasone, vincristine and asparaginase)
- Intermediate risk (around 20-30%)
    - All children ≥10 yrs or with WBC ≥ 50 x 10^{9}/l without any high-risk cytogenetics-regimen B (four drug; Dexamethasone, vincristine, daunorubicin and asparaginase)
- High risk (around 10-12%)
    - All children, who are ser, BCR-ABL +ve, hypodiploidy (<44 ch), MLL rearrangement-regimen C (four drug; Dexamethasone, vincristine, daunorubicin and asparaginase)
- **CNS prophylaxis;** Methotrexate ITs,
- **Treatment duration**: 4 weeks
- Bone marrow aspiration day 8/15/29 to assess remission status.

PROGNOSTIC FACTORS

- Major prognostic factors include.
    - The clinical features that are present at diagnosis,
    - Biologic and genetic features of leukaemia cells, and
    - Early response to treatment.

PROGNOSTIC FACTORS OF ALL

Variable	Favorable Factor	Adverse Factor	Use in Risk Stratification
Age	>1 to <10 years	< 1 or ≥ 10 years	Yes in NCI
Gender	Female	Male	No
Race	White, Asian	Black, Hispanic	No
Initial WBC count	Lower (<50,000/mm3)	Higher (≥50,000/mm3)	Yes
Immunophenotyping	B-cell lineage	T-cell lineage	used to select therapy backbone
Cytogenetic features	Trisomies ETV6-RUNX1, hyperdiploidy	BCR-ABL1, MLL rearrangement hypodiploidy	Often used to select treatment intensity, HSCT

CNS disease: an adverse prognostic factor			
Early response to treatment			
Response to 1 wk of glucocorticoid therapy	Good response to prednisone (<1000 blasts/mm3)	Poor response to prednisone (≥1000 blasts/mm3)	Easy to measure and used by many groups
Marrow blasts after 1–2 weeks of Chemo	M1 marrow (<5% blasts) by day 8 or 15	No M1 marrow (≥5% blasts) by day 8 or 15	Easy to measure and used previously by many groups; now being supplanted by MRD
MRD quantitation during or at end of induction	Reaching low (<0.01%) or undetectable MRD by specific time point	Persistence of MRD ≥0.01% at specific time points; the higher it is, the worse the prognosis	Most important single prognostic factor for contemporary therapy; critical for modern risk stratification
MRD at 3–4 mo	Low (<0.01%), preferably undetectable	Persistence of MRD ≥0.01%	May help select patients for HSCT or new therapies in first remission

POST-REMISSION THERAPY IN STANDARD-RISK ALL

- Consolidation Phase
- Interim Maintenance
- Delayed Intensification
- Maintenance therapy:
    - Vincristine on 4 weekly basis.
    - Dexamethasone for 5 days every 4 weeks
    - Methotrexate weekly PO
    - 6 Mercaptopurine daily PO
    - CNS prophylaxis- IT MTX every 12 weeks
- Duration; - 2 yrs from Day 1 of Interim Maintenance

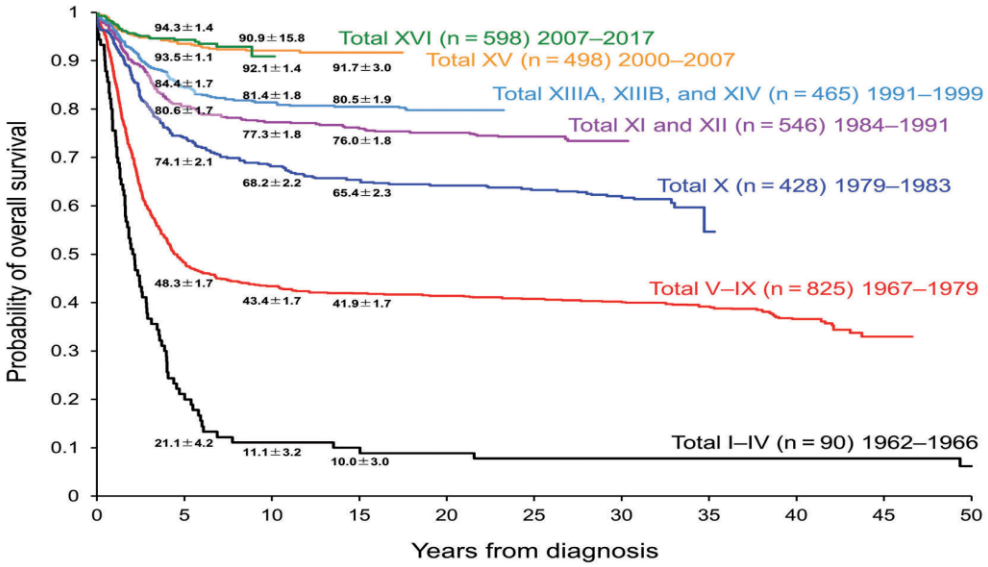
ALLOGENEIC SCT IN ALL; Allogeneic transplant in first CR is recommended for the following groups:

- iAMP21 with >5% blasts at day 29.
- MLL rearrangement positive or hypodiploid < 44 with M2 marrow (>5% blasts) at day 29
- M3 marrow at day 29
- BCR: ABL positive, follow guidance within Philadelphia ALL protocol.
- t (17;19) (E2A-HLF) positive

PROGNOSIS- ALL

- The overall 5-year event free survival (EFS) rate for Paediatric ALL currently approaches 87 % in the developed world.

Change in overall survival of pediatric patients treated on the historical St. Jude Total Therapy studies.



TREATMENT -AML

STANDARD INDUCTION THERAPY

- ADE chemotherapy course 1 (A10, D3, E5)
- ADE chemotherapy course 2 (A 8, D3, E5)
    - Cytosine Arabinoside, Daunorubicin, Etoposide
    - All drug doses in course 1 and 2 should be reduced by 25% for children aged less than one year and/or weighing 10kg or less.
- 80%-90% achieve hematologic CR

POST-REMISSION THERAPY

- Historical controls suggest **High dose Ara-C** consolidation improves outcome.
- 60-70% of children with matched family donors achieved cure with Allo transplant, but data is conflicting

MAINTENANCE THERAPY: No data demonstrates efficacy.

Session 8: Childhood Brain Tumors

SESSION DURATION

- 14:30 - 15:00 pm (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session, participants will learn and consider CNS tumours in the differential diagnosis for children with headache, vomiting, lethargy, ataxia, visual changes, prolonged torticollis, nystagmus, papilledema, or seizures, and should consider appropriate imaging and specialist referral according to the history and a comprehensive physical examination.

KEY POINTS

- Brain tumours are the 2nd most common cancers in children.
- They account for about 20% of all childhood cancers.
- More than 4,000 brain and spinal cord tumours are diagnosed each year in children and teens in USA.
- Most childhood brain tumours (60–70%) arise from glial cells and tend not to metastasize outside the CNS.
- Most are infratentorial in location.
- **There are no pathognomonic features of brain tumours**, making their diagnosis in children difficult. Headache, vomiting, lethargy and seizures are the most common symptoms associated with central nervous system tumours, but these occur at greater frequency with other, more benign conditions.
- Psychologic changes are frequent among children with central nervous system lesions.

TYPES OF BRAIN TUMOURS

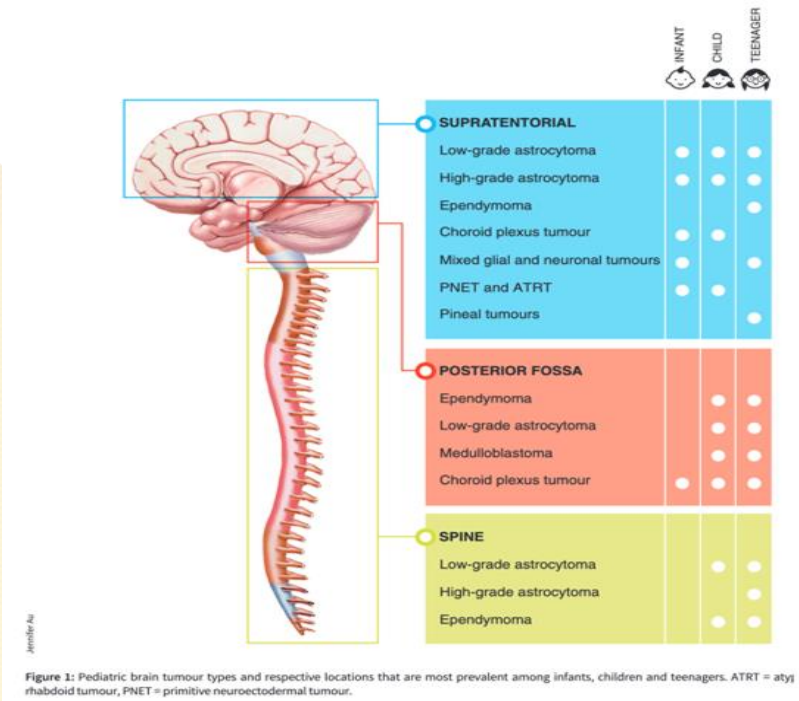
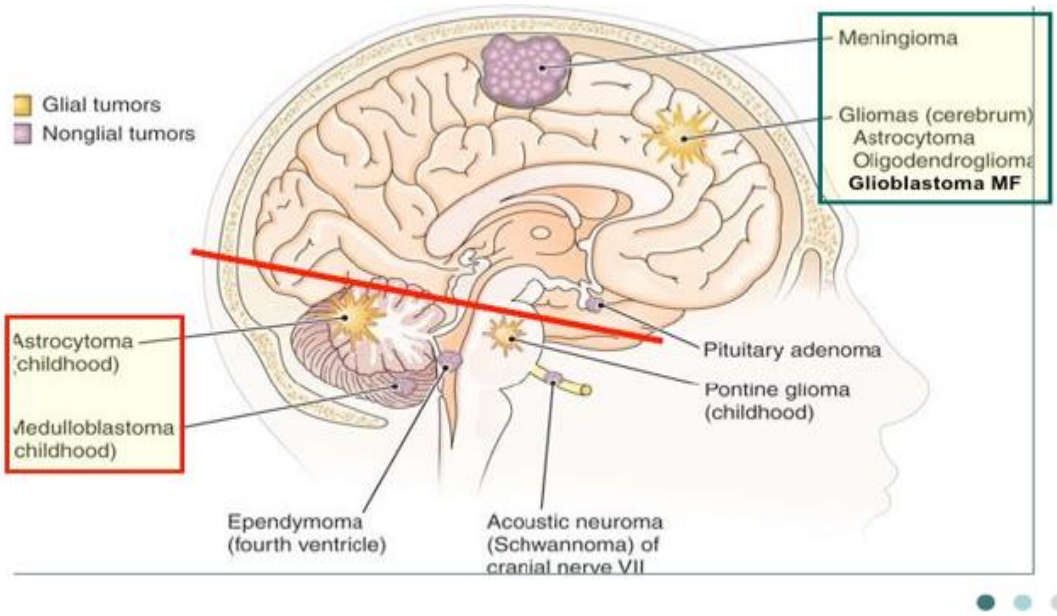
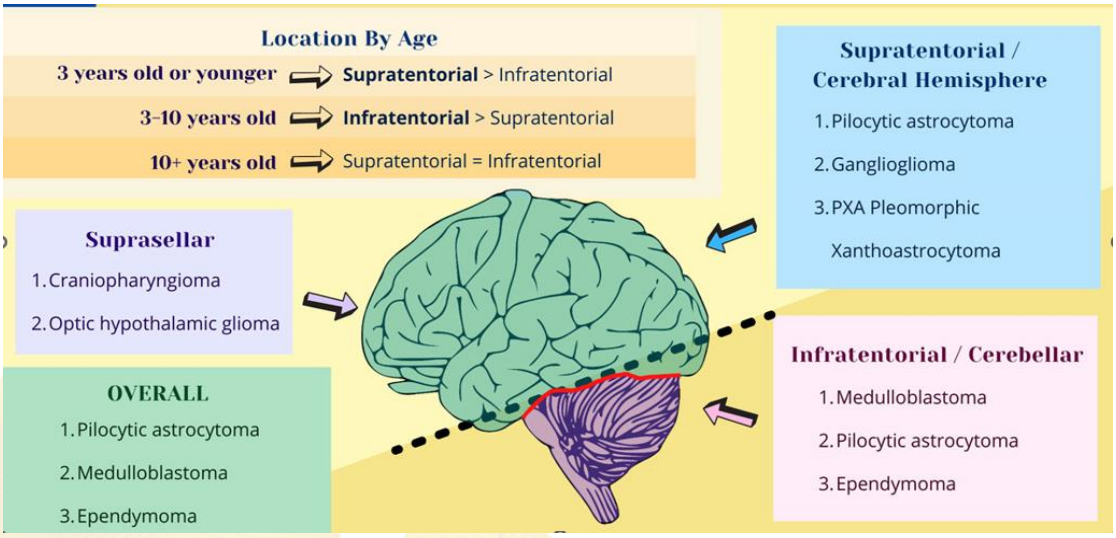


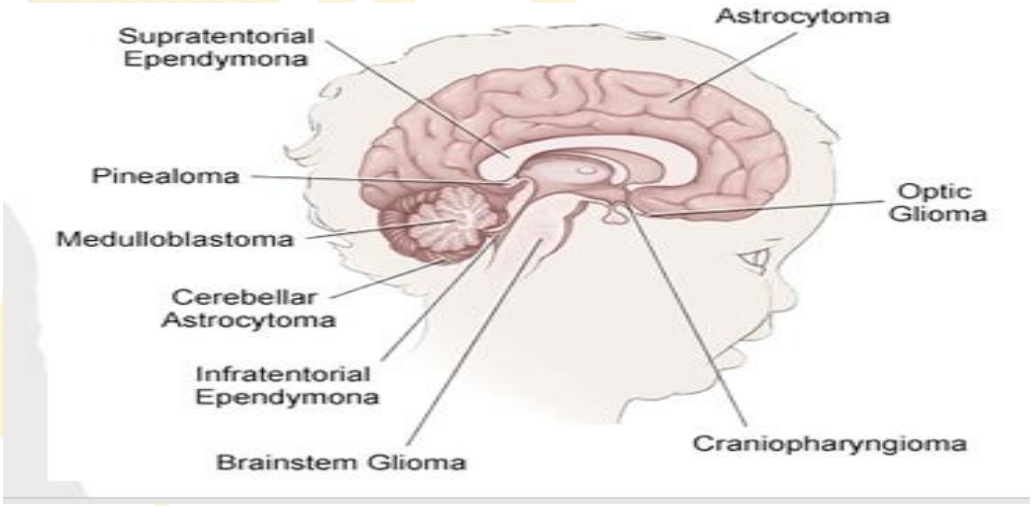
Figure 1: Pediatric brain tumour types and respective locations that are most prevalent among infants, children and teenagers. ATRT = atyp rhabdoid tumour, PNET = primitive neuroectodermal tumour.



MOST COMMON PAEDIATRIC BRAIN TUMOURS



TYPES AND LOCATION OF BRAIN TUMOURS



MOST COMMON CNS TUMOURS

THE 10 MOST COMMON SYMPTOMS

- Headache
- Seizure
- Nausea or Vomiting
- Issues with the vision
- Peripheral neuropathy & neurological symptoms
- Confusion and issues with self-identity
- Memory loss and issues with perception & judgement
- Sleep-wake disturbances.
- Communication Issues (Language impairment)
- Hearing loss/issues & issues with balance

BRAIN TUMOURS - SIGNS/SYMPTOMS

INCREASED INTRACRANIAL PRESSURE - SYMPTOMS

- Headache (am)
- Nausea/vomiting (am)
- Double vision
- Head tilt
- Decreased alertness.
- Lethargy/irritability
- Poor feeding, Failure to thrive (FTT)
- Endocrine dysfunction
- Unexplained behaviour changes
- Change in affect, motivation, energy level.

INCREASED ICP – SIGNS

- Papilledema, optic atrophy
- Loss of vision
- OFC (head circumference) increased.
- Bulging fontanelles, spreading sutures
- "Setting sun" sign (Parinaud syndrome)
- Increased blood pressure, low pulse

POSTERIOR FOSSA & BRAINSTEM TUMOURS - CLINICAL FEATURES

POSTERIOR FOSSA PRIMARY

- Ataxia
- Tremors
- Dysarthria
- Stiff neck
- Papilledema

BRAINSTEM PRIMARY

- Extremity weakness
- Cranial nerve signs
    - double vision
    - facial weakness
    - swallowing dysfunction

HEMISPHERIC TUMOURS – CLINICAL FEATURES

- Hemiparesis
- Hemianopsia
- Aphasia
- Seizures

PHYSICAL EXAMINATION FINDINGS

CRANIAL NERVES

- Double vision
- Nystagmus
- Head tilt
- Facial palsy
- Abnormal eye movement
- Downward deviation of eyes
- Difficulty swallowing
- Deviation of tongue
- Reduced hearing

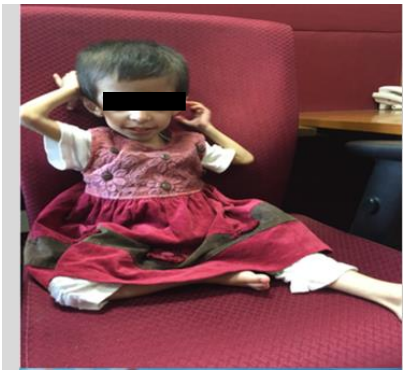
OTHERS

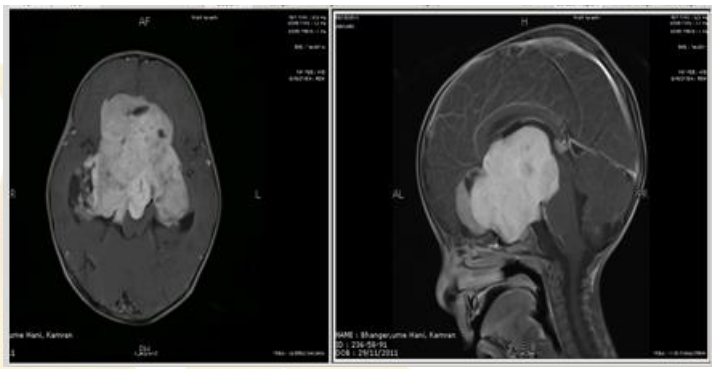
- Paresis
- Dysmetria

- Hyperreflexia/Hyporeflexia
- Papilledema
- Positive Romberg sign
- Increased muscle tone
- Clonus
- Decreased muscle tone.
- Heel–knee–shin ataxia.

CASE-1 DIENCEPHALIC SYNDROME

- 4 years old girl with malnutrition.
- Normal Calorie intake
- Weight 4.8 kg



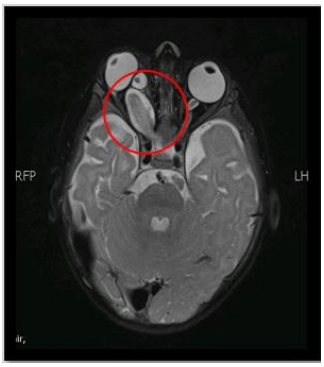


DIENCEPHALIC SYNDROME

- A rare disorder caused by a tumour that is usually located in the diencephalon. The diencephalon includes the hypothalamus and the thalamus.
- Affected infants and young children may develop symptoms that include the failure to gain weight and grow as would be expected based upon age and gender (***failure to thrive***) and abnormal progressive thinness and weakness (***emaciation***).
- Affected infants and children may behave in an alert and ***happy*** manner, or more frequently, infants and young children are ***irritable***.
- May have additional symptoms as ***vomiting***, ***vision*** abnormalities, ***nystagmus***, ***headaches***.
- Diencephalic syndrome can progress to cause severe, life-threatening complications.
- **Treated** by surgery, radiation, chemotherapy and/or molecular-targeted therapy.

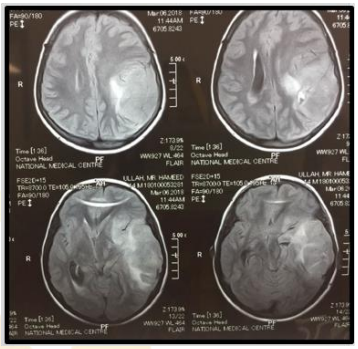
CASE-2 OPTIC NERVE GLIOMA

- 10 months old presented with **proptosis**.
- Went to multiple pediatricians then referred to an ophthalmologist who did this MRI Brain



CASE-3 DIAGNOSIS GBM

- 14 years old boy GTC seizures for the last 8 months.
- Have been to various pediatricians and neurologists
- MRI done after 8 months.



Died within one month of diagnosis.

Final Diagnosis; Left frontal tumor

- Glioblastoma, IDH-mutant COMMENT
    - WHO grade IV
    - IDH1R132H positive by immunohistochemistry
    - P53 positive, ATRX retained.
    - Mismatch repair deficient (see comment)

Comment

Immunostaining shows loss of MSH6 in tumor cells with retention in normal cells. MSH2 is weak or absent in tumor cells. This is suggestive of a possible monoallelic germline mutation in MSHS. Genetic counseling is recommended.

HOW TO AVOID DELAY IN THE DIAGNOSIS

- ***Early detection is essential*** to allow the best possible treatment by an experienced team of paediatric neurosurgeons and oncologists, to optimize outcomes.
- CNS tumours in children are ***often initially misdiagnosed*** as more common paediatric conditions, such as migraine, gastroenteritis, or psychologic or behavioural problems.
- ***Headache, vomiting, lethargy, and seizures*** are the most common symptoms associated with CNS tumours, but they are nonspecific and present more frequently with other, more benign conditions.
- The diagnosis of CNS tumours necessitates a ***comprehensive clinical history and complete examination***, in addition to advanced imaging, such as ***CT scan or MRI*** to confirm clinical suspicion.
- Initial management should include ***imaging*** after ***four weeks*** of persistent headache, after four weeks of persistent lethargy or withdrawal (in preschool children), after ***two weeks*** of persistent nausea or vomiting (or both), or after two weeks of persistent visual changes.
- Patients should be referred to a paediatrician or a paediatric neurologist if symptoms persist or if physical examination suggests any of the signs and symptoms listed below.

CONCLUSION

- Physicians should consider CNS tumours in the ***differential diagnosis*** for children with headache, vomiting, lethargy, ataxia, visual changes, prolonged torticollis, nystagmus, papilledema or seizures, and should consider appropriate imaging and specialist referral according to the history and a comprehensive physical examination.
- For patients with nonspecific symptoms and normal neurologic examination, ***imaging*** should be considered if the symptoms do not resolve as expected.
- Standards for acceptable prediagnostic symptomatic intervals must be established to avoid delay in diagnosis and suboptimal outcomes.
- For patients with ***paresis or unsteadiness***, ***prompt imaging*** should be strongly considered.
- For those with headache or vomiting and normal results on a detailed neurologic examination, imaging should be considered if symptoms do not resolve after several weeks.

MANAGEMENT

SURGERY

- The purpose of ***neurosurgical intervention*** is threefold.
    - To provide a tissue ***biopsy*** for purposes of histopathology and cytogenetics.
    - To attain ***maximum tumour removal*** with fewest neurologic sequelae.
    - To ***relieve associated increased ICP due to CSF obstruction***.
- Use of pre-operative ***dexamethasone*** can significantly decrease peri-tumoral oedema, thus decreasing focal symptoms and often eliminating the need for emergency surgery.
- For patients with increased hydrocephalus that is moderate to severe, endoscopic, or standard ***ventriculostomy*** can decrease ICP.
- Tumour resection is safer when performed 1–2 days following reduction in oedema and ICP by these means.

CHEMOTHERAPY

- In newly diagnosed, progressive ***LGG*** in patients < 5 yrs of age Vincristine & Carboplatin is recommended.

- In HGG **multi-agent adjuvant chemotherapy** added to postoperative radiation results in a significant (but modest) improvement in disease-free survival compared with postoperative radiation alone.
- But without a reasonable resection, chemotherapy is ineffective. Chemotherapy includes Procarbazine (or prednisone), CCNU, vincristine and Temozolomide.

RADIOTHERAPY

- XRT is used when chemotherapy has failed in unrespectable symptomatic tumours, especially in older patients.

PROGNOSIS

THE 5- AND 10-YEAR OS RATES

- For **completely resected low-grade supratentorial astrocytoma** treated with surgery alone are 76–100% and 69–100%, respectively.
- In the **posterior fossa** these rates approach 100%.
- In patients with **partially resected low-grade astrocytoma** who are observed without treatment or who are treated with postoperative radiotherapy the 5- and 10-year survival rates are 67–87% and 67–94%, respectively.

RECURRENCE

- Recurrent low-grade astrocytoma should be approached surgically when possible.
- If not completely resectable, chemotherapy and/or radiation should be given, depending on prior therapy received.

session 9: Lymphoma

SESSION DURATION

- 15:00 - 15:30 pm (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session Participants can identify childhood lymphoma, its signs and symptoms through observation, questions related to the clinical history, and a complete physical examination.

KEY POINTS

- Hodgkin lymphoma (HL) is diagnosed in approximately 1100 children and adolescents less than 20 years of age in the United States each year, accounting for 6% of overall childhood cancer diagnoses, and ranks as the most common malignancy among adolescents 15 to 19 years old[8].
- It is one of the most curable forms of childhood cancer, with estimated 5-year survival rates exceeding 98%, yet long-term overall survival declines primarily from delayed effects of therapy.

LYMPHADENOPATHY

- Lymphadenopathy is **most common in young children** whose naïve immune systems respond more frequently to newly encountered infections.
- There are many different causes of lymphadenopathy, and thus, a **thorough history and physical** are critical in establishing a diagnosis.
- **Enlargement of lymph nodes** is often secondary to **infection** and is frequently **benign and self-limited**.
- **Viral or bacterial infections** lead to localized responses from lymphocytes and macrophages, leading to enlargement of nodes. There may also be localized infiltration by inflammatory cells in response to an infection of the nodes themselves. This is known as a **lymphadenitis**.
- Finally, it is crucial to rule out rarer, more serious causes such as **lymphomas or leukaemias,** which are due to proliferation of neoplastic lymphocytes or macrophage.
- Some questions that will help narrow the differential include:

Less concerning findings	Increased risk of malignancy
Localized	Generalized adenopathy
Cervical, inguinal, and axillary regions	Occipital, auricular, supraclavicular, mediastinal, epitrochlear or posterior cervical nodes
< 1-2 cm (depending on location)	> 2 cm
Erythema	Firm and matted
Tender	Nontender
Warm	Systemic symptoms
Fluctuant	Generalized adenopathy

HODGKIN LYMPHOMA

[8] Allen CE, Kelly KM, Bollard CM. Pediatric lymphomas and histiocytic disorders of childhood. Pediatr Clin North Am. 2015 Feb;62(1):139-65. doi: 10.1016/j.pcl.2014.09.010. PMID: 25435117; PMCID: PMC4250829

- HL formerly called HD accounts for approximately **7 %** of childhood cancers[9]
- The **incidence** of HL in childhood **varies by age.**
    - Rare in infants but is the most common cancer in the 15- to 19-year-old age group.
- HL arises from germinal centre or post-germinal centre **B cells**.
- The malignant cells of HL are clonal **Hodgkin/Reed-Sternberg (HRS) cells** which usually constitute <1 % of the cells in involved lymph nodes.
- The rest of the lymph node contains a **heterogeneous cellular infiltrate** consisting of lymphocytes, eosinophils, macrophages, plasma cells, and fibroblasts.

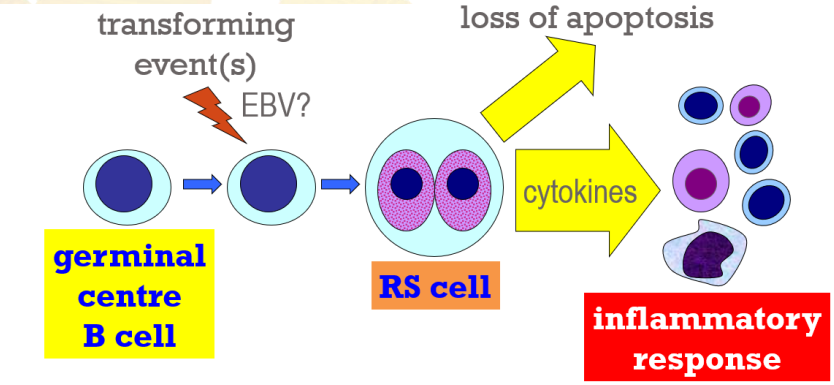
HL-Subgroups

- HL can be divided into **two major sub-groups**, based on the appearance and immunophenotype of the tumour cells.
- **Classical HL** – The **tumour cells** in this group are derived from **germinal centre B cells.** These tumour cells — **Hodgkin and Reed-Sternberg (HRS) cells** — are usually very rare in the tissue. Although HRS cells are **derived from mature B cells**, they have largely lost their B cell phenotype and show a very unusual co-expression of markers of various hematopoietic cell types.
- **Nodular lymphocyte predominant HL** – The tumour cells in this subtype retain the immuno-phenotypic features of germinal centre B cells.

Histology

- Based on the characteristics of the reactive infiltrate and the morphology of the Reed-Sternberg cells, **four subtypes of classic Hodgkin lymphoma** are distinguished in the WHO classification.
    - **Lymphocyte-rich** Hodgkin lymphoma (LRHL),
    - **Lymphocyte-depleted** Hodgkin lymphoma (LDHL),
    - **Mixed-cellularity** Hodgkin lymphoma (MCHL), and
    - **Nodular sclerosis** Hodgkin lymphoma (NSHL).
- **Nodular lymphocyte predominant HL (NLPHL)** is non-classical HL with expression of different immuno-phenotypic features.

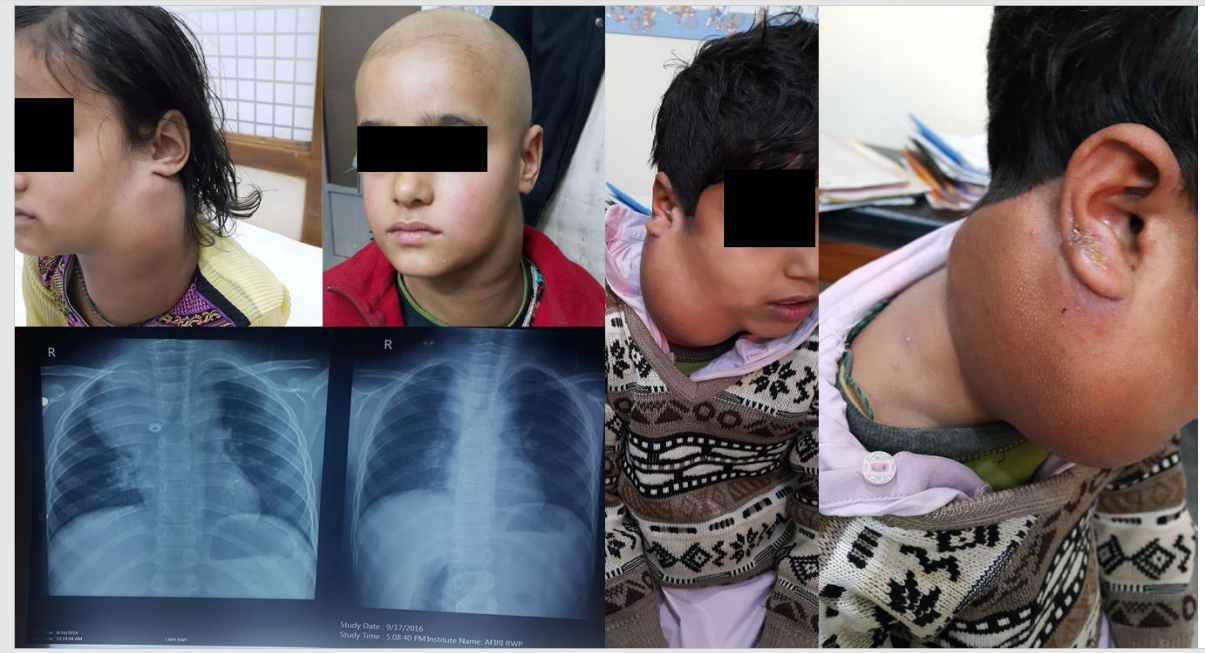
A possible model of pathogenesis



[9] (CA Cancer J Clin. 2014 Mar-Apr;64(2):83-103)

Signs and symptoms

- **Clinical features of Hodgkin lymphoma** include the following:
- Asymptomatic lymphadenopathy
- Unexplained weight loss, unexplained fever, night sweats
- Chest pain, cough, shortness of breath
- Pruritus
- Splenomegaly and/or hepatomegaly
- Superior vena cava syndrome may develop in patients with massive mediastinal lymphadenopathy.



Cervical and mediastinal lymphadenopathy in Hodgkin Lymphoma and response to chemotherapy

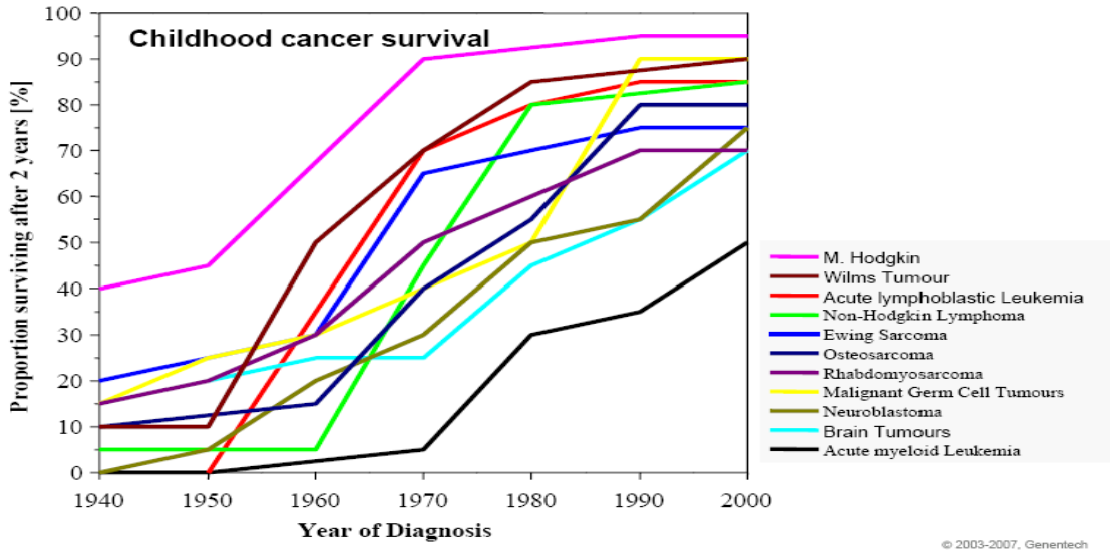
TREATMENT

- Current treatment protocols
  - **Risk-based** and **response-adapted approach.**
  - **Multi-agent chemotherapy** with or without low-dose involved-field or involved-site **radiation therapy.**

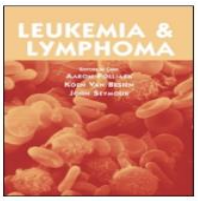
Outcome

- In developed countries, **the 5-year survival rate** of PHL increased from 81% to **more than 95%** between 1975 and 2010[10].
- Survival in **developing countries** is still significantly lower, due to **late presentation, abandonment of therapy and inadequate supportive and critical care**[11].
- Data of few published studies from **Pakistan** shows overall survival ranging from **76% to 84%**[12].

[10] Smith MA et al. Cancer. 2014;120(16):2497-506, White Y et al. The Journal of pediatrics. 2013;162(6):1090
[11] Ghafoor T. Prognostic factors in PHL: Leuk Lymphoma. 2020;61(2):344-350
[12] Faizan M et al JCPSP. 2016;26(11):904-7.



Prognostic factors [11]



Leukemia & Lymphoma

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Prognostic factors in pediatric Hodgkin lymphoma: experience from a developing country

Tariq Ghafoor

- **Delay in starting treatmen**t for more than one year, use of **anti-tuberculosis treatment**, **malnutrition**, presence of **B symptoms** and advanced stage disease adversely affected the treatment outcome.
- **OS** was **95.7%** in children getting treatment within one year from the onset of symptoms and decreased to **61.5%** in children getting treatment after one year (p <.001)
- **OS** was **100%** in stage I, **91.2%** in stage II, **95.3%** in stage III, and **77.8%** in stage IV disease.
- With a median follow-up time of 36.26 ± 27.47 months, **EFS and OS** was 80.2% and 91.5% respectively.

NON-HODGKIN LYMPHOMA

- Childhood non-Hodgkin lymphoma (NHL) is distinguished from adult NHL by **differing frequencies of histopathologic types** and by the greater frequency of **extra-nodal presentations**.
- With current combination chemotherapy regimens, **survival is generally excellent** (85 to 90%) for all patients, including those with **disseminated disease**, bone marrow, central nervous system involvement, and high serum lactate dehydrogenase (LDH).
- NHL represents approximately **8%** of all malignancies in patients < 20 years of age.
- **750--800 cases per year** in children up to 19 years of age in the United States.

- Paediatric NHL is mostly (more than 95%) of **high grade** and includes the following **four major subtypes**:
    - B- and T- **lymphoblastic lymphoma** (LL) (**20%** of NHL in children and teens)
    - **Burkitt Lymphoma** (**40%** of NHL in children and teens)
    - **Diffuse large B-cell lymphoma** (DLBCL) (15-**20%** of NHL in children and teens)
    - **Anaplastic Large Cell Lymphoma** (ALCL) (**10%** of NHL in children and teens)

Signs and Symptoms of NHL

- NHL can cause many **different signs and symptoms**, depending on the type of NHL and location in the body. Common symptoms include:
- **Lymphadenopathy**
- **Abdominal** swelling /pain, constipation, or urinary retention
    - Feeling full after eating only a small amount of food
- **Shortness of breath**, wheezing, or cough
- **B Symptoms** (Fever, Weight loss, Night sweats)
- Some lymphomas can affect the **skin** and can cause itchy, red skin nodules.

Treatment of NHL

- **Chemotherapy**
    - the main treatment for children and teens with NHL, because it can reach all parts of the body and kill lymphoma cells wherever they may be.
    - Even if the lymphoma appears to be limited to a single lymph node based on exams and tests, the lymphoma cells have often spread to other parts of the body by the time it is diagnosed.
- **High-dose chemotherapy** followed by a stem cell transplant may be needed in relapse cases.
- **Surgery** is not required as chemotherapy can resolve symptoms caused by tumour masses

session 10: Solid tumours

SESSION DURATION

- 15:45 - 16:15 pm (30 mins)

LEARNING TARGETS/OBJECTIVES

- After this session Participants can identify childhood Solid tumours, its signs and symptoms through observation, questions related to the clinical history, and a complete physical examination.

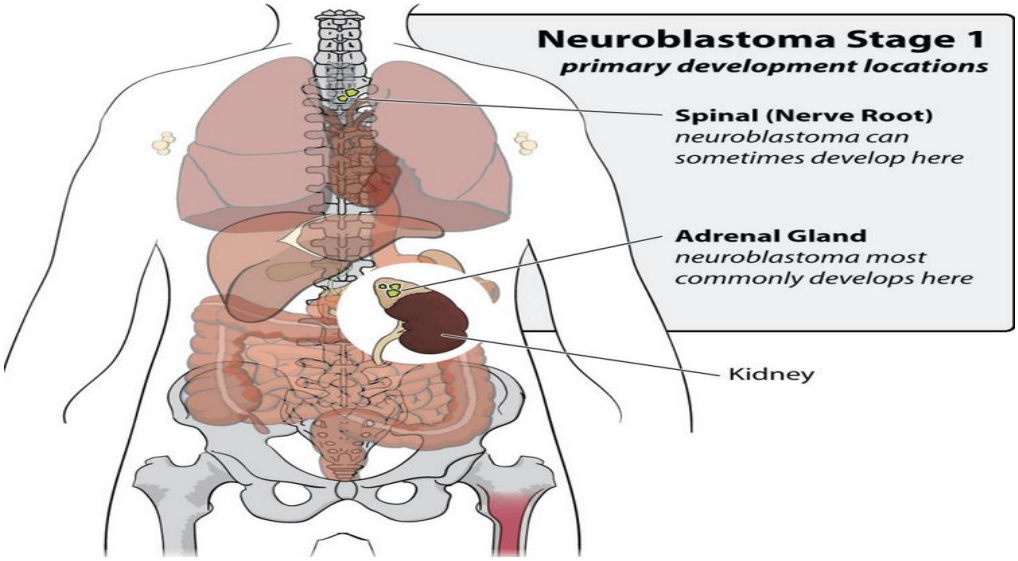
KEY POINTS

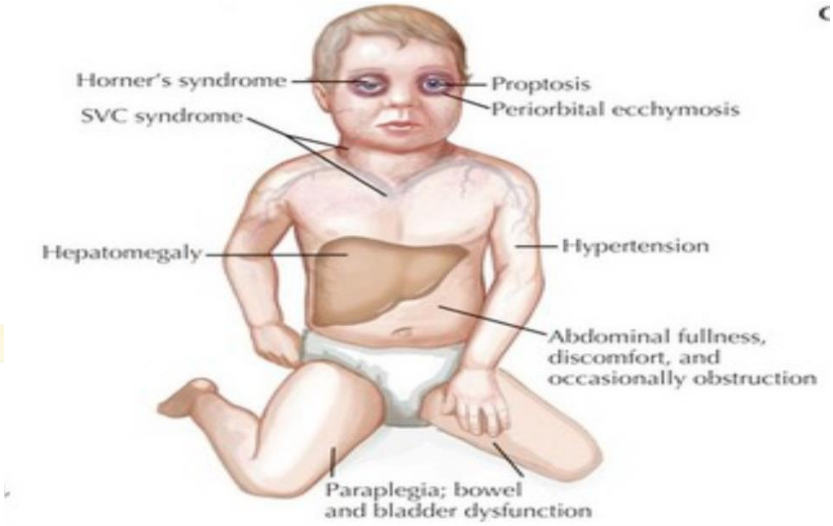
Malignant Abdominal Masses

- **Most common:**
    - Burkitt's lymphoma
    - Neuroblastoma
    - Wilms Tumour
- **Others:**
    - Hepatoblastoma
    - Rhabdomyosarcoma
        - Pelvic
    - Ovarian germ cell tumours
        - pelvic

NEUROBLASTOMA

- About 6% of all cancers in children.
- There are 700 new cases/ yr in US.
- **Age**
    - The most common cancer in infants
    - 50% < 2 years and 90% < 5 years.
    - Occasional USG detection *in utero*
- **Location:** any neural crest tissue
    - Adrenal
    - Paraspinal sympathetic tissue
        - Cervical, Thoracic, Pelvic
- **Often metastatic at diagnosis**
    - Bone and/or bone marrow
        - > 1 y/o: 70%
    - Abdominal mass
        - Often crosses midline.
        - Infants; massive hepatomegaly
    - Lower extremity weakness
        - Spinal cord compression
            - Thoracic
            - Abdominal
    - Cervical, high thoracic mass
        - **Horner's syndrome**
            - Miosis, ptosis, anhidrosis



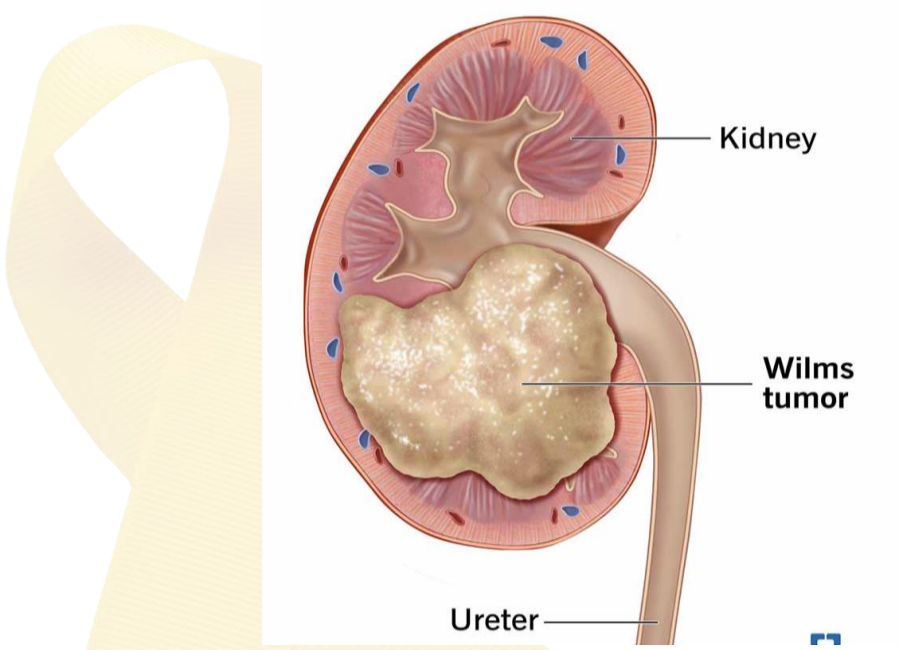


- **Signs of metastatic disease**
  - Irritability
  - Weight loss
  - Bone pain
  - Fever
  - Proptosis
  - Bone lesions
  - Periorbital ecchymoses
- Symptoms of **paraneoplastic syndromes** can include:
  - Opsoclonus-myoclonus, cerebellar ataxia
  - Constant diarrhoea
  - Fever
  - Tachycardia and / or Hypertension (causing irritability)
  - Reddening (flushing) of the skin
  - Sweating

		
Periorbital Ecchymoses	Periorbital Ecchymoses At diagnosis	Periorbital Ecchymoses After two weeks of chemo
Metastatic Neuroblastoma: * *Pictures with permission of the family*		

WILMS TUMOUR (WT)

- Wilms tumour, or nephroblastoma, is **the most common renal cancer** in children.
- Wilms tumour is the **most common paediatric abdominal cancer** and
- The **fourth most common paediatric cancer** overall.
- Typically found in children younger than five years old.



Wilms Tumour

Presentation of Wilms tumour

- **Asymptomatic abdominal mass** in most common presentation in children.
    - The mother may have discovered the mass during bathing the infant.
- Abdominal **pain** (Abdominal pain is the most common initial presenting symptom (30% to 40%))
- **Hypertension** (25-30%), normalizes after nephrectomy)
- Gross **haematuria** (12% to 25%).
- **Other features** include:
    - Urinary tract infections
    - Varicocele
    - Fever
    - Anaemia
- If the patient has **lung metastases**, dyspnoea or tachypnoea may occur.

Associated syndromes

- **Beckwith-Wiedemann syndrome (overgrowth syndrome)**
    - Children with this syndrome have a 5% to 10% risk of developing Wilms.
- **WAGR syndrome: (WT, Aniridia, Genital, Renal)**
    - Children with this syndrome have a 50% chance of developing WT.
    - Other complications include Aniridia and Genital or the Renal issues.
- **Denys-Drash syndrome**
    - Have a 90% chance of developing Wilms.
    - Other issues involve their genitals and kidneys.

Management

- Pre-Op Chemotherapy
- Nephrectomy and removal of lymph nodes
- Post-op chemotherapy and / or radiation therapy
- CT every 6 months for 3 years
- Chest x-rays every 3 months for 3 years.

Conclusions

- **Stage of the disease** is the most important prognostic factor. **Delayed presentation** with metastatic disease has a poor outcome.

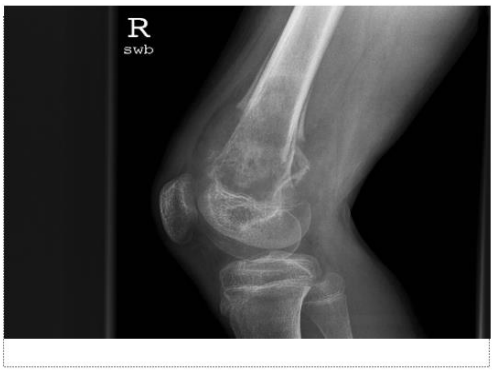
BONE TUMOURS

- **Age** – Adolescents > younger children
- **Signs and symptoms**
    - Bone pain, ± palpable mass
    - Often History of sports injury (coincidental)
- **OSTEOGENIC SARCOMA**
    - Metaphyses of long bones:
    - Distal femur
    - Proximal tibia
    - Proximal humerus
    - Pelvis
- **EWING SARCOMA**
    - All bones:
        - Long: diaphyses
        - Flat

- Pelvis
- Skull

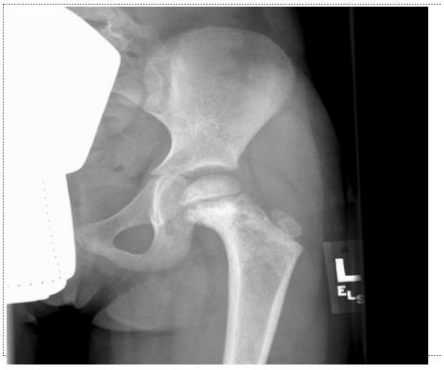
- **Radiology**

Classic X-ray of O.S



"Sunburst pattern"
Periosteal reaction
Soft tissue mass + calcium

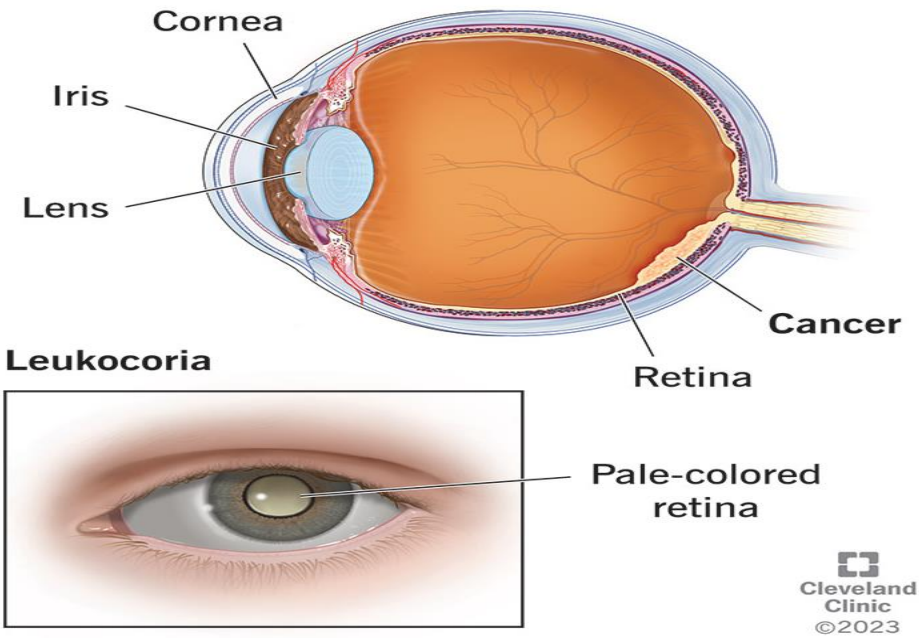
Classic X-ray of Ewing:



Moth-eaten lytic lesion

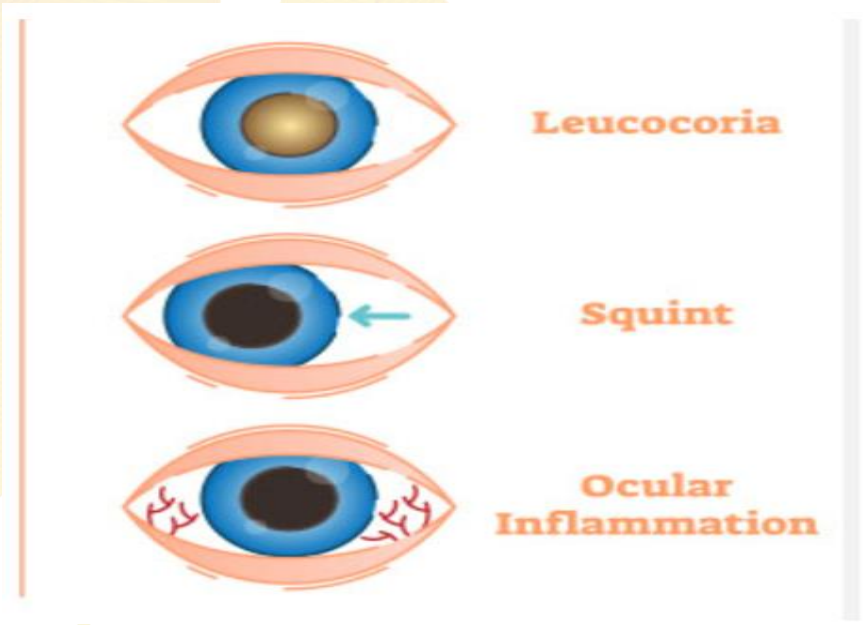
RETINOBLASTOMA (RB)

- RB is the most common intraocular malignancy of childhood.
- Incidence; 12 cases /Million < 5 yrs
- Around 300 new cases / yr in the U.S.
- Slightly under 9,000 new cases worldwide.
- The median age at diagnosis is 2 years.
- Approximately 50% of cases are heritable.



Presentation of RB

- Leukocoria
    - A pupil that appears white instead of black occurs when light reflects against the tumour's white surface).
- Strabismus / squint
- Poor vision or vision loss
- Inflammatory changes.
- Hyphema.
- Proptosis: A bulging pupil
- Buphthalmos;
    - An enlarged pupil or eyeball
- Vitreous haemorrhage,



Diagnostic Procedures

- **Screening**
  - **All children should have screening performed.**
  - as part of well-child check-ups, primarily by eliciting red reflexes in the eye.
  - However, most cases of RB are diagnosed after a parent or other relative notices an abnormality of the eye and this prompts further evaluation.
- **Siblings of children with RB** should be screened by ophthalmology at regular intervals at least through age 2 to 3 years unless their genetic testing has revealed they do not carry the RB1 gene mutation.
- **Diagnosis of Intraocular RB**
  - Diagnosis is made by a combination of an ophthalmologic examination generally performed under sedation or anesthesia, together with retinal camera (RetCam) imaging, ultrasound, CT or MRI
  - Due to concern about rupturing the tumour and causing both intraocular and extraocular spread, surgical biopsies are not performed for confirmation.

Table 6:International Classification of Retinoblastoma

Group	Defining Features
Group A- **Small tumour < 3 mm in size**	*Small intraretinal tumors away from foveola and disc*
Group B- **Large tumour > 3 mm in size**	*All remaining discrete tumors confined to the retina*
Group C- **Focal seeds ,<3 mm**	*Discrete local disease with minimal subretinal or vitreous seeding*
Group D- **Diffuse seeds**	*Diffuse disease with significant vitreous or subretinal seeding*
Group E- **Extensive RB** ***Presence of any one or more of these poor prognostic features***	Tumour touching the lens. Tumour anterior to the anterior vitreous Diffuse infiltrating retinoblastoma Neovascular glaucoma Opaque media from haemorrhage Tumour necrosis with aseptic orbital cellulites Phthisis bulb

Treatment of RB

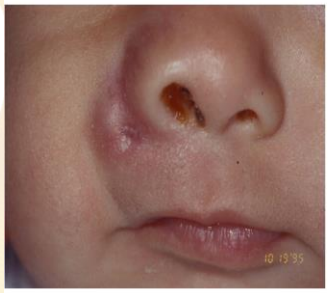
Group	Focal Treatments	Chemotherapy	Radiation
A	+	-	If PD
B	+	VCR 0.05 mg/kg CBP 18.6 mg/kg X 2 – 6 courses	If PD
C – D	+ +/- subtenon CBP x 3	VCR 0.05 mg/kg CBP 14 mg/kg x 2 ETO 6 mg/kg x 2 X 6 courses	If PD If massive seeding, consider early RT
E	Enucleation		

Prognosis

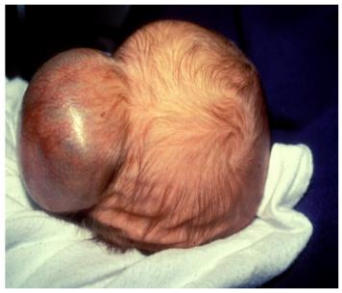
- Early diagnosis and treatment are crucial to prevent vision loss and the metastasis of retinoblastoma beyond the eye.
- Almost all children who are treated for retinoblastoma live for five years or more after finishing treatment. Those who are cancer-free after five years are considered cured.
- Due to the same genetic mutations that led to retinoblastoma, and to the effects of chemotherapy and radiation, people who had cancer do have an increased risk of other cancers later in life.

SOFT TISSUE SARCOMAS (STS)

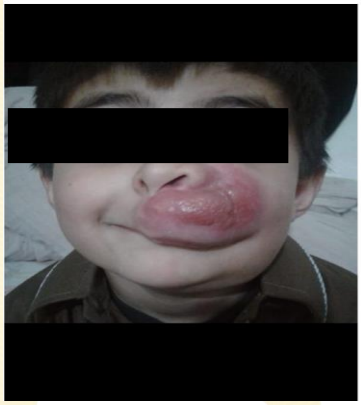
- **Presentation**
    - **STS** usually presents as painless mass/swelling.
    - Symptoms depends upon the location of the tumour
    - **Rhabdomyosarcoma – most common**
        - **Age**
            - Birth to > 20 y/o
            - 70% < 10 y/o
        - **Sites**
            - Head and neck – 40%.
            - Genitourinary – 20%
            - Extremities – 20%
            - Trunk – 10%
            - Retroperitoneal – 10%
        - Signs and symptoms depend on age and site.



6 weeks old



Newborn



Pre-treatment

Post treatment

Session 11: post test

SESSION DURATION

- 16:15 – 16:30 (15 mins)

Session 12: closing

SESSION DURATION

- 16:30 – 17:00 (30 mins)
- Concluding remarks
- Vote of thanks
- Certificate distribution

For more information, please contact:

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