

Early Diagnosis of Childhood Cancer



Pan American
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REGIONAL OFFICE FOR THE Americas



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I INTRODUCTION

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 tumors is 12.45 per 100,000 children under 15 years. Fortunately, great progress has been made in the treatment of childhood cancer in recent years, to the extent that in the last twenty years, there have been few specialties that can claim therapeutic outcomes comparable to those of pediatric oncology.

One example is acute leukemia, a disease that 30 years ago was considered inevitably fatal, with occasional, yet unsustainable, temporary remissions. At present, acute lymphoblastic leukemia, the most frequent childhood cancer, has a five-year survival exceeding 70%, meaning that most patients can be cured.

Similar advances have been made in treatment of solid tumors. Initially, when surgery was the only available treatment, two-year survival ranged from 0% to 20%, with very high perioperative mortality. Shortly after radiation therapy was introduced as a systematic treatment in pediatric oncology, favorable results began to be seen in Hodgkin's disease and Wilms' tumor. Chemotherapy, in turn, began to be used for relapses, as a last resort; but once its usefulness had been proven, it began to be used as a third therapeutic option, as a complement to surgery or radiation therapy. What is certain, is that since these methods have been used in combination, long-term survival of childhood cancer has significantly increased.⁽¹⁾

This progress has led to the development of new standardized clinical protocols, which have made it possible to resolve uncertainties and select the most appropriate guidelines for each neoplasm and, more importantly, for each patient's specific situation.

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 pediatric hematology/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."**

Table 1. Differences between pediatric and adult cancers

Parameter	Children	Adults
Site	tissues	organs
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

"Pediatric cancer is not preventable, but it can be detected at early stages."

Delay in referral of a patient with cancer and late initiation or suspension of treatment can mean the difference between life and death. Where does the delay happen?

Can a delay occur because the parents do not recognize the symptoms? Can a delay occur in the response of the nurse, the general practitioner, the pediatrician, the health system? Who is responsible for timely diagnosis? **In truth, the responsibility is everyone's.** The delay should not occur in health services, which is our commitment to the children.

If the time between appearance of the first signs or symptoms and referral to an oncology center for confirmation of a cancer diagnosis is to be shortened, more effort is needed in the human resources area that includes undergraduate and graduate medical and nursing education and the training of primary care staff, so that they know how to identify the early signs of cancer. **To contribute in this direction is the purpose of this particular module for the Integrated Management of Childhood Illness (IMCI).**

- ☒ When a child is examined and vague signs and symptoms are found that might be associated with malignancy, **cancer must be suspected and action taken accordingly to prevent late diagnosis.**



General practitioners and pediatricians must know the signs and symptoms of possible pediatric cancer.

Cancer is rarely on the list of differential diagnoses of physicians who see children and yet, for some reason, parents do suspect it. Parents frequently say, “I knew that my child was seriously ill, but the doctor did not listen to me.”

The vast majority of diagnostic errors are due to the lack of a thorough interview, clinical history review, and physical examination, as well as to the common mistake of ignoring some symptom that the parents report, or not giving it the importance it deserves.(2) In pediatrics, there are two major groups of neoplasms: hematolymphoid malignancies (leukemias and lymphomas) and solid tumors, of which the most frequent are those that attack the central nervous system (Table 2).

II RISK FACTORS FOR CHILDHOOD CANCER

Although little may be known about the etiology of cancer in children, there are several factors that are known to be associated with the appearance of some types of dysplasias.

☑ **Ionizing radiation.** Exposure to X-rays during pregnancy may increase the risk of cancer in the resulting children.

☑ **Chemicals and drugs.** Although it has not been demonstrated conclusively, some drugs may have carcinogenic effects on the children when they are administered to the mother during pregnancy; one example is diethylstilbestrol, which was used in the 1970s. Likewise, pesticide exposure has been associated with leukemia, non-Hodgkin's lymphoma, and neuroblastoma, and solvents such as benzene are a risk factor for leukemia in children. N-nitroso compounds, found in some processed foods and in tobacco, can induce tumors of the central nervous system (CNS) when consumed during pregnancy, while alcohol and some diuretics used during pregnancy have been linked to childhood cancers such as neuroblastoma and Wilms' tumor.(4)

Table 2. Incidence of cancer in children under and over 15 years of age, by groups and subgroups in the International Classification of Diseases(3).

Type of Cancer	< 15 years	≥ 15 years
Acute lymphoid leukemia	23.5%	5.6%
Acute myeloid leukemia	4.7%	4.3%
Hodgkin's disease	3.6%	16.8%
Non-Hodgkin's lymphoma	5.7%	8.3%
Tumors of the central nervous system	22.1%	9.8%
Neuroblastoma	0.9%	0.2%
Retinoblastoma	3.2%	0%
Wilms' tumor	6%	0.3%
Hepatoblastoma	1.3%	0%
Osteosarcoma	2.6%	4.2%
Ewing sarcoma	1.5%	2.4%
Rhabdomyosarcoma	3.6%	1.7%
Germ cell tumors	3.5%	7.3%
Thyroid carcinoma	1.1%	7.3%
Malignant melanoma	1.1%	7.6%

Source: Vizcaino M, De los Reyes I. Diagnóstico oportuno del cáncer en niños. Memorias del 24 Congreso Colombiano de Pediatría, Cartagena 2005.

☑ **Biological factors.** Some viruses, such as the Epstein Barr virus, human immunodeficiency virus (HIV), hepatitis B and C, human T-cell lymphotropic virus type 1 (HTLV1), and human papillomavirus (HPV), are associated with specific cancers, according to the virus and the tissues affected.(4)

Genetic and familial factors. Among family risk factors, embryonal tumors may be either inherited or sporadic. Not all are inherited, but of those that are, retinoblastoma and bilateral Wilms' tumor are the most important. Furthermore, certain genetic illnesses predispose to cancer. For example, children with Down syndrome are 20 to 30 times more likely to develop acute leukemia and children with Klinefelter syndrome have a 20 times greater risk of breast cancer and a 30 to 50 times greater risk of germ cell tumors of the mediastinum.^(1, 4)

✓ **Age.** As in any pediatric disease, there are cancers that appear more frequently in infants, others in preschool or school-age children, and others that are characteristic in adolescents (Table 3).

III MOST FREQUENT CANCERS IN CHILDREN

Not all cancer cells grow at the same rate, or have the same characteristics, or tend to spread to the same places—the biology of each tumor is different. Thus, certain tumors, even some with the same name, behave differently depending on the characteristics of their component cells.⁽⁵⁻⁷⁾ Given the importance of timely diagnosis, risk factors, and characteristic ages of some frequent oncological diseases of childhood, they are briefly described below, to aid in suspecting and identifying them when assessing children who presents signs that may be suggestive of cancer and, if necessary, in referring them to a specialized center.

a. Leukemia⁽⁸⁻²⁷⁾

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 can be cured 90% of the time. 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 months (average of two or three weeks), pallor, petechiae, ecchymoses, signs of bleeding, hepatosplenomegaly, adenomegaly, and infiltration of other organs (testis, central nervous system, or kidneys). Weight loss is rare. Leukemia has a characteristic triad of fever, anemia, and bleeding. Definitive diagnosis is made by bone marrow aspiration done in a specialized center.

Table 3. Most frequent cancers in children, by age group (3).

Most frequent cancers		
<5 years	5-10 years	>10 years
Leukemias	Leukemias	Leukemias
Neuroblastoma	Non-Hodgkin's lymphoma	Non-Hodgkin's lymphoma
Wilms' tumor	Hodgkin's lymphoma	Hodgkin's lymphoma
Testicular tumors (yolk sac)	Tumors of the CNS	Tumors of the CNS
Retinoblastoma	Soft tissue sarcoma	Germ cell tumor (ovarian, extragonadal GCT)

b. Lymphomas⁽²⁸⁻³⁷⁾

This group of diseases of the lymphatic system are fast growing and are called solid hematological tumors to differentiate them from leukemias.

They are the third most common of child cancers, following leukemias and tumors of the central nervous system.

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, anemia, weight loss, and drenching night sweats.

Hodgkin's lymphoma mainly affects the lymphatic system. Its usual clinical presentation is asymptomatic cervical or supraclavicular lymphadenopathy, displaying progressive growth and increased consistency, and adhesion in deeper layers, and is often painful.



c. Tumors of the central nervous system⁽³⁸⁻⁵³⁾

These are solid tumors 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 tumor'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 awakens 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 behavior (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. Progressive blindness may occur in one eye due to a tumor of the optic nerve on that side.
- ✓ 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.

d. Wilms' tumor⁽⁵⁴⁻⁶²⁾

This is a malignant neoplasm of the kidney cells, which compromises one of the two kidneys, although it can also be bilateral. 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, hematuria, and hypertension.
- ✓ Other less frequent signs include anemia, fever, and constipation.

e. Neuroblastoma⁽⁶³⁻⁷⁶⁾

This is an extracranial malignant solid tumor 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.
- ✓ Tumors can grow in any part of the nervous system. Symptoms depend on the mass effect of the tumor in the affected region, which can be the head, neck, thorax, or paraspinal or lumbar-sacral region.
- ✓ Neuroblastoma most frequently metastasizes to the following sites: bones, lymph nodes, bone marrow, liver, and skin.

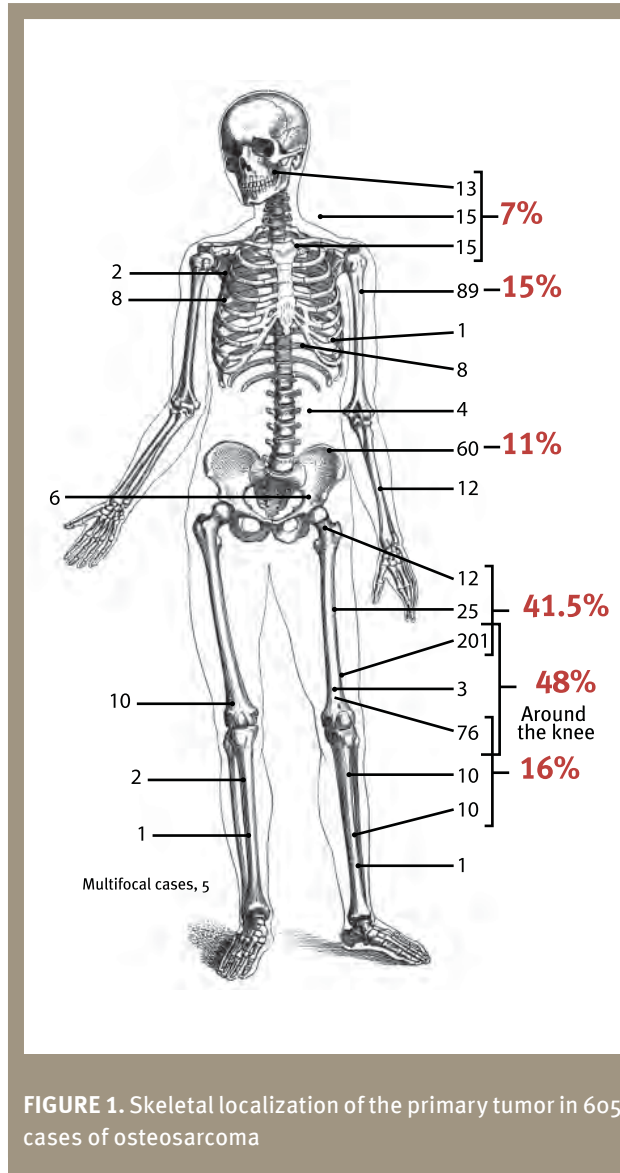
f. Osteosarcoma and Ewing sarcoma⁽⁷⁷⁻⁸³⁾

Osteosarcoma and Ewing sarcoma are the most common primary tumors of the bone. These malignant neoplasms are more frequent in men, 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.
- ✓ 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.
- ✓ Osteosarcoma is located at sites of rapid growth—metaphyses (e.g. femur, tibia, and humerus).
- ✓ Osteosarcoma affects the diaphysis of long and flat bones.
- ✓ Late diagnosis worsens the prognosis, which is directly related to the number and size of the metastases. Survival is close to 70%.
- ✓ Normally, there are no clinical metastases at the time of diagnosis.

g. Retinoblastoma⁽⁸⁴⁻⁸⁹⁾

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, suggesting that it is due to exposure to infectious agents, particularly adenovirus and human papillomavirus, and other factors such as lack of vitamin A and folate in the diet.



- ✓ 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 colored 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.

h. Rhabdomyosarcoma⁽⁹⁰⁻⁹⁷⁾

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 tumor's location. A mechanical mass effect can occur.
- ✓ It is aggressive, with rapid local growth, and directly invades neighboring structures. Its clinical presentation will depend on the structures it affects.

i. Germ cell tumor⁽⁹⁸⁻¹⁰³⁾

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 tumors of the ovary, over half are benign.
- ✓ It presents with general clinical symptoms, such as fever, vomiting, weight loss, anorexia, and weakness.
- ✓ When the tumor is located in the ovary, the most common symptom is chronic pain. A mass may be felt that, if it is very large, produces constipation, genitourinary disorders, and absence of menstruation.
- ✓ When it is located in the testes, it appears as a hard, slightly painful mass that does not transilluminate.

IV HOW TO ASSESS THE POSSIBILITY OF CANCER

This module will teach you to use the IMCI strategy to assess the possibility of cancer in a child, using a procedure through which you should:

- ☑ **Check for and identify** suspected cancer signs through observation, questions related to the clinical history, and a complete physical examination.
- ☑ **Classify**, through color 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**).

- ✓ **Treat the child.** After classifying the child's condition, if urgent referral is needed, administer essential treatment before referring. If the child needs treatment but can go home, prepare an integrated treatment plan and administer the first dose of treatment in the clinic.

- ✓ **Teach the parent** or caretaker how to care for the child's health; for example, how to give (oral) treatments at home. Schedule a follow-up visit with a specific date and teach ***how to recognize danger signs that require bringing the child to the clinic immediately.***

- ✓ **Ensure counseling** on key practices, such as feeding and home care by parents and family.

- ✓ **Provide follow-up care**, according to the management charts, to identify how the child is doing—the same, better, or worse—and find out if there are new signs, symptoms, or problems.

In EVERY case, you must ask the mother about the child's problem, check for general danger signs in the child, and ask whether the child has cough or difficult breathing, diarrhea, fever, or ear and throat problems. In EVERY case, you must assess the child's nutritional status, possibility of anemia, development, and vaccination status.

Then determine whether the child COULD HAVE CANCER



ASK

- Has the child had fever for more than 7 days and/or heavy sweating?
- Has the child recently had a headache that has been intensifying?
- Does the headache waken the child?
- Is it accompanied by another symptom, such as vomiting?
- Has the child had bone pain in the last month?
 - That interrupts the child's activities?
 - That has been increasing?
- Has the child shown changes, such as loss of appetite, weight loss, or fatigue, in the last 3 months?

OBSERVE, FEEL, AND IDENTIFY:

- Petechiae, bruises, or bleeding
- Severe palmar and/or conjunctival pallor
- Any eye abnormality:
 - Leukokoria (white eye)
 - New strabismus
 - Aniridia (lack of iris)
 - Heterochromia (different colored eyes)
 - Hyphema (blood in the eye)
 - Proptosis (bulging eye)
- Swollen lymph nodes: Larger than 2.5 cm, hard, painless, lasting ≥ 4 weeks
- Focal neurological signs and symptoms, with sudden and/or progressive onset:
 - 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
- Enlargement of some area of the body (mass)

CLASSIFY



Remember that you should think and look in order to find cancer. Diagnosing cancer early makes the difference between life and 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 leukemia, 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 anemia + purpura + fever appears in two-thirds of leukemia 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 hemogram 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 tumor.**

Tumors of the central nervous system are manifested by **continuous, persistent, and disabling headaches.** These headaches worsens 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 tumor and referral of the child to a specialized center should not be delayed. It is important to keep in mind that brain tumors are most likely to occur in children aged 5 to 10 years, when headaches of other etiologies are infrequent. Brain tumors 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 pediatrician 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 tumors 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 tumors 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 tumor disease.

Bone (and joint) pain is also one of the initial symptoms of leukemia, especially acute lymphocytic leukemia, 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. ^(2, 3, 21-24)



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 tumors 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 leukemias 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 leukemia, 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.

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

Anemia is defined as a decline in hemoglobin concentration, hematocrit, or the number of red cells per cubic millimeter, with different normal lower limits according to age, sex, and altitude. In general, hemoglobin levels are higher in newborns, decline in the first 6 to 8 weeks of life, and from then on rise slowly until adolescence, when they reach adult levels. They are lower in women and, as with hematocrit levels, increase with elevation above sea level.

When only red blood cells are compromised (that is, there is no change in other blood cells), there can be three causes of anemia, and each requires different treatment: low production (lack of substrate, such as iron; problems of maturity and proliferation in chronic diseases), rapid destruction (hemolytic anemias), or blood loss (acute or chronic).

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.



FIGURE 2. Acute Leukemia

- ✓ **Infections.**
- ✓ **Parasites, such as hookworm or whipworm,** which can cause blood loss.
- ✓ **Malaria,** which rapidly destroys red blood cells.
- ✓ **Oncological diseases, mainly leukemia.**

According to World Health Organization criteria, children aged 6 months to 6 years should be diagnosed as anemic when their hemoglobin levels are lower than **11 g/dl**. One sign of anemia 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 color 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.

The decision to use palmar pallor to assess anemia is based on difficulty in measuring hematocrit and hemoglobin levels in many places that provide the first level of care. Given the high mortality associated with severe anemia and the diseases that cause it, the clinical signs to detect it, and as a result refer the patient to a specialized center, should be as sensitive and specific as possible.

Another clinical test that can be used to detect anemia is conjunctival pallor, but in places where conjunctivitis is common, pallor is replaced by conjunctival hyperemia. 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 color 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

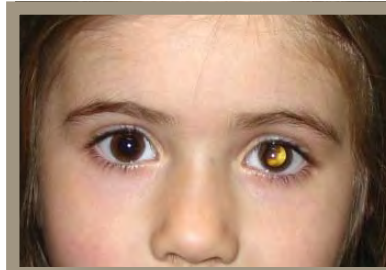


FIGURE 3. Unilateral retinoblastoma, leukokoria (white eye on left), and normal red reflex on right



FIGURE 4. Bilateral retinoblastoma



FIGURE 5. LEUKOKORIA (WHITE EYE)

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' tumor, 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 tumor. Retinoblastoma can cause strabismus when vision is lost in the eye where the tumor is located and is usually accompanied by leukokoria.



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

The malignant causes of lymphadenopathy are:

- ✓ Lymphoma.
- ✓ Leukemia.
- ✓ Langerhans cell histiocytosis.
- ✓ Metastatic: rhabdomyosarcoma, thyroid, neuroblastoma, nasopharyngeal.

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.

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 leukemia 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 needle biopsy needs to be done and will select the node.



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 tumors. Changes can also be seen in consciousness, mental status, or behavior; 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 tumor 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



FIGURE 6. Children with cervical lymphadenopathy

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 tumors 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 tumors are asymptomatic in their first stages and are only detected if a good physical assessment is done.

Malignant tumor masses are hard, with a firm consistency and, depending on the affected organ, are located in the flank (renal tumors), in the right hypochondrium (liver tumors), and in the hypogastrium (bladder or ovarian tumors). Neuroblastomas are found in the retroperitoneum, as is Wilms' tumor, but usually cross the midline. Burkitt's lymphoma (a very fast growing lymphoma) is located 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 center. Masses felt in the newborn are usually of benign origin.



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 tumors, 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



FIGURE 7. Child with Wilms' tumor



FIGURE 8. Child with Burkitt's lymphoma



FIGURE 9.
Adolescent with
osteosarcoma



FIGURE 10.
Adolescent with
Ewing Sarcoma



FIGURE 11. Child
with Langerhans
cell histiocytosis

tend to present subcutaneous mobile painless nodules, which look blue through the skin. Subcutaneous nodules can also be detected in some acute leukemias, as well as in Langerhans cell histiocytosis (especially on the scalp).

Remember:
If you seek, you shall find.



HOW TO CLASSIFY THE POSSIBILITY OF CANCER

When a child has any suspected sign or symptom of cancer, the *only* procedure is to refer the patient immediately to a specialized center, 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. Furthermore, if a biopsy is indicated, it will be safest and the most appropriate to have it done by a pathologist experienced in child oncology, in a laboratory that can perform or has easy access to immunohistochemistry tests. That is, all the delays and paperwork can be reduced if the child is referred directly to a specialized center that has all those resources or has access to high-tech testing. Plus, if a test needs to be repeated, the child will be exposed again to tests that are often invasive.

It is possible that some children will be referred whose tests results will be negative, but what is important is that the health team at the first level of care will have the satisfaction of having made a timely referral of a child with cancer. If cancer is not confirmed, the child and his family will be happy, and if it is confirmed, they will have collaborated in giving a child the chance to receive appropriate treatment in time and the possibility of being cured.

The classification of a child according to the probability that he or she has cancer is done using traffic-light colors to identify the severity of clinical symptoms. According to the child's combination of 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"

You see a child who comes in because of some illness or for growth and development monitoring, or immunization, and you see that the child has some

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 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 follow-up 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



of the signs or symptoms included in the red area of the IMCI classification (see Table 4). This child should be studied immediately because the cause might be a neoplasm or another very severe disease.

The safest, most appropriate thing to do is to refer the child to a specialized center immediately, which will prevent wasting days or weeks on laboratory testing and imaging that will probably need to be repeated later. But even if the diagnosis can be confirmed, very valuable time for achieving a better response to treatment will have been wasted. In any case, before referring, stabilize the child so that he can travel under the best possible conditions. If a brain tumor is suspected and the child shows neurological deterioration, treatment for intracranial hypertension should be started before referring.

Yellow area: “Some risk of cancer”

You see a child who comes in because of any disease or for growth and development monitoring, or immunization, and you see that the child has 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, among them neoplasms and infectious diseases, such as tuberculosis and HIV/AIDS. Therefore, these children should be referred to pediatric consultation for studies to identify the causes of those signs and to begin appropriate treatment and follow-up.

Anemia in children is usually secondary to causes such as iron deficiency, infections, or parasites, among others, but it can also be a manifestation of a neoplasm, such as leukemia. As a result, if iron is prescribed, it has to be for a limited time. Schedule the child for an appointment every 14 days to give him more iron and reexamine him: if the anemia has worsened clinically, refer immediately, and if the anemia still persists clinically following one month of treatment with iron, studies need to be done, including a complete hemogram and peripheral blood smear.

Lymphadenopathy and enlargement with inflammatory characteristics in some region of the

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.

body 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.

HOW TO TREAT THE CHILD WITH POSSIBLE CANCER



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.

HOW TO TREAT THE CHILD CLASSIFIED WITH “POSSIBLE CANCER OR VERY SEVERE DISEASE”

The management objective for a child with a diagnosis compatible with cancer is to get him to a specialized center as soon as possible. This objective means that the staff rapidly resolves all administrative problems that occur and, without taking a long time to conduct paraclinical tests, sends the child to a specialized center where in the end any diagnosis will be confirmed or ruled out.

I HOW TO TREAT THE CHILD WITH POSSIBLE CANCER

Over the last several decades, protocols have been developed to manage the different cancers that affect children. Systematic use of these protocols is the factor that has made the biggest difference in improving pediatric cancer cure rates—at present, some 70% of children diagnosed with cancer survive. Even more, it is expected that these high cure rates will mean that in coming years, one out of every thousand young people will be a survivor of childhood cancer. For this reason, the current treatment focus for pediatric cancer is aimed at curing, but with the fewest adverse effects possible. These statistics and these goals, however, are still not the reality in Latin America and the Caribbean. This is because in our countries, and even when health services use the same protocols as developed countries, children with signs and symptoms of cancer do not visit the clinic, or they go very late, or they drop out of treatment, or, for various reasons, they do not receive the right treatment at the right time.

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.

If the cancer diagnosis is fortunately ruled out, in any case the symptoms reported are critical and study is needed to diagnose the underlying disease causing them.

Once we have a child with a probable diagnosis of cancer, based on a proper clinical history, a complete physical exam, and the identification of suspicious signs or symptoms, the final diagnosis is anatomopathological, carried out in a referral facility. Hence, the importance of understanding that, when there is a suspected possibility of cancer, the child should be referred to a center 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 definitely need to be stabilized before being sent to a specialized center, as described below.

a. 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.

There is no ideal method for providing oxygen, nor is there one method that is better than another. 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.

b. Hemodynamic stability

A child with signs of severe dehydration, or with hypovolemia of another etiology, or shock should be stabilized before referral. Lack of a pediatric 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 to 30 mL/kg in 30 minutes or less if necessary. It is important to remember, however, that some children with cancer can have severe anemia, which means that a rapid load of fluids can produce pulmonary edema in them. In these



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

c. Administration of fluids

For the infant under two months of age, dextrose (dextrose in distilled water- D/DW) is recommended. In the newborn, 10% dextrose should be administered without electrolytes at 80 mL/kg/day, via umbilical catheter or, if possible, by peripheral vein. From the second day of life, sodium chloride (10 ml/500 ml solution) should be added to the fluids, and from the third day, potassium chloride (5 ml/500 ml solution). The infant older than 2 months referred with intravenous fluids should receive, if there is no dehydration or shock, 5% dextrose with electrolytes in volumes calculated as follows (Holliday-Segar method, based on water and calorie requirements):

<10 kg:	100 ml/kg/day
10-20 kg:	1000 ml + (50 ml/kg per each kg >10 kg) per day
>20 kg:	1500 ml + (20 ml/kg per each kg >20 kg) per day

Example of fluid calculation:

Child weighing 25 kg:

1500 ml + (20 x 5 kg) 5 kg are the kg above 20 kg for a child weighing 25 kg.

1500 ml + 100 = 1600 ml in 24 hours

1600 ml/24 hours = 66.6 ml/hour

This means that a child weighing 25kg needs an intravenous solution of 5% dextrose with electrolytes at 66 ml/hour. It is always necessary to add electrolytes to this solution to contribute to requirements. Ideally, from 3 to 5 mEq/kg/day of sodium and 2 to 3 mEq/kg/day of potassium should be provided.

A practical way to organize intravenous fluids is by the age of the child, as follows:

For the newborn	First day of life: 10% D/DW without electrolytes
	Second day of life: 500 ml 10% D/DW + 10 ml sodium chloride
	Third day of life up to 2 months: 500 ml 10% D/DW + 10 ml sodium chloride + 5 ml potassium chloride
For babies >2 months old	5% D/DW by weight + 15 ml sodium chloride + 5 ml potassium chloride

These are maintenance fluids in a child without oral access or that requires venous access, but does not have dehydration or shock.

d. Pain management

If the child is in pain, treat before referring:

- ✓ Mild pain:
 - Paracetamol 10-20 mg/kg/dose every 4-6 hours
- ✓ Mild or moderate pain:
 - Ibuprofen: 5-10 mg/kg/dose every 6 hours
 - Diclofenac: 1-1.5 mg/kg/dose every 8-12 hours
 - Naproxen: 5-7.5 mg/kg/dose every 8-12 hours

e. Management of intracranial hypertension

If a patient with a suspected brain tumor 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: intramuscular or intravenous dexamethasone at a rate of 0.15 to 0.25 mg/kg/dose and/or insulin at a rate of 0.25 to 0.5 g/kg/dose.
- ✓ 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.⁽¹⁾

f. Recommendations in case of bleeding and severe anemia

If the child has a very low hematocrit and hemodynamic disturbances, packed red blood cells should be transfused at 10 mL/kg; however, whenever possible, transfusion should be avoided until the child is studied and the transfusion done in the referral facility. Transfuse only if the child's life is in danger.

If there is thrombocytopenia with a blood platelet count $\leq 50,000/\text{mm}^3$ with serious hemorrhagic manifestations, a platelet button should be transfused; however, if there are no severe hemorrhagic manifestations, do not transfuse and wait for the specialized center to decide when to transfuse. Keep the child at rest to prevent bleeding.

g. 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, which tends not to be available in many of the region's health facilities. 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.

h. 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 and everything necessary to properly diagnose and treat their 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 it 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.

i. 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.

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

Children with this classification have clinical signs shared by many diseases, among them cancer, although without being strictly suggestive. Moreover, since cancer perhaps produces these signs at a much lower percentage than other diseases, children should be treated based on the most frequent etiology. 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. Tumors 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 tumors 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. Anemia 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 leukemia triad, anemia alone, without other symptoms such as purpura, should be considered to have another etiology and should primarily be treated with iron. Nevertheless, if at the one-month follow-up, there is no clinical improvement, a hemogram and peripheral blood smear should be done to study the cause of anemia and the absence of response to treatment with iron. Fortunately, cancer will be the cause in a minority of children, and this will be evident from the hemogram, 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 (cefalexin or dicloxacillin 50 mg/kg/day in 3 doses).

If no improvement is seen at the follow-up visit, or if lymphadenopathy persists after treatment for infection, the child should be referred to study the cause—which could be a neoplasm. 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 etiology 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 center.

In this group, proper counseling of the parents is of the utmost importance, so they can detect danger signs and know when to return immediately.

III 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.

COUNSELING THE CHILD’S PARENTS OR CARETAKER

The child with cancer requires treatment and follow-up at a specialized center 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 center in counseling 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 center.
- ✓ Reinforce danger signs and remind parents that they should seek immediate attention if the child shows any change or associated symptom.
- ✓ You will recommend that the child return to school based on the treatment protocol and degree of immunosuppression.

“Insist on the importance of following these recommendations.”

IV 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 care he needs for the new classification. 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 difficult breathing.
- ✓ Is very pale.
- ✓ Does not look well or is worsening.

V CASE EXAMPLES**1. Martín's case**

Martín is a 4 year old boy. His mother took him to the clinic because Martín had been sick for four weeks, first with bronchitis symptoms that were managed with cough syrup. After that, he got an ear infection and took amoxicillin for 7 days. His mother notes that her son has not gotten completely better; his ears no longer hurt, but he is not eating well, he is very weak, and he only wants to play for short periods. She does not like her son's color—he looks very pale— and two days ago some kind of rash broke out on his skin, especially on his torso, which worsened today.

The physician did a complete IMCI assessment. He found that Martín weighs 15 kg, his height is 98 cm, his heart rate (HR) is 110 per minute (x'), respiration rate (RR) 28 x', and his temperature is 36.6° C. After the complete IMCI assessment, the physician assesses the possibility of cancer in Martín and asks:

Has he had a fever?

The mother says that he has had some fever the entire month, but not now.

Has he had changes, such as loss of appetite, weight loss, or fatigue?

The mother says yes, and that she is worried because Martín was a very active child and now he is quiet, like he is tired all the time, and he is eating much less.

Has he had headache or bone pain?

The mother says not really, that he has been somewhat achy, but no headache, and a little bit in his bones—he complains at night about his legs.

Then the physician examines Martín:

He observes pallor on the palm of the hand, but it is not severe; there are petechiae on his torso and on parts of his limbs where there is rubbing; he has multiple small ecchymoses on his legs.

Martín does not have any disturbances in his eyes, he does not have ataxia, and he has multiple small adenopathies on his neck, none over 2.5 cm. There were no palpable masses in the abdomen, but the edge of the liver is palpable 3 cm below the right costal margin and he was able to feel the edge of the spleen about one cm below the left costal margin. He did not find enlargement in any other region of the body, or any other significant disturbance.

Read the case recording form on the next page and the classification of Martín and discuss any doubts with your facilitator.



CHILD CANCER REGISTRATION FORM DETECTION

Name: MARTIN

Date: FEB 10/10 Age: 4 YEARS OF AGE

What problem has the child? *TABLE OF 4 WEEKS INITIALLY BRONCHITIS, THEN OTITIS WITH ANTIBIOTIC AND SINCE THEN DECLINED MANAGEMENT, DOES NOT EAT WELL, DOES NOT WANT TO PLAY, OF *MAL COLOR, INCREASINGLY PALE, AND DOES 2 DAYS HAS SPECIES OF OUTBREAK IN THE SKIN THAT TODAY WORSENS*

First consultation: X Control: Weight: 15 KG Size: 98 CM. ...PC:

FC: 110 X' FR: 28 X' T°: 36,6°C

ASK	OBSERVE AND DETERMINE: (encompass in a circle what	CLASSIFY
Has it had fever for more than 7 days and/or important perspiration? YES ☐ NO ☒ Recent headache that has been worsening? YES ☐ NO ☒ Since when? Does it awaken headache to the child? YES ☐ NO ☒ Is it accompanied by some other symptom as vomit? YES ☐ NO ☒ Does it present bone pains in the last month? YES ☐ NO ☒ What interrupts its activities? YES ☐ NO ☒ Has been what increasing? YES ☐ NO ☒ Has it presented changes as loss of appetite, weight loss, or fatigue in the last 3 months? YES ☐ NO ☒ Which and since when? <i>4 WEEKS AGO. LOSS OF APPETITE, WEARINESS</i>	■ <u>Petechiae, mores,</u> or bleeding ■ <u>Palmar and/or conjunctival pallor:</u> Mild ☒ Intense ☐ ■ Abnormality in the eyes: white eye ☐ Lack of iris ☐ Acquired strabismus ☐ different color eyes ☐ Blood within the eye ☐ left ☐ ■ Nodes: Size 2.5 cm Without pain nor inflammation. Hard and firm consistency Lasting 4 weeks of evolution ■ Signs and focal neurological symptoms of sudden or progressive onset: ■ Unilateral weakness: unilateral weakness, one of the limbs or of a side of the body ■ Physical asymmetry (facial) ■ Changes in the state of conscience or mental (in the behavior, confusion) ■ Loss of the balance to the walks ■ Limbs by pain ■ Difficulty in speaking ■ Alteration in the vision: (blurred, double, sudden blindness) ■ Presence of abdominal palpable mass ■ `Hepatomegaly` and/or `splenomegaly` ■ Increase of volume in some regions of the body (mass)	POSSIBLE CANCER OR VERY SEVERE DISEASE SOME RISK OF CANCER DOES NOT HAVE CANCER

COMMENTS:

Notes:

`Cranial` perimeter; FC: Heart rate; FR: Respiration rate; T°: Temperature

2. Raúl's case

Raúl is 12 years old and he went to the emergency service because he has had a headache for 1 month and he tells his mother that he does not feel right, that he feels like he cannot see properly.

His mother says that the pain began a month ago, which was intermittent at first, but caught her attention because he had never complained of headaches before. She took him to the pediatrician, who diagnosed sinusitis, and started treatment with antibiotics and antihistamines. Two weeks later he returned to the doctor and was referred for an ophthalmology assessment, but the appointment is a month off and since the pain is worsening he decided to visit the emergency service today.

Raúl is a previously healthy child, with no outstanding history, a good student and athlete. Raúl says that in the last month he has not been able to play sports well because the exercise makes the pain worse and he feels that he cannot see the soccer ball well.

On examination: Height: 150 cm. Weight: 45 kg. HR: 60 x'. RR: 16 x'. T°: 36.2° C. BP: 100/50

Findings: He is a cooperative child, pink, without difficult breathing, hydrated, and afebrile.

The complete IMCI assessment was done, no danger signs were found; no cough or difficult breathing, no diarrhea or dehydration, no fever, no ear or throat problems, nutritional status is good, and there is no anemia.

The physician assessed the possibility of cancer and found that:

Raúl has not had fever, weight loss, or fatigue. He has had a headache for one month, and in the last few days it occasionally awakened him at night; there is no associated emesis (vomiting), but he does report visual disturbances and double vision. Pain occurs at any time of day. He does not have bone pain.

Examination found no manifestations of bleeding, pallor, or lymphadenopathy; examination of the eyes showed pupils equal and reactive to light, there was mild lack of coordination and he failed the finger-to-nose test, with bilateral bitemporal hemianopsia. Gait, tone, and strength were normally symmetrical; no other disturbance was found; eye fundus exam could not be done due to lack of equipment.

Use the above information to fill out the case recording form on the next page.

Then answer the following questions:

1. According to the procedure chart, how should the health professional approach the child and his family?
2. What signs of disease did the health professional identify during the assessment?
3. Are there any other questions or something else to assess to have all the information necessary to classify the child?
4. How would the health professional classify Raúl based on his findings?
5. What treatment should Raúl be given and what recommendations should his mother be given?



CHILD CANCER REGISTRATION FORM DETECTION

Name:

Date: Age:

What problem has the child?

First consultation: Control: Weight: Size: PC:

FC: FR: T°:.....

ASK	OBSERVE AND DETERMINE: (encompass in a circle what	CLASSIFY
Has it had fever for more than 7 days and/or important perspiration? YES ☐ NO ☐ Recent headache that has been worsening? YES ☐ NO ☐ Since when? Does it awaken headache to the child? YES ☐ NO ☐ Is it accompanied by some other symptom as vomit? YES ☐ NO ☐ Does it present bone pains in the last month? YES ☐ NO ☐ What interrupts its activities? YES ☐ NO ☐ Has been what increasing? YES ☐ NO ☐ Has it presented changes as loss of appetite, weight loss, or fatigue in the last 3 months? YES ☐ NO ☐ Which and since when?	■ Petechiae, moretes, or bleeding ■ Palmar and/or conjunctival pallor: Mild ☐ Intense ☐ ■ Abnormality in the eyes: white eye ☐ Lack of iris ☐ Acquired strabismus ☐ different color eyes ☐ Blood within the eye ☐ left ☐ ■ Nodes: Size 2.5 cm Without pain nor inflammation. Hard and firm consistency Lasting 4 weeks of evolution ■ Signs and focal neurological symptoms of sudden or progressive onset: ■ Unilateral weakness: unilateral weakness, one of the limbs or of a side of the body ■ Physical asymmetry (facial) ■ Changes in the state of conscience or mental (in the behavior, confusion) ■ Loss of the balance to the walks ■ Limps by pain ■ Difficulty in speaking ■ Alteration in the vision: (blurred, double, sudden blindness) ■ Presence of abdominal palpable mass ■ `Hepatomegaly` and/or `splenomegaly` ■ Increase of volume in some regions of the body (mass)	POSSIBLE CANCER OR VERY SEVERE DISEASE SOME RISK OF CANCER DOES NOT HAVE CANCER

COMMENTS:

3. Alejandra's case

Alejandra is 7 years old and her mother brought her to the clinic because for the past 6 weeks she has been eating little, has a cough mainly at night, and is losing weight; she has also had a fever, irregular and not lasting all day, but in the last 3 weeks her fever has spiked at times. She has not consulted before because she was not able to travel from the countryside to the clinic.

The physician asked whether Alejandra had any significant medical history and the mother said no; the girl has not had her 5-year vaccine boosters and her grandfather is hospitalized for a lung disease (the mother does not know which one); Alejandra used to take care of him at home.

Upon examination, the physician finds that Alejandra has: weight of 18 kg, height of 114 cm.

HR: 90 x'. RR: 35 x'. T°: 37.4°

The physician does a complete IMCI assessment and obtains the following classifications:

Cough or cold (chronic cough), no diarrhea, low-risk febrile disease, no ear or throat problems, and is malnourished, with mild palmar pallor.

The physician assesses the possibility of cancer and finds that the girl:

Has had intermittent fever for >7 days; in the last 6 weeks, she has lost her appetite, she has lost weight, and (the mother says) she gets tired. She does not have bone pains or headache.

On examination, the physician finds multiple 1 cm cervical and axillary adenopathies; there are no manifestations of bleeding, no visual disturbances, no palpable masses; no focal neurological disturbances, and only some palmar pallor.

Use the above information to fill out the case recording form on the next page.

Then answer the following questions:

1. What positive signs did the physician find to classify Alejandra?
2. How does the physician classify Alejandra?
3. What procedure does the physician decide to follow?
4. Should Alejandra be referred or treated on an ambulatory basis? If treated ambulatorially, when should the patient return for follow-up?
5. What recommendations will the physician give to Alejandra's mother?



CHILD CANCER REGISTRATION FORM DETECTION

Name:

Date: Age:

What problem has the child?

First consultation: Control: Weight: Size: PC:

FC: FR: T°:.....

ASK	OBSERVE AND DETERMINE: (encompass in a circle what	CLASSIFY
Has it had fever for more than 7 days and/or important perspiration? YES ☐ NO ☐ Recent headache that has been worsening? YES ☐ NO ☐ Since when? Does it awaken headache to the child? YES ☐ NO ☐ Is it accompanied by some other symptom as vomit? YES ☐ NO ☐ Does it present bone pains in the last month? YES ☐ NO ☐ What interrupts its activities? YES ☐ NO ☐ Has been what increasing? YES ☐ NO ☐ Has it presented changes as loss of appetite, weight loss, or fatigue in the last 3 months? YES ☐ NO ☐ Which and since when? 	■ Petechiae, moretes, or bleeding ■ Palmar and/or conjunctival pallor: Mild ☐ Intense ☐ ■ Abnormality in the eyes: white eye ☐ Lack of iris ☐ Acquired strabismus ☐ different color eyes ☐ Blood within the eye ☐ left ☐ ■ Nodes: Size 2.5 cm Without pain nor inflammation. Hard and firm consistency Lasting 4 weeks of evolution ■ Signs and focal neurological symptoms of sudden or progressive onset: ■ Unilateral weakness: unilateral weakness, one of the limbs or of a side of the body ■ Physical asymmetry (facial) ■ Changes in the state of conscience or mental (in the behavior, confusion) ■ Loss of the balance to the walks ■ Limbs by pain ■ Difficulty in speaking ■ Alteration in the vision: (blurred, double, sudden blindness) ■ Presence of abdominal palpable mass ■ `Hepatomegaly` and/or `splenomegaly` ■ Increase of volume in some regions of the body (mass)	POSSIBLE CANCER OR VERY SEVERE DISEASE SOME RISK OF CANCER DOES NOT HAVE CANCER

COMMENTS:

4. Ricardo's case

Ricardo is 4 years old and he was brought to the emergency service for intense abdominal pain that began 4 hours ago. When the emergency physician asks Ricardo's mother what is happening, she answers that during the morning Ricardo complained of abdominal pain and that it is now worse—so she decided to bring him in. When the physician asks if Ricardo has been healthy, the mother says yes, although in the last month he had already had abdominal pain for which he had seen the doctor twice: the first time he was diagnosed with constipation and prescribed milk of magnesia; the second time he was told he had parasites and was prescribed medication for parasites and amebas, which he took 10 days ago. He had never been sick before; he is a healthy child who has had all his vaccinations.

On examination, the physician found:

Weight: 19 kg. Height: 103 cm. HR: 110 x'. RR: 28 x'. T°: 36.3°

Based on the IMCI assessment, Ricardo did not have danger signs; he had no cough, diarrhea, fever, or ear or throat problem. His nutritional status was adequate and he did not have pallor.

The physician assesses the possibility of cancer and finds that Ricardo has no headache, no bone pain, no history of weight loss, no loss of appetite, and no fever. On examination, he does not have lymphadenopathy, or manifestations of bleeding; the eye examination and neurological examination are also normal. However, when feeling his abdomen, he finds a large mass (about 10 x 10 cm) on the left side, compromising the whole flank; abdominal palpation is painful, with no signs of peritoneal irritation. There are no other disturbances.

Use the above information to fill out the case recording form on the next page.

Then answer the following questions:

1. What signs does the physician use to classify Ricardo?
2. How does he classify Ricardo?
3. What should the physician now do?
4. The clinic can do sonography; should they do it and begin to study Ricardo?
5. What should the physician tell Ricardo's mother?



CHILD CANCER REGISTRATION FORM DETECTION

Name:

Date: Age:

What problem has the child?

.....

First consultation: Control: Weight: Size: PC:

FC: FR: T°:.....

ASK	OBSERVE AND DETERMINE: (encompass in a circle what	CLASSIFY
Has it had fever for more than 7 days and/or important perspiration? YES ☐ NO ☐ Recent headache that has been worsening? YES ☐ NO ☐ Since when? Does it awaken headache to the child? YES ☐ NO ☐ Is it accompanied by some other symptom as vomit? YES ☐ NO ☐ Does it present bone pains in the last month? YES ☐ NO ☐ What interrupts its activities? YES ☐ NO ☐ Has been what increasing? YES ☐ NO ☐ Has it presented changes as loss of appetite, weight loss, or fatigue in the last 3 months? YES ☐ NO ☐ Which and since when?	■ Petechiae, moretes, or bleeding ■ Palmar and/or conjunctival pallor: Mild ☐ Intense ☐ ■ Abnormality in the eyes: white eye ☐ Lack of iris ☐ Acquired strabismus ☐ different color eyes ☐ Blood within the eye ☐ left ☐ ■ Nodes: Size 2.5 cm Without pain nor inflammation. Hard and firm consistency Lasting 4 weeks of evolution ■ Signs and focal neurological symptoms of sudden or progressive onset: ■ Unilateral weakness: unilateral weakness, one of the limbs or of a side of the body ■ Physical asymmetry (facial) ■ Changes in the state of conscience or mental (in the behavior, confusion) ■ Loss of the balance to the walks ■ Limps by pain ■ Difficulty in speaking ■ Alteration in the vision: (blurred, double, sudden blindness) ■ Presence of abdominal palpable mass ■ `Hepatomegaly` and/or `splenomegaly` ■ Increase of volume in some regions of the body (mass)	POSSIBLE CANCER OR VERY SEVERE DISEASE SOME RISK OF CANCER DOES NOT HAVE CANCER

COMMENTS:

VI 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 pediatric 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 or enlargement 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 to a specialized center.

VII THE CHILD WITH A CANCER DIAGNOSIS SEEN IN THE FIRST LEVEL OF CARE

As mentioned earlier, the child with cancer will receive integrated management in a specialized hematology/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 center—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

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, and impaired immunity, among others. Nevertheless, 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 cytostatics, transfusions, allergic reactions, or from the tumor 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 bacteremia.

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 germs 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 corticoids or other immunosuppressive drugs.

Every child with leukemia or cancer who is in treatment and who goes to the emergency service with a high fever and whose hemogram reveals leukopenia and a neutrophil count less than 500, should be hospitalized immediately on a hematology/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.

Despite the lower frequency of gram-negative bacterial infections, antibiotics will continue to be prescribed for this type of bacteria because of the fulminant nature of the infection and its high mortality. In many countries, initial empirical therapy is as follows:

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

☑ **Tumor lysis syndrome**

Tumor lysis refers to significant destruction of tumor cells, which can occur spontaneously when tumors are very large, or, in leukemias with hyperleukocytosis, when administering chemotherapy to destroy malignant cells. Tumor lysis can lead to life-threatening metabolic changes (e.g., hiperkalemia—increase of potassium in the blood, hypocalcemia—reduction of calcium in blood, hyperphosphatemia—increase of phosphorus in the blood, hyperuricemia—increase of uric acid in the blood) from renal failure, arrhythmia, or cardiac arrest.

The classical triad is hyperuricemia, hyperphosphatemia, and hiperkalemia.

- ✓ **Hyperuricemia:** This is produced by increased nucleic acid degradation secondary to tumor cell destruction. Uric acid precipitates in the renal medulla, distal and collecting tubule, where urinary concentration and acidity is greater.
- ✓ **Hiperkalemia:** Potassium accumulates from tumor cell destruction, producing secondary renal failure.
- ✓ **Hyperphosphatemia:** Lymphoblasts contain four times more phosphates than normal lymphocytes. With tumor cell destruction, phosphorus is elevated. When the calcium:phosphorus ratio is greater than 60, the calcium phosphate precipitates in the microvasculature, producing hypocalcemia, metabolic acidosis, and acute renal failure.
- ✓ **Acute renal failure:** Oliguresis before the beginning of treatment accompanied by calcium phosphate precipitation favors development of acute renal

failure. It is manifested by cardiac disturbances; neuromuscular symptoms, such as paresthesia, weakness, and hyporeflexia; and respiratory failure from hiperkalemia. Hypocalcemia is manifested by abdominal pain, fine tremor, muscular fibrillation, tetany, convulsions, and impaired consciousness.

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

1. **Hyperhydration:** 3,000 to 4,000 ml/mt2/day with 5% dextrose solution in water in order to ensure urinary volume $\rightarrow 3$ mL/kg/h or $\rightarrow 100$ ml/mt2/hour and urinary density $\leftarrow 1010$.
2. **Alkalinization:** 60 to 100 mEq/L of bicarbonate to maintain urinary pH between 7 and 7.5 if applicable.
3. **Reduction of uric acid** with allopurinol at 10 mg/kg/day or 300 mg/mt2/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 etiology is malignant neoplasm, such as non-Hodgkin's lymphoma, Hodgkin's lymphoma, and T-cell type acute lymphoblastic leukemia. 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 edema, jugular distension, and superficial collateral thoracic circulation. If there is compression of the windpipe, there will be symptoms of airway obstruction: cough, dyspnea, orthopnea, and stridor.

General measures include airway maintenance, elevation of the head of the bed, oxygen, and diuretics with caution, and immediate referral to the specialized center where this is being treated.

☑ **Hemorrhagic cystitis**

This is the most common cause of macroscopic hematuria in cancer patients. It is due to treatment with drugs such as ciclosporin and ifosfamide that are metabolized in the liver into acrolein, which is toxic to the vesical mucosa. This also occurs in patients who have received pelvic radiation therapy. It can appear hours, days, or months later. It manifests

with urinary tract symptoms, such as dysuria, urinary urgency, pollakiuria, epigastric pain, and micro- or macroscopic hematuria.

Treatment includes preventive measures: forced diuresis and administration of MESNA (sodium 2-mercaptoethanesulfonate), which binds with the

toxic metabolite and protects the vesical mucosa.

As the number of children treated for cancer who use primary care services is small, it helps to have a special file, or use different markings to locate them immediately and provide the most personalized care that the service permits.



VIII GLOSSARY

Adenitis	Inflammation of a lymph node.
Adynamia	Lack of movement or reaction, which can lead to prostration. The cause may be physical or psychological.
Aphasia	Loss of the ability to produce or understand language.
Amenorrhea	Absence of menstruation greater than 90 days.
Anemia	In children aged 6 months to 6 years, hemoglobin ≤ 11 g/dL.
Aniridia	Absence of the iris in the eye.
Asthenia	General feeling of physical and psychological weariness, fatigue, and weakness.
Ataxia	Lack of coordination of movements of the parts of the body, causing an abnormal swaying gait ("drunken gait").
Headache	Headache.
Diplopia	Double vision.
Dysarthria	A speech impairment due to an underlying neurological disorder.
Dysphagia	Difficulty swallowing.
Dysphasia	Partial loss of speech from a cortical lesion.
Dyspnea	Difficult breathing or increased respiratory effort.
Dysuria	Difficult urination.
Enophthalmos	Posterior displacement of the eyeball within the orbit.
Epistaxis	Any bleeding from the nose.
Ecchymosis	Discoloration caused by superficial bleeding in the skin or mucous membranes, due to rupture of blood vessels as a result of a blow or coagulation problem.
Gingival bleeding	Spontaneous bleeding of the gums.
Hematuria	Blood in the urine.
Hemianopsia	Lack of vision in the outer visual field of both eyes.
Hemiparesis	Motor weakness of limbs on one side of the body.
Heterochromia	Different colored eyes in the same person.



Hyphema	Blood in the anterior chamber of the eye.
Leukemias	Group of malignant diseases of the bone marrow.
Leukocytosis	An increased number of white cells in the blood (leukocytes).
Leukokoria	White reflex or white spot on the pupil.
Leukopenia	A reduced number of total leukocytes ($<4000 \text{ mm}^3$).
Leucoria	White pupil.
Leukosis	Suggested name to designate leukemic states; i.e., the various acute or chronic disorders characterized by the proliferation of leukocyte forming tissue, which are accompanied by the invasion or not of the blood by white blood cells (myeloid, lymphoid, or acute leukemias).
Lymphadenopathy	Enlarged lymph nodes.
Lymphomas	Group of neoplastic diseases that develop in the lymphatic system.
Metastasis	The spread of a cancer to an organ other than the one where it originated.
Myosis	Contraction of the pupil of the eye.
Monoparesis	Slight paralysis of one limb or part.
Nystagmus	Involuntary and uncontrollable movement of the eyes.
Osteolysis	When one or more areas of a bone wear out and get thin.
Petechiae	Small red lesions, formed by extravasation of a small number of erythrocytes when a capillary is damaged.
Pollakiuria	Frequent urination not associated with an increase in volume of urine.
Proptosis	Forward displacement of the eyeball.
Ptosis	Falling of the upper eyelid over the eye (drooping eyelid).
Purpura	Leaking by small blood vessels, causing a purplish color under the skin, secondary to reduction in the number of blood platelets.
Thrombocytopenia	Decreased number of platelets in the blood

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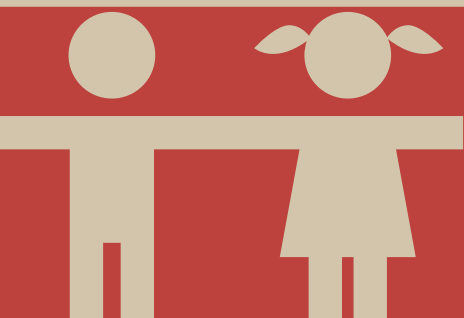
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Photographs

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