Qure
Center for Complete Care
Blood Diseases, Cancer, Stem Cell Transplantation

Childhood Rhabdomyosarcoma

What is rhabdomyosarcoma (RMS)?

Childhood rhabdomyosarcoma (RMS) is a cancer arising within muscle cells and can be found throughout the body with the main site of tumor equally common in 1) head and neck 2) bladder, scrotum and vagina 3) limbs 4) other miscellaneous sites. With modern treatment programs using multiagent chemotherapy, surgery and radiation therapy, over two-third of children with RMS will be cured. Cure rates vary depending on the risk factors and your doctor will give you a better estimate after taking those all into account.

What are the signs of childhood RMS?

Typically RMS presents as a painless growing lump and the symptoms are related to where the tumor is located, e.g. involvement of the orbit of the eye may cause the eyeball to bulge out whereas RMS involving the base of the bladder causes difficulty in urination.

What causes RMS?

Nobody knows for sure, nothing in the diet or environment causes this. It not inherited, (except in *rare* genetic syndromes such as TP53 Li-Fraumeni syndrome and DICER1 mutations pleuropulmonary blastoma) so other children in the family should not be at risk.

How is RMS diagnosed?

Biopsy of the tumor (with removal of the whole tumor if possible) is the key test in which tumor tissue is removed by a surgeon and sent to a pathologist who reviews the cancer tissue under a microscope looking at the appearance of cancerous cells, and looking at markers on the surface of tumor cells, and doing special genetic tests which allows an accurate diagnosis and sub-type. Depending on the site of the tumor, the surgeon may also sample regional lymph nodes to check for tumor spread.

How is the likelihood of cure in RMS determined?

Before doing a biopsy a careful physical exam and history, and blood tests such as complete blood count (CBC), blood chemistry are done. Bilateral bone marrow aspirates and biopsies, in which liquid bone marrow and a tiny piece of bone is removed by inserting a needle into the hipbone while the child is sedated, can determine spread to the bone marrow. Imaging can help define the tumor and where it has spread, which will determine risk category and likelihood of cure.

- Chest x-ray.
- Computed tomography (CT) scan of the chest.
- CT scan of the abdomen and pelvis (for lower extremity or genitourinary tumors).
- Magnetic resonance imaging (MRI) of the skull/brain (for parameningeal tumors).
- PET-CT scan is a special kind of scan that can show where RMS has spread in the body (and later can also show whether it is responding to treatment).
- Bone scan

RMS is divided into two main types based on the appearance under the microscope:

- **Embryonal:** which constitutes two-thirds of cases, commonly seen in younger children, and usually with better outcomes.
- **Alveolar:** which constitutes less than one-third of cases, found equally in all childhood ages, but harder to cure. Alveolar RMS has a specific genetic abnormality in which two genes from different chromosomes are fused together (*PAX3* or *PAX7* and *FOXO1*), and testing for this can be helpful in confirming that a patient needs more intensive chemotherapy.
- **Spindle cell/sclerosing:** is rare, and in infants has gene rearrangements and fusions that are different from adults, with better outcomes.

Determining the risk category of RMS depends on multiple factors, so is complicated, but essentially takes into account the **stage** and **group** of the tumor, as seen in the table below.

- The **stage** ranks patients from 1 to 4 (1 being the best) based on:
  - How large the tumor is and how far it has spread
  - Whether the site of the tumor is favorable such as those listed below:
    - Eye or area around the eye.
    - Head or neck (but not near the ear, nose, sinuses, or base of the skull).
    - Gallbladder and bile ducts.
    - Ureter or urethra.
    - Testes, ovary, vagina, or uterus
  - Whether the tumor is embryonal, or lacks *FOXO1* gene fusion, which is favorable

- The **group** ranks patients from I to IV (I being the best) based on:
  - Whether the tumor was completely removed, or whether the surgeon had to leave small or large amounts behind

Risk	**Tumor type**	**Stage**	**Group**
Low	Embryonal	1, 2	I, II
		1	III (favorable site only)
Intermediate	Embryonal	All tumors not high or low risk	
	Alveolar	All tumors not high risk	
High	Alveolar/Embryonal	4	IV

How is RMS treated?

Chemotherapy or cancer fighting drugs are given as a combination to increase the chance of killing all the cancer cells, and are injected into a vein to reach cancer cells throughout the body. RMS chemotherapy is most commonly a combination of three chemotherapy drugs (vincristine, actinomycin and cyclophosphamide) commonly referred to as “VAC” given for 9 months. Low risk patients may receive only “VA” for 11 months or a combinations of VAC and VA. The exact chemotherapy protocol will depend on whether the RMS is low, intermediate or high risk, and your doctor will confirm which category your child is in.

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All people who receive cancer treatment are at risk of having side effects, some of which are mild but others of which can be life-threatening. In addition to killing tumor cells, chemotherapy can damage normal tissue. Side effects usually get better when the medication is stopped but sometimes last a long time or never go away. Common side effects include nausea, vomiting, hair loss, low blood counts and fatigue (tiredness). Drugs are given to prevent nausea and vomiting. Hair loss is usually temporary but very rarely it may be permanent. Low blood counts may require transfusion or increase the risk of infection. Chemotherapy side effects for each medication are listed on the sheets your doctor will give you. It is important to remember the treatment is essential for cure and most patients have very few of the **side effects** listed.

In addition local control of the tumor is key to achieving a cure, and requires good coordination between the surgeon, radiation expert and oncologist.

Surgery is performed before chemotherapy if it will not result in disfigurement, or damage to organs. Surgery that leaves behind visible tumor (debulking) has no benefit over biopsy alone, so if complete removal is not possible, only an initial biopsy will be done. Later it may be possible to have delayed surgery to remove all tumor, to allows less radiation to be given but this will not be attempted unless the surgeon can remove all the tumor.

Radiation is given to all patients *except* those with embryonal tumors who have had a complete resection (Group I). Radiation uses high energy X-rays to destroy or damage rapidly dividing cancer cells. It affects only the area of the body where the radiation is given, so it is ideal for local control of RMS. Your radiation oncologist will create a plan to target your child's cancer, sparing healthy organs, and the area to be treated (radiation field) will be carefully marked on your child's body in a process called "simulation." The dose of radiation varies with risk category.

External beam radiation therapy is delivered by a machine called a linear accelerator which generates a narrow beam of high energy X-rays. Sometimes for vaginal or bladder sites a radioactive implant is used instead (brachytherapy). Sophisticated machines can use protons to deliver radiation energy more precisely, however their use in RMS remains limited, as it is unclear how much long-term benefit they provide. Your child won't see, taste, or smell the radiation; it is like getting an X-ray. Each session lasts 10-30 minutes, with most of the time spent in making sure everything is set up precisely. Treatments are given five days a week, for a total of 4-7 weeks, thus allowing enough radiation to reach and kill the cancer, while giving surrounding healthy cells time to recover.

Any side effects from radiation are due to damage caused as radiation passes through healthy cells. The most common side effect is mild fatigue. Skin in the area treated may become red and sensitive, similar to sunburn (radiation dermatitis), and careful skin care is needed. Widespread radiation can lead to blood cell count decrease. Other side effects depend on where radiation is being given.

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What dietary and what other precautions should I take?

Chemotherapy suppresses your child's immune system so infections are a concern. We place diet and activity restrictions, especially for young children and prohibit street/outside food and recommend home food be thoroughly cooked. No special foods will help with cure. Visits to movie theaters, malls, weddings, or other crowded places are discouraged. You should contact your doctor *immediately* if in spite of these precautions your child develops a fever >100.4F, diarrhea, cough, vomiting, abdominal pain, headaches or looks unwell.

What are long term outcomes?

As mentioned above, for low risk patients, outcomes with the right treatment are surprisingly good with over 80% patients having a long-term cure. Unfortunately patients with high risk disease are more likely to have the disease come back (relapse) at which point it is usually incurable. Discuss with your doctor any short and long-term side effects from treatment you may have concerns about.