Medulloblastoma
A Word About ABTA

Founded in 1973, the not-for-profit American Brain Tumor Association has a proud history of funding research, providing patient services, and educating people about brain tumors. Our mission is to eliminate brain tumors through research and to meet the needs of brain tumor patients and their families.

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**Introduction**

Medulloblastoma is a rapidly-growing tumor of the cerebellum — the lower, rear portion of the brain. Also called the “posterior fossa,” this area controls balance, posture, and complex motor functions such as speech and balance. Tumors located in the cerebellum are referred to as “infratentorial” tumors. That means the tumor is located below the “tentorium,” a thick membrane that separates the larger, cerebral hemispheres of the brain from the cerebellum. In children, medulloblastoma arises most often near the vermis, the narrow worm-like bridge that connects the cerebellum’s two sides. In adults this tumor tends to occur in the body of the cerebellum, especially toward the edges.

**THE TENTORIUM**

**THE CEREBELLUM**
Medulloblastoma is the most common of the embryonal tumors — tumors that arise from “embryonal” or “immature” cells at the earliest stage of their development. Other embryonal tumors include histologically similar tumors such as supratentorial primitive neuroectodermal tumors, central neuroblastomas, and ependymoblastomas. These tumors are now known to be molecularly different than medulloblastoma, as are other embryonal tumors such as medulloepithelioma and atypical teratoid/rhabdoid tumors.

To a neurosurgeon, this tumor looks like a pinkish gray mass with a thickened “sugar-coating.” But under the microscope, classic medulloblastoma tissue looks like sheets of densely packed, small round cells with large colorful centers called nuclei. While this classic pattern is found in the majority of both pediatric and adult tumors, four other notable tissue patterns include desmoplastic nodular medulloblastoma, which contains scattered islands of tumor cells in the tissue and small cysts; large-cell or anaplastic medulloblastoma, with large round tumor cells; medulloblastoma with neuroblastic or neuronal differentiation, in which the tumor cells look similar to abnormal nerve cells; and medulloblastoma with glial differentiation, whose cells look similar to the supportive, glial brain cells. Two other variants, medulloepithelioma and melanotic medulloblastoma, are rarer and generally
found only in children. These “histologic” tissue patterns are used for grouping and naming these tumors, and may someday be useful for targeting therapies. For now, though, the subtype of medulloblastoma does not influence the treatment plan.

Significant strides have been made in diagnosing and treating medulloblastoma. Yet these tumors remain among the most challenging pediatric brain tumors.

**Incidence**

About 1,000 new patients — children and adults — are diagnosed in the US each year, more often in males than females. Medulloblastoma is relatively rare, accounting for less than 2% of all primary brain tumors (tumors that begin in the brain or its coverings) and 18% of all pediatric brain tumors. More than 70% of all pediatric medulloblastomas are diagnosed in children under age 10. Very few occur in infancy or under age 1.

Typically a tumor of childhood, medulloblastoma in adults is not common, but does occur. About one-third of all medulloblastomas diagnosed in the United States are found in adults between the ages of 20 – 44. The incidence in adults sharply decreases in frequency after age 45, with very few older adults having this tumor.

**Cause**

Although the cause of medulloblastoma is unknown, scientists are making significant progress in understanding its biology. Changes have been identified in genes and chromosomes (the cell’s DNA blueprints) that may play a role in the development of this tumor. For example, one-third to one-half of all pediatric medulloblastomas contain a change on chromosome 17. Similar changes on chromosomes 1, 7, 8, 9, 10q, 11 and 16 may also play a part.
There are a few rare, genetic health syndromes that are associated with increased risk for developing this tumor. For instance, a small number of people with Gorlin’s Syndrome develop medulloblastoma. (Gorlin’s Syndrome is an inherited tendency to develop basal cell carcinoma in combination with other conditions.) Scientists have identified alterations on a gene called \textit{PTCH} which may be the common link. Similarly, genetic changes in the \textit{APC} and \textit{TP53} genes are involved in two other inherited syndromes, Turcot and Li-Fraumeni. People with these syndromes tend to develop multiple colon polyps and malignant brain tumors.

**GENETIC VERSUS INHERITED**

“Genetic” does not mean “inherited.” Genetic changes are those that occur in the DNA, or the inside blueprint, of a cell. No one knows what triggers these changes. Some, but not all, genetic changes can be inherited. Inherited means abnormal genes are passed from one generation to another. Medulloblastoma is not an “inherited” disease.

Researchers are also exploring normal brain activity pathways, such as communication patterns among cells or genes. Changes in the genes involved in cell-signaling pathways such as \textit{SHH}, \textit{WNT} and \textit{ERBB}, have been linked to the development of medulloblastoma. Several therapies targeted at proteins in these pathways are being studied. With increased understanding of how these genetic changes contribute to medulloblastoma, researchers may one day be able to correct or compensate for these changes.
Symptoms

The early “flu-like” signs of this tumor — lethargy, irritability and loss of appetite — are often so non-specific that the disease first goes unnoticed. In infants, increased head size and irritability may be the first symptoms. Older children and adults may experience headaches and vomiting upon awakening. Typically, the person feels better after vomiting and as the day goes on. As the pressure in the brain increases due to a growing tumor or blocked fluid passages, the headaches, vomiting and drowsiness may increase. Other symptoms depend on the nerves and brain structures affected by the tumor. Since medulloblastomas appear in the cerebellum, the center of balance and movement, problems with dizziness and coordination are common. Tumors growing close to the brain’s fourth ventricle may expand into that cavity, blocking the normal flow of cerebrospinal fluid. This can result in hydrocephalus — the buildup of cerebrospinal fluid within one of the cavities of the brain. The pressure of this buildup triggers the tumor’s characteristic symptoms: Morning headaches, nausea, vomiting and lethargy.
Children with this tumor may exhibit a clumsy, staggered walking pattern. They may also complain of visual problems. For instance, if the tumor involves the sixth cranial nerve which controls outward muscle movement of the eye, diplopia (double vision) can occur. Nystagmus (involuntary jerking of the eye) may also be a problem. While seizures are not common with medulloblastoma, other symptoms such as mild neck stiffness and a tilt of the head may occur.

As many as 2 out of every 10 children with medulloblastomas may be less than 2 years of age at the time of diagnosis. In infants, symptoms can be more subtle and include intermittent vomiting, failure to thrive, weight loss, an enlarging head with or without a bulging of the soft spot of the head (fontanelle), and inability to raise the eyes upward (the so-called “sun-setting” sign).

**Diagnosis**

Obtaining a symptom history and performing a neurological examination will be your doctor’s first steps in making a diagnosis. Magnetic resonance imaging (MRI), done both with and without a contrast dye, is then used to identify the presence of a tumor in the brain. The contrast dye is given intravenously (into the vein) to enhance the pictures. By concentrating in abnormal tissue, the dye makes a tumor appear much brighter than other areas.

If a tumor suspected of being a medulloblastoma is identified, an MRI of the entire spine can be done to look for tumor in that area. PET (positron emission tomography) and MRS (magnetic resonance spectroscopy) may be used to determine if what is seen on the scan is growing, live tumor as opposed to radiation effects or non-growing tissue.
While scans provide important and intricate details, microscopic examination of tissue obtained during a surgical procedure, such as a biopsy or tumor removal, confirms the diagnosis. The pathologist, a doctor who specializes in studying tissue samples, will be looking for cell patterns that identify the tumor type. A pathology report usually takes about a week to be completed. It is sent to your neurosurgeon’s office, and the results then shared with you.

**Treatment**

If the tumor is determined to be a medulloblastoma, current treatment consists of surgically removing as much tumor as possible, followed by craniospinal (brain and spine) radiation and/or chemotherapy. Your doctor will suggest a treatment plan based on factors that indicate the risk of tumor recurrence — either “average-risk” or “high-risk.” To determine risk, doctors look at the age of the patient; the amount of tumor remaining following surgery; and the amount of metastases, or tumor spread (also called M stage).

Children are considered at “average-risk” of recurrence if they are diagnosed after age 3; if all, or nearly all, of the tumor is surgically removed; and if there is no evidence of metastases or tumor spread. All other pediatric medulloblastomas are
considered to be at “high-risk” of recurrence. High-risk patients include those under age 3; if more than 1.5 cm (about 1/2 inch) of tumor volume remains following surgery; or if there is any evidence that the disease has spread.

For adults, risk is generally determined by the amount of remaining tumor, and the presence or absence of tumor spread.

The present staging system for medulloblastoma is of major importance. However, a variety of molecular changes were recently identified in childhood medulloblastoma tumors. Researchers are studying whether these findings will be helpful in determining whether children are of average or high-risk disease, or if the information might help to predict the chances of recurrence or spread. Researchers are also studying ways to obtain this biologic information in real-time (meaning within days after surgery).
Surgery

Removing as much tumor as possible is the most important step in treating medulloblastoma. The neurosurgeon has three goals for the surgery: To relieve cerebrospinal fluid buildup caused by tumor or swelling; to confirm the diagnosis by obtaining a tissue sample; and to remove as much tumor as possible with minimal neurological damage. Several studies have shown the best chance for long-term tumor control is when all of the medulloblastoma visible to the neurosurgeon’s eye can be removed safely.

Many technologically-advanced surgical tools are now available. MRI scanning combined with computer-aided navigation tools help the neurosurgeon map the exact tumor location before the operation, and track its removal during the procedure. High-powered microscopes provide visual enhancement. Ultrasound and gentle suction devices are used to remove tumor during the actual procedure. These techniques assist the surgeon in navigating around adjacent healthy structures. To read more, and see pictures from an actual craniotomy, please call us at 800-886-2282 and request a free copy of our publication, Surgery.

While the goal is to eliminate the tumor, some medulloblastomas cannot be removed completely. In one-third of patients, the tumor grows into the brain stem, making total removal difficult because of potential neurological damage. If the tumor is determined to be inoperable, a biopsy may still be done to confirm the diagnosis.

Steroids are drugs used before and after surgery to reduce swelling around the tumor. Occasionally, a ventriculostomy (an external drainage device) may be placed to divert excess cerebrospinal fluid from the brain. A permanent shunt, a long catheter-like tube that drains fluid from the brain to the abdomen, is sometimes necessary. In most
cases, however, removing the tumor opens the cerebrospinal pathways, which restores both normal fluid flow and pressure. It also eliminates the need for a shunt or drainage device.

Within two days following surgery, an MRI will be done to visualize the amount of remaining tumor. (If an MRI scanner is available in the operating room, the scan may be done during surgery.) The amount of “residual” or remaining tumor will be a strong factor in determining further treatment.

**Radiation**

Following surgery, medulloblastoma is usually treated with radiation therapy. It is an important “next-step” because microscopic tumor cells can remain in the surrounding brain tissue even after surgery has successfully removed the entire visible tumor. Since these remaining cells can lead to tumor regrowth, the goal of radiation therapy is to reduce the number of left-over cells.

Doctors consider several factors in planning radiation therapy: The age of the patient, the location of the tumor, the amount of remaining tumor, and any tumor spread. Since radiating the brain and central nervous system can be damaging to a developing brain, it is usually delayed in children under age 3. Initial treatment for these young children includes surgery followed by chemotherapy to control the tumor. Radiation may be delivered later, if needed.

For older children and adults, conventional external beam radiation therapy is given to the brain and spine. This area is called the craniospinal axis. This form of radiation is given 5 days a week for 5 to 6 weeks. A “boost” is given to the posterior fossa, the region most at-risk because it housed the original tumor. An additional boost may be given to areas of tumor spread. Age and risk factors determine the total doses of radiation given to each area.
While radiation therapy has proven effective, scientists are still looking for new ways to lower the potential side effects of this treatment. Techniques such as focused radiation, also called stereotactic radiosurgery, aims converged beams of radiation at the tumor. Conformal radiation allows doctors to shape the radiation beams to match the tumor’s contour. The goal of these focused forms of radiation is to spare normal brain tissue while treating tumor. Your radiation oncologist, a doctor specially trained in the use of radiation therapy, can talk with you about the best method of radiating you/your child’s tumor.

**Chemotherapy**

Chemotherapy uses powerful drugs to kill cancer cells. For children with medulloblastoma, chemotherapy is used to reduce the risk of tumor cells spreading through the spinal fluid. For adults, this benefit is not quite as clear since their tumors tend to regrow in the cerebellum. Because different drugs are effective during different phases of a cell’s life cycle, a combination of drugs may be given. The combination increases the likelihood of more tumor cells being destroyed.

Chemotherapy is now a standard part of treatment for children with medulloblastoma. Most children are treated in clinical trials — organized studies that are helping determine which treatments are most effective. Clinical trials also offer a formal way to test new therapies against existing therapies to learn which is better.

In children at average-risk of recurrence, current studies are exploring the use of chemotherapy as a way to reduce the total amount of craniospinal radiation. There are several treatment plans in use, but most focus on a combination of vincristine, cisplatin, lomustine, and/or cyclophosphamide.
For children at high-risk, the drugs vincristine, cisplatin, and cyclophosphamide tend to be the main focus, but others are being tested in clinical trials. Researchers are also looking at the use of chemotherapy as a radiation sensitizer, and at “post-radiation” high-dose chemotherapy accompanied by a stem cell transplant.

For infants under the age of 3, chemotherapy is used to delay or even eliminate radiation therapy. Cyclophosphamide, vincristine, cisplatin, etoposide, carmustine, procarbazine, cytarabine, and/or hydroxyurea may be found in these treatment plans. New drugs are under consideration, but their effectiveness is generally determined in older children prior to use in infants. Some treatment plans use higher doses of chemotherapy, supported by peripheral stem cell rescue, for infants. There is also interest in instilling chemotherapy directly into the cerebrospinal fluid (either “intrathecally” — into the lumbar spine by spinal taps, or “intraventricularly” — into the ventricular fluids of the brain via an Ommaya reservoir). This is being done in attempts to deliver high doses of therapy to the coating regions of the brain and reduce disease relapse in these areas. In addition, studies are underway evaluating the efficacy and safety of utilizing local radiation therapy (radiation therapy only to the primary tumor site) after chemotherapy in infants whose initial disease was limited to the posterior fossa.

In adults, the usefulness of chemotherapy is less clear. Although large scale studies have not been done, some smaller studies indicate adult tumors may likewise respond to some of the above combinations. But adults seem less able to withstand potential side effects, especially those of the lomustine and cisplatin used in some treatment plans. Studies are exploring the use of cyclophosphamide, ifosfamide, etoposide, or carboplatin in adults, and other studies are exploring pre-radiation chemotherapy plans as alternatives.
Research continues into defining the best use of chemotherapy in average-risk patients; the best tolerated drugs in adults; and new drugs targeted to specific genetic changes found in medulloblastomas. Your doctor will outline a treatment plan based on current studies, the patient’s age, the amount of remaining tumor, and the risk of further disease.

Side Effects

Despite its impact on increasing survival, the tumor and its treatment can cause significant side effects. Your healthcare team can speak with you about the potential side effects of your/your child’s personalized treatment plan, and help you weigh risks against the benefits. Some of the more common effects are discussed here.

In a recent study, about 25% of children undergoing surgery for their tumor developed delayed onset (usually 6 to 24 hours after awakening) loss of speech which was often associated with decreased muscle tone, unsteadiness, emotional lability, and irritability. This syndrome, called “posterior fossa mutism syndrome” or “cerebellar mutism” seems to occur predominantly after surgery in children with medulloblastoma, and has not been clearly related to tumor size or surgical approach. Many of these children recover, but the study noted that some children still have significant neurologic problems—such as abnormal speech and unsteadiness—a year after surgery.

If mutism occurs, a speech pathologist can help outline a temporary communication plan for your child, and help initiate a rehabilitation evaluation. The rehab team can plan a program specialized to your child’s needs and strengths.

Understandably so, parents and adult patients often express concern about the effects of radiation therapy. In the short-term, fatigue, lack of appetite, nausea, sore throat, difficulty swallowing,
and hair loss in the path of the radiation beams are the most common acute effects of this treatment. Adults seem to experience these temporary, short-term effects to a greater degree than children. Children appear to experience greater intensity of the long-term effects. Radiation may trigger a decrease in IQ or intellectual ability, accompanied by learning disabilities, attention deficit and memory loss. Most of this research has focused on children: The younger the child during treatment, the greater the potential subsequent learning challenges. Infants and children less than 3 years of age are particularly vulnerable because the brain is maturing rapidly during this time. For any age group, however, the radiation oncologist will be able to talk with you about what you can expect based on age and the planned dose of radiation.

Radiation can also have long-term effects on the hypothalamus and pituitary, two glands that contribute important hormones for bodily function and growth. Since these glands are directly in the pathway of the radiation beam,
their normal function may be disturbed by the treatment. As a consequence, patients can have problems with obesity and hypothyroidism (thyroid deficiencies). They also may experience short stature and scoliosis (curvature of the spine) if the spinal cord is irradiated. Patients should be evaluated carefully for hypothalamic or pituitary dysfunction and receive replacement therapy. Studies have not shown that children treated with growth hormone replacement are at a higher risk for tumor recurrence.

Hearing loss may accompany the use of the drug cisplatin in children. Because this drug has an important role in treating childhood medulloblastoma, scientists are testing “protective” drugs that may be able to defend a child’s hearing mechanisms from cisplatin. This research is ongoing. Hearing may also be affected if radiation beams pass near the ears; an otolaryngologist (an ear, nose and throat doctor) can be of help in diagnosing and treating this effect.

The short-term effects of chemotherapy are similar to those of radiation: Hair loss, nausea, vomiting, fatigue and weakness. But chemotherapy can also lead to reduced blood counts and kidney problems. As patients live longer, there’s the added risk of secondary malignancies, such as leukemia.

Doctors continue to study the long-term effects of both radiation and chemotherapy in hopes of developing new agents and combinations of agents. Discoveries continue to emerge about the molecular mechanisms used by tumor cells to evade the body’s normal growth controls, and the methods by which tumor cells move through the brain or spine.
**Follow-up**

MRI scanning of the brain will be done every 2-3 months and spinal MRI every 4-6 months for the first two years following surgery. The scans help determine the effectiveness of treatment, and are used to monitor for early evidence of a recurrence. Scans will be done less frequently thereafter, unless specific symptoms develop that might indicate further growth. Your doctor will determine the appropriate schedule.

Children should be carefully evaluated for long-term cognitive problems, and should receive early aggressive learning support.

Neuropsychological testing before treatment can serve as a baseline for followup evaluations. If learning concerns arise after treatment, these baseline results can be used as a tool for comparison. Children should be carefully evaluated for long-term cognitive problems, and should receive early aggressive learning support. In addition, your doctor may refer you to other specialists, such as an endocrinologist (a physician specially trained in treating growth or hormone imbalances), or an oncologist (a physician trained in treating cancer, particularly with chemotherapy drugs). Rehabilitation and special education programs will play a vital role in returning children to school.

**Recurrence**

Tumors recur when all the tumor cells cannot be removed by surgery or killed by other treatments. In children, medulloblastoma tends to “seed” or drop tumor cells into the spinal fluid. These cells can give rise to tumor growth in the spine. This type of spread may or may not be accompanied by tumor regrowth in the cerebellum. In adults, the tumor tends to first regrow in the cerebellum. On very rare occasions, the tumor may spread elsewhere in, and outside, of the central nervous system.
Recurring medulloblastoma is treated aggressively with repeated surgery, re-irradiation if possible, and chemotherapy. Recurrences limited to the cerebellum (the posterior fossa) offer the best chance of long-term survival since treatment can be aimed at the “local” site. Surgery or radiation therapy focused on the regrowth may be a choice. Chemotherapy may be of benefit if the tumor spreads beyond the local area. If chemotherapy was not used for the initial tumor, it may now be a consideration. Patients who previously received chemotherapy can be given different drugs for the recurrence. High-dose chemotherapy may be considered, as might a clinical trial investigating new therapies.

**Prognosis**

How well a patient responds to treatment is affected by their age at the time of diagnosis; the size and extent of the tumor; the amount of mass that can be removed safely; and the level of metastatic disease (the M stage).

Overall, the Central Brain Tumor Registry of the United States reports about 65% – 70% of adults (age 20+) with medulloblastoma are alive at 5 years following diagnosis. It is important to realize these statistics do not reflect differences in outcome between low risk and high risks groups (since high risk groups may not do as well), differences in patient characteristics, nor differences between patient responses to treatment.

With current therapies, 70% – 80% of children with average-risk medulloblastoma can be expected to be alive and free of disease five years from diagnosis. Even in those children with high-risk disease, effective therapy is possible and results in long-term disease control in as high as 60% – 65% of patients. Outcome for infants is poorer, but for those infants with localized disease at the time of diagnosis, survival rates in the 30% – 50% range are being seen.
Take the opportunity to speak with the healthcare team treating you or your child to learn how these statistics apply to your individual situation.

**Resources**

Medulloblastoma patients have a significantly increased chance of survival, thanks to improved treatment techniques. The best results, however, occur when patients are cared for by an experienced multi-disciplinary team of medical professionals at an established pediatric or adult cancer center.

Additional treatment information about this tumor can be obtained from the Cancer Information Service (CIS) at 800-422-6237. CIS can provide you with information about medulloblastomas in adults or children, and/or a listing of clinical trials (research treatments) for medulloblastoma.

Support groups and pen-pal programs allow you to share experiences with others in the same situation. ABTA social workers and information specialists can help you find these networks, as well as sources of financial assistance, transportation help, educational resources, or rehabilitation programs. We also offer a video/DVD, Alex’s Journey, for children ages 9–13 diagnosed with a brain tumor. Please call us at 800-886-2282 for these and other services.
A Next Step

Our web site — www.abta.org — offers extensive brain tumor information, treatment and research updates, and patient/family stories. A pen-pal program, Connections, links people interested in this disease with others. ABTA social workers can help parents explain this disease, and provide support, in language children understand. Parent/teacher education packets help ease your child’s return to their classroom. Our memory retraining, rehabilitative medicine, and employment resources may be of help to survivors and their families. Please call us at 800-886-2282 or visit our web site to access these programs. The thread that runs through each of our services and programs is hope. Become involved — join us in some way to move towards a cure, and ultimately, prevention of brain tumors.

We hope that the information in this booklet helps you communicate better with the people caring for you or your child. Our purpose is not to provide answers; rather, we encourage you to ask questions.
Questions I Want to Ask
Publications & Services

BUILDING KNOWLEDGE
Dictionary for Brain Tumor Patients
Living with a Brain Tumor
A Primer of Brain Tumors

FOCUSING ON TUMORS
Ependymoma
Glioblastoma Multiforme and Anaplastic Astrocytoma
Medulloblastoma
Meningioma
Metastatic Brain Tumors
Oligodendroglioma and Oligoastrocytoma
Pituitary Tumors

FOCUSING ON TREATMENT
Chemotherapy
Conventional Radiation Therapy
Stereotactic Radiosurgery
Steroids
Surgery
Physician Resource List: Physicians Offering Clinical Trials for Brain Tumors

FOR & ABOUT CHILDREN
Alex’s Journey: The Story of a Child with a Brain Tumor (Video or DVD)
Education Packet (Parent or Teacher)
When Your Child Returns to School

SUPPORT RESOURCES
Bibliography
Care Options
Emergency Alert Wallet Cards
Employment Information
End-of-Life Care
Financial Aid Resources
Health Insurance Resources
Housing During Treatment Resources
Net-Working Links
Neuropsychology Resources
Scholarship & Educational Financial Aid Resources
Social Security Disability Resources
Spanish-Language Resources
Transportation Assistance Resources
Wig and Head Covering Resources
Wish Fulfillment Resources

NEWSLETTER
Messageline Newsletter
Sharing Knowledge, Sharing Hope e-News

FOCUSING ON SUPPORT
Listing of Brain Tumor Support Groups
Listing of Bereavement (Grief) Support Groups
Organizing and Facilitating Support Groups
Pen Pal Programs
Connections (program for patients and family members)
Bridges (program for those who have lost someone to a brain tumor)
Resources for Online Support
TLC (Tips for Living and Coping) e-bulletin

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Sharing knowledge. Sharing hope.